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ESC GUIDELINES

2024 ESC Guidelines for the management of peripheral arterial and aortic diseases

Developed by the task force on the management of peripheral arterial and aortic diseases of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS), the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN), and the European Society of Vascular Medicine (ESVM)

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Abbreviations and acronyms

^{18}F–NaF	Fluorine-18–sodium fluoride
6MWD	Six-minute walking distance
6MWT	Six-minute walk test
AA	Abdominal aorta
AAA	Abdominal aortic aneurysm
AAD	Acute aortic dissection
AAE	Aortic adverse events
AAL	Ascending aortic length
AAS	Acute aortic syndrome
ABI	Ankle–brachial index
ACAS	Asymptomatic Carotid Atherosclerosis Study
ACB	Asymptomatic Cervical Bruit Study
ACC/AHA	American College of Cardiology and American Heart Association
ACEI	Angiotensin-converting enzyme inhibitor
ACS	Acute coronary syndrome
ACST	Asymptomatic Carotid Surgery Trial
ACTA2	Alpha-actin gene
AD	Aortic dissection
ADAM	American Aneurysm Detection and Management
ADD-RS	Aortic dissection detection-risk score
AF	Atrial fibrillation
AHI	Aortic height index
ALI	Acute limb ischaemia
AMI	Acute mesenteric ischaemia
AP	Antero-posterior
ARB	Angiotensin receptor blocker
ARR	Absolute risk reduction
ASCVD	Atherosclerotic cardiovascular disease
ASE	American Society of Echocardiography

ASI	Aortic size index
BASIL	Bypass versus Angioplasty in Severe Ischaemia of the Leg trial
BAV	Bicuspid aortic valve
BB	Beta-blocker
BEST-CLI	Best Endovascular versus Best Surgical Therapy for Patients with Critical Limb Ischemia trial
b.i.d.	Bis in die (twice daily)
BMI	Body mass index
BP	Blood pressure
b.p.m.	Beats per minute
BSA	Body surface area
BTK	Below-the-knee
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CANTOS	Canakinumab Anti-Inflammatory Thrombosis Outcomes Study
CANVAS	Canagliflozin Cardiovascular Assessment Study
CAS	Carotid artery stenting
CCA	Common carotid artery
CCB	Calcium channel blocker
CCT	Cardiovascular computed tomography
CDT	Catheter-based thrombectomy
cdTLR	Clinically driven target lesion revascularization
CEA	Carotid endarterectomy
CEUS	Contrast-enhanced ultrasound
CHA_2DS_2-VASc	Congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female)
CI	Confidence interval
cIMT	Carotid intima media thickness
CK	Creatinine kinase
CKD	Chronic kidney disease
CLTI	Chronic limb-threatening ischaemia
CMI	Chronic mesenteric ischaemia
CMR	Cardiovascular magnetic resonance
CoA	Coarctation of the aorta
COMPASS	Cardiovascular Outcomes for People Using Anticoagulation Strategies
COPD	Chronic obstructive pulmonary disease
CP	Carotid plaque
CREDENCE	Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation
CREST-2	Carotid Revascularization Endartectomy vs. Stenting Trial 2
CRP	C-reactive protein
CS	Carotid artery stenosis
CSA/h	Cross-sectional area-to-height ratio
CT	Computed tomography
CTA	Computed tomography angiography
CV	Cardiovascular
CVD	Cardiovascular disease
CVRF	Cardiovascular risk factor
DAPT	Dual antiplatelet therapy
DBP	Diastolic blood pressure
DD	D-dimer
DISSECT	Duration, Intimal tear, Size, Segmental Extent, Clinical complications, Thrombosis
DPI	Dual pathway inhibition
DSA	Digital subtraction angiography
DTA	Descending thoracic aorta
DUS	Duplex ultrasound
DWI	Diffusion-weighted imaging
ECG	Electrocardiogram
ECST	European Carotid Surgery Trial
eGFR	Estimated glomerular filtration rate
EMPA-REG OUTCOME	(Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients
ESC	European Society of Cardiology
ESH	European Society of Hypertension
ESRD	End-stage renal disease
EUCLID	Examining Use of tiCagreLor In peripheral artery Disease
FDA	(United States) Food and Drug Administration
FDG	Fluorodeoxyglucose
FDR	First-degree relative
FET	Frozen elephant trunk
FID	Focal intimal disruption
FL	False lumen
GERAADA	German Registry of Acute Aortic Dissection Type A
GFR	Glomerular filtration rate
GLP-1RA	Glucagon-like peptide-1 receptor agonist
GSV	Great saphenous vein
HADS	Hospital anxiety and depression score
HbA1c	Glycated haemoglobin
HBET	Home-based exercise training
HF	Heart failure
HITS	High-intensity transient signal
HOME	Hyperinsulinaemia: the Outcomes of its Metabolic Effects
HR	Hazard ratio
HRQoL	Health-related quality of life
hs-CRP	High-sensitivity C-reactive protein
HSR	High surgical risk
HTAD	Heritable thoracic aortic disease
IC	Intermittent claudication
ICA	Internal carotid artery
ID	Intimal disruption
IL	Interleukin
ILT	Intensive lipid-lowering therapy
IMA	Inferior mesenteric artery
IMH	Intramural haematoma
IMPROVE-AD	The Improving outcomes in vascular disease—aortic dissection trial
IMPROVE-IT	IMProved Reduction of Outcomes: Vytorin Efficacy International Trial
IPE	Icosapent ethyl
IRAD	International Registry of Acute Aortic Dissection
ISTH	International Society on Thrombosis and Haemostasis
i.v.	Intravenous
IVUS	Intravascular ultrasound
LDL-C	Low-density lipoprotein cholesterol
LEADER	Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results trial
LSA	Left subclavian artery
LV	Left ventricular
MACE	Major adverse cardiac event

MAD	Multisite artery disease
MALE	Major adverse limb event
MAP	Mean arterial pressure
MESA	Multi-Ethnic Study of Atherosclerosis
MFS	Marfan syndrome
MHV	Mechanical heart valve
MI	Myocardial infarction
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MWD	Maximal walking distance
NASCET	North American Symptomatic Carotid Endarterectomy Trial
OAC	Oral anticoagulation
o.d.	Once daily
OMT	Optimal medical treatment
OR	Odds ratio
PAAD	Peripheral arterial and aortic diseases
PA	Popliteal aneurysm
PAD	Peripheral arterial disease
PAU	Penetrating atherosclerotic ulcer
PC-AKI	Post-contrast acute kidney injury
PCSK9	Proprotein convertase subtilisin/kexin type 9
PET	Positron emission tomography
PET-CT	PET-computed tomography
PFWD	Pain-free walking distance
PROM	Patient-reported outcome measure
PSV	Peak systolic velocity
PSVr	Peak systolic velocity ratio
PVD	Polyvascular disease
QoL	Quality of life
RAR	Renal-aortic peak flow velocity ratio
RAS	Renal artery stenosis
RCT	Randomized controlled trial
REACH	The REduction of Atherothrombosis for Continued Health
REDUCE-IT	Reduction of Cardiovascular Events With Icosapent Ethyl–Intervention Trial
ROMS	Retrograde open mesenteric stenting
ROPAC	Registry Of Pregnancy And Cardiac disease
RPE	Rate of perceived exertion
RR	Relative risk
SAMMPRIS	Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis trial
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial
SAPT	Single antiplatelet therapy
SBP	Systolic blood pressure
SCI	Spinal cord ischaemia
SCS	Spinal cord stimulation
SET	Supervised exercise training
SF-36	Short-form 36-item health questionnaire
SGLT2i	Sodium-glucose co-transporter-2 inhibitor
SMA	Superior mesenteric artery
SMART	Secondary Manifestation of ARTerial disease
SOCRATES	Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes trial
SCORE2	Systematic Coronary Risk Evaluation 2
SCORE2-Diabetes	Systematic Coronary Risk Evaluation 2 - diabetes
SCORE2-OP	Systematic Coronary Risk Evaluation 2–Older Persons
SPACE-2	Stent Protected Angioplasty versus Carotid Endarterectomy study
SPPB	Short physical performance battery
SRUCC	Society of Radiologists in Ultrasound
SS	Subclavian stenosis
SSFP	Steady-state free precession
STJ	Sinotubular junction
STS/AATS	Society of Thoracic Surgeons/American Association for Thoracic Surgery
SUSTAIN-6	Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes
SVS	Society for Vascular Surgery
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TAA	Thoracic aortic aneurysm
TAAA	Thoracoabdominal aortic aneurysm
TAAD	Type A aortic dissection
TAD	Thoracic aortic disease
TAI	Traumatic aortic injury
TAV	Tricuspid aortic valve
TAVI	Transcatheter aortic valve implantation
TBAD	Type B aortic dissection
TBI	Toe–brachial index
TCAR	Transcarotid artery revascularization
$TcPO_2$	Transcutaneous oxygen pressure
TOE	Transoesophageal echocardiography
TEM	Type entry malperfusion classification
TEVAR/EVAR	Thoracic endovascular aortic aneurysm repair
TFCAS	Transfemoral carotid artery stenting
THALES	Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and acetylsalicylic acid for Prevention of Stroke and Death trial
TIA	Transient ischaemic attack
TIMI	Thrombolysis in myocardial infarction
TP	Toe pressure
TS	Turner syndrome
TTE	Transthoracic echocardiography
UEAD	Upper-limb artery disease
UKPDS	United Kingdom Prospective Diabetes Study: clinical and therapeutic implications for type 2 diabetes
uTBAD	Uncomplicated type B aortic dissection
VascuQoL	Vascular quality of life questionnaire
VAST	Vertebral Artery Stenting Trial
vEDS	Vascular Ehlers–Danlos syndrome
VIST	Vertebral Artery Ischaemia Stenting Trial
VKA	Vitamin K antagonist
WELCH	Walking Estimated Limitation Calculated by History
WIfI	Wound, Ischaemia, foot Infection classification
WIQ	Walking Impairment Questionnaire

1. Preamble

Guidelines evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. Guidelines are intended for use by health professionals and the European Society of Cardiology (ESC) makes its guidelines freely available.

ESC Guidelines do not override the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated when warranted by new evidence. ESC Policies and Procedures for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). This guideline updates and replaces the previous peripheral arterial disease and aortic disease guidelines from 2017 and 2014, respectively.

The Members of this task force were selected by the ESC to include professionals involved with the medical care of patients with this pathology as well as patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the whole of the ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity and inclusion, notably with respect to gender and country of origin.

The task force performed a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. The strength of every recommendation and the level of evidence supporting them were weighed and scored according to pre-defined scales as outlined in *Tables 1* and *2* below. Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) were also evaluated as the basis for recommendations and/or discussion in these guidelines. The task force followed ESC voting procedures and all approved recommendations were subject to a vote and achieved at least 75% agreement among voting members. Members of the task force with declared interests on specific topics were asked to abstain from voting on related recommendations.

The experts of the writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest were reviewed according to the ESC declaration of interest rules which can be found on the ESC website (http://www.escardio.org/guidelines) and have been compiled in a report published in a supplementary document with the guidelines. Funding for the development of ESC Guidelines is derived entirely from the ESC with no involvement of the healthcare industry.

The ESC Clinical Practice Guidelines (CPG) Committee supervises and co-ordinates the preparation of new guidelines and is responsible for the approval process. In addition to review by the CPG Committee, ESC Guidelines undergo multiple rounds of double-blind peer review by external experts, including members from across the whole of the ESC region, all National Cardiac Societies of the ESC and from relevant ESC Subspecialty Communities. After appropriate

Table 1 Classes of recommendations

Classes of recommendations	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Table 2 **Levels of evidence**

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

revisions, the guidelines are signed off by all the experts in the task force. The finalized document is signed off by the CPG Committee for publication in the *European Heart Journal*.

ESC Guidelines are based on analyses of published evidence, chiefly on clinical trials and meta-analyses of trials, but potentially including other types of studies. Evidence tables summarizing key information from relevant studies are generated early in the guideline development process to facilitate the formulation of recommendations, to enhance comprehension of recommendations after publication, and reinforce transparency in the guidelines development process. The tables are published in their own section of ESC Guidelines and reference specific recommendation tables.

Off-label use of medication may be presented in this guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, the final decisions concerning an individual patient must be made by the responsible health professional giving special consideration to:

- The specific situation of the patient. Unless otherwise provided for by national regulations, off-label use of medication should be limited to situations where it is in the patient's interest with regard to the quality, safety, and efficacy of care, and only after the patient has been informed and has provided consent.
- Country-specific health regulations, indications by governmental drug regulatory agencies, and the ethical rules to which health professionals are subject, where applicable.

2. Introduction

Peripheral arterial and aortic diseases (PAAD) are highly prevalent and significantly increase cardiovascular (CV) mortality and morbidity in the general population,[1,2] consequently, intensive preventive strategies are needed. However, patients with PAAD are generally underdiagnosed and undertreated[3,4] compared with patients with coronary artery disease (CAD).[5] Common risk factors in PAAD often coexist, requiring a multidisciplinary approach for effective management.[5] Early diagnosis is crucial for better outcomes. These guidelines address PAAD, updating and merging the 2017 peripheral arterial diseases and 2014 aortic diseases guidelines. The focus is primarily on atherosclerotic arterial diseases, but they also address some non-atherosclerotic genetic conditions. While not exhaustive, these 2024 guidelines offer guidance on diagnosis, surveillance, and treatment. A number of new and revised recommendations are summarized in *Tables 3* and *4*, respectively. Readers should consider non-atherosclerotic conditions and refer to specific documents.[6–9]

A general approach to PAAD is provided in the central illustration (*Figure 1*).

In the management of PAAD, the following aspects must be highlighted:

- ***Shared decision-making*** to involve patients, explore treatment options, assess patient values, and reach decisions collaboratively.
- ***Multidisciplinary approach (Figure 1) in expert and high-volume PAAD centres for complex patients or procedures***. These centres provide diverse services, including diagnosis, treatment planning, minimally invasive procedures, open surgery, post-operative and outpatient care, and ideally, research and innovation. They should provide continuous clinical service (24/7) and have access to digital imaging. These guidelines recognize variations in healthcare systems, population sizes, and needs, impacting the definition of 'high volume' in PAAD care across countries.

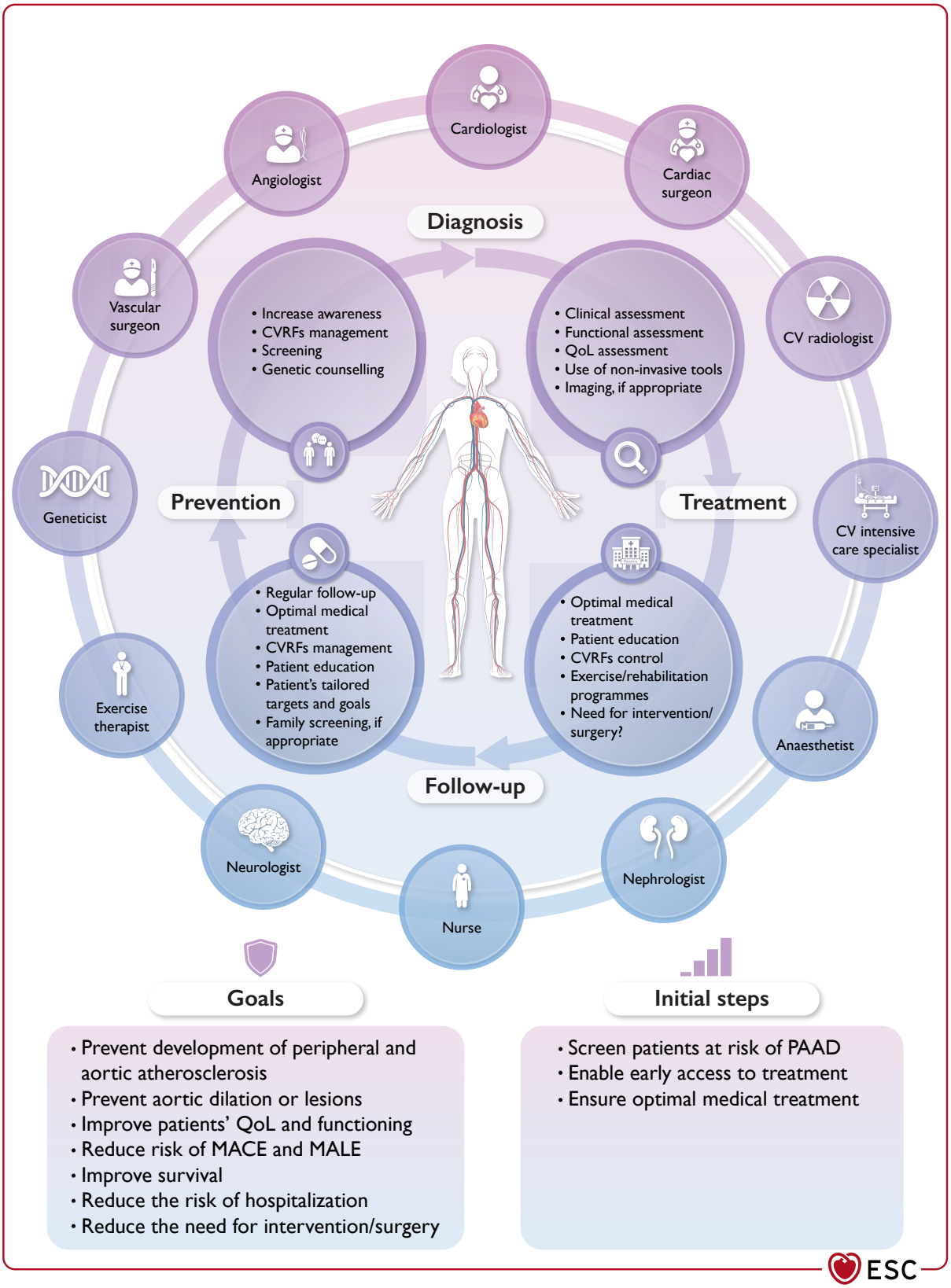

Figure 1 Central illustration: from diagnosis to treatment, a holistic multidisciplinary peripheral arterial and aortic diseases approach. CV, cardiovascular; CVRFs, cardiovascular risk factors; MACE, major adverse cardiac event; MALE, major adverse limb event; PAAD, peripheral arterial and aortic diseases; QoL, quality of life.

3. What is new

Table 3 New recommendations

Recommendations	Class	Level
Recommendations for clinical and laboratory, and for functional quality of life, assessment in patients with peripheral arterial and aortic disease		
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of arterial circulation.	I	B
Recommendations for peripheral arterial disease screening		
In patients with AAA, femoro-popliteal aneurysm screening with DUS should be considered.	IIa	C
In patients needing intervention with transfemoral access, screening for iliofemoral artery disease may be considered.	IIb	C
In patients with two or more CVRFs, screening for asymptomatic CS may be considered.	IIb	C
Recommendations for abdominal aortic aneurysm screening		
Opportunistic AAA screening with DUS should be considered in symptomatic/asymptomatic PAD patients.	IIa	B
Recommendations for lifestyle, physical activity, and patient education		
Use of web- or app-based secondary prevention risk calculators should be considered in the shared decision-making to improve patient adherence to treatment and lifestyle changes.	IIa	C
E-cigarettes may be considered as an aid to quitting tobacco smoking, but it is advisable to limit their use and avoid simultaneous use with conventional cigarettes due to unknown long-term effects.	IIb	C
Recommendations for lipid-lowering therapy in patients with peripheral arterial and aortic diseases		
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.	I	B
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.	I	B
Statins for the reduction of growth and rupture of AAA should be considered.	IIa	B
Statins for the reduction of growth and rupture of TAA may be considered.	IIb	B
In high-risk patients with PAAD and triglycerides >1.5 mmol/L despite lifestyle measures and statin therapy, icosapent ethyl 2 g b.i.d. may be considered in addition to a statin.	IIb	B
Fibrates are not recommended for cholesterol lowering.	III	B
Recommendations for exercise therapy in patients with peripheral arterial disease		
In patients with symptomatic PAD, SET is recommended.	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.	I	A
When SET is not available or feasible, a structured and monitored (calls, logbooks, connected devices) HBET programme should be considered.	IIa	A
Walking should be considered as the first-line training modality. When walking exercise is not an option, alternative exercise modes (strength training, arm cranking, cycling, and combinations of different training modes) should also be considered.	IIa	A
Walking training performed at high intensity (77%–95% of maximal heart rate or 14–17 self-perceived exertion on Borg's scale) should be considered to improve walking performance, and high-intensity exercise training (various aerobic training modes) should be considered to improve cardiorespiratory fitness.	IIa	A
Training frequency of at least three times per week, training session duration of at least 30 min, and training programme duration of at least 12 weeks should be considered.	IIa	B
In patients with PAD, exercise training to moderate-severe claudication pain may be considered to improve walking performance. However, improvements are also achievable with lesser claudication pain severities (low-mild pain or pain-free).	IIb	B
Based on patient's tolerance, a progressive increase (every 1–2 weeks) in exercise training load may be considered.	IIb	C

Continued

Recommendations for antithrombotic therapy in patients with peripheral arterial disease		
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and high ischaemic risk, and non-high bleeding risk.	IIa	A
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and non-high bleeding risk following lower-limb revascularization.	IIa	B
Aspirin (75–100 mg) for primary prevention may be considered in patients with asymptomatic PAD and DM, in the absence of contraindications.	IIb	A
Recommendations for interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)		
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.	I	C
In patients with symptomatic PAD and impaired PAD-related QoL after a 3 month period of OMT and exercise therapy, revascularization may be considered.	IIb	B
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.	III	B
In patients with asymptomatic PAD, revascularization is not recommended.	III	C
Recommendations for interventional treatment of patients with symptomatic peripheral arterial disease (per arterial bed)		
In femoro-popliteal lesions, drug-eluting treatment should be considered as the first-choice strategy.	IIa	A
In femoro-popliteal lesions, if revascularization is indicated, an open surgical approach should be considered when an autologous vein (e.g. GSV) is available in patients with low surgical risk.	IIa	C
In patients with severe IC undergoing endovascular femoro-popliteal revascularization, treatment of BTK arteries may be considered in the same intervention.	IIb	C
Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease		
It is recommended to regularly, at least once a year, follow-up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.	I	C
Recommendations for the management of chronic limb-threatening ischaemia		
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.	I	C
Recommendations for medical treatment in patients with chronic limb-threatening ischaemia		
It is recommended that patients with CLTI are managed by a vascular team.	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is indicated to allow wound healing.	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.	III	C
Recommendations for interventional treatment of chronic limb-threatening ischaemia		
In CLTI patients, it is recommended to perform revascularization as soon as possible.	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
In CLTI patients with good autologous veins and low surgical risk (<5% peri-operative mortality, >50% 2 year survival), infra-inguinal bypass may be considered.	IIb	B
In CLTI patients, endovascular treatment may be considered as first-line therapy, especially in patients with increased surgical risk or inadequate autologous veins.	IIb	B
Recommendations for follow-up in patients with chronic limb-threatening ischaemia		
In patients with CLTI, following revascularization it is recommended to follow-up patients on a regular basis.	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.	I	C
Recommendations for carotid artery stenosis assessment		
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.	I	B
It is not recommended to use the ECST method for ICA stenosis assessment.	III	C
Recommendations for the management of subclavian artery stenosis		
Bilateral arm BP measurement is recommended for all patients with PAAD.	I	B
Endovascular revascularization may be considered over surgery, despite similar long-term outcomes, due to lower complication rates.	IIb	B
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.	III	C
Recommendations for diagnostic strategies for renal artery disease		
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.	I	B

Continued

Recommendations for treatment strategies for renal artery disease		
Revascularization		
In patients with atherosclerotic unilateral >70% RAS, concomitant high-risk features, and signs of kidney viability, renal artery revascularization should be considered after OMT has been established.	IIa	B
In patients with atherosclerotic bilateral (>70%) RAS or RAS in a solitary kidney, concomitant high risk features, and signs of kidney viability, renal artery revascularization should be considered.	IIa	B
In patients with hypertension and/or signs of renal dysfunction due to RAS caused by fibromuscular dysplasia, concomitant high-risk features, and signs of kidney viability, revascularization with primary balloon angioplasty and bailout stenting should be considered.	IIa	B
In patients with an indication for renal artery revascularization and complex anatomy, or after failed endovascular revascularization, open surgical revascularization should be considered.	IIa	B
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.	III	A
Recommendations in patients with visceral artery stenosis		
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve		
In patients with dilatation of the tubular ascending aorta who can be offered surgery with low predicted risk, ascending aortic replacement should be considered at a maximum diameter >52 mm.	IIa	B
In patients undergoing surgery for tricuspid aortic valve disease who have concomitant dilatation of the aortic root or ascending tubular aorta, and low predicted surgical risk, ascending aorta or root replacement should be considered at a maximum diameter ≥45 mm, otherwise ≥50 mm.	IIa	B
SAPT with low-dose aspirin (75–100 mg/day) should be considered for the first 3 months after valve-sparing aortic surgery when there are no other baseline indications for OAC.	IIa	C
In patients undergoing non-aortic-valve cardiac surgery who have concomitant dilatation of the ascending aorta or aortic root with a maximum diameter ≥50 mm, concomitant aortic surgery should be considered.	IIa	C
Recommendations for surgery in aortic arch aneurysms		
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.	I	C
In patients undergoing open surgical repair of an aortic arch aneurysm, an elephant trunk or frozen elephant trunk procedure should be considered if the aneurysmal disease extends into the proximal descending thoracic aorta.	IIa	C
Recommendations for follow-up after treatment of aortic aneurysms		
After open repair of TAA, an early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.	I	B
After 5 post-operative years without complications, continuing long-term follow-up of TEVAR by CCT every 5 years should be considered.	IIa	B
If growth of the excluded aneurysm is observed, without evidence of type I or III endoleak, repeating CCT every 6–12 months, depending on the growth rate observed, should be considered.	IIa	C
In low-risk patients, from 1 year post-operatively after EVAR, repeating DUS/CEUS every 2 years should be considered.	IIa	B
If any abnormality during DUS/CEUS is found, confirmation should be considered using additional CCT or CMR (based on potential artefacts).	IIa	B
Recommendations for diagnostic work-up of acute aortic syndrome		
CCT from neck to pelvis is recommended as the first-line imaging technique in patients with suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendations for medical treatment in acute aortic syndromes		
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents is recommended after 24 h if gastrointestinal transit is preserved.	I	B
If the patient has a contraindication for BBs, a non-dihydropyridine calcium blocker should be considered.	IIa	B
Recommendations for intervention in type A acute aortic dissection		
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.	I	B
In patients presenting with acute TAAD, transfer from a low- to a high-volume aortic centre with the presence of a multidisciplinary team should be considered to improve survival if transfer can be accomplished without significant delay in surgery.	IIa	B
In selected patients, a valve-sparing root repair may be considered, when performed by experienced surgeons.	IIb	B

Continued

Recommendations for aortic repair strategies in type A acute aortic dissection		
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.	I	B
In patients with acute TAAD and a secondary intimal tear in the arch or proximal DTA, extended aortic repair with stenting of the proximal DTA (e.g. by the frozen elephant technique) may be considered to reduce late distal aortic complications (e.g. aneurysm evolution of the remaining dissected descending aorta).	IIb	C
Recommendations for the management of malperfusion in the setting of acute aortic dissection		
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.	I	B
In patients with acute TAAD presenting with cerebral malperfusion or non-haemorrhagic stroke, immediate aortic surgery should be considered to improve neurological outcome and reduce mortality.	IIa	B
In patients with acute TAAD presenting with clinically significant mesenteric malperfusion syndrome, immediate invasive angiographic diagnostics to evaluate percutaneous malperfusion repair before or directly after aortic surgery, in aortic centres with expertise, should be considered.	IIa	C
Recommendations for the management of patients presenting with acute type B aortic dissection		
In patients with uncomplicated acute TBAD, TEVAR in the subacute phase (between 14 and 90 days) should be considered in selected patients with high-risk features to prevent aortic complications.	IIa	B
Recommendations for the management of patients presenting with chronic type B aortic dissection		
In chronic TBAD and with a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.	I	B
In patients with chronic TBAD and a descending thoracic aortic diameter ≥55 mm, an indication for intervention should be considered in patients with low procedural risk.	IIa	C
In patients with chronic post-dissection thoracoabdominal aortic aneurysms, the use of fenestrated/branched stent grafts may be considered, when treatment is indicated.	IIb	C
Recommendations for the management of penetrating atherosclerotic ulcer		
In uncomplicated type B PAU with high-risk imaging features, endovascular treatment should be considered.	IIa	C
Recommendations for traumatic aortic injury		
In cases of severe aortic injury (grade 4), immediate repair is recommended.	I	A
In minimal aortic injury (grades 1 or 2), initial medical therapy under careful clinical and imaging surveillance should be considered.	IIa	C
In cases of progression of the IMH (grade 2), semi-elective repair (within 24–72 h) should be considered.	IIa	C
Recommendations for follow-up after treatment of acute aortic syndrome		
In medically treated type B AAS or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.	I	C
After open surgery for AAS, follow-up imaging by CCT and TTE within 6 months, then CCT at 12 months and then yearly if findings are stable, should be considered.	IIa	B
If no complications occur within the first 5 years, CCT every 2 years thereafter should be considered.	IIa	B
If no residual patent FL is documented for 3 post-operative years, subsequent surveillance by CCT every 2–3 years should be considered.	IIa	C
In the follow-up of medically treated PAU, after 2 years of imaging stability, larger intervals should be considered in low-risk patients.	IIa	C
Recommendations for the management of patients with heritable thoracic aortic disease		
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.	I	C
Recommendations for genetic testing and aortic screening in aortic disease		
In patients with HTAD, guidance of clinical management by the underlying gene/variant, when known, should be considered.	IIa	B

Continued

Recommendations for imaging in women with Turner syndrome		
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.	I	C
Recommendations for aortic surgery in women with Turner syndrome		
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered in women with TS who are ≥15 years of age, have an ascending ASI >23 mm/m^2, an AHI >23 mm/m, a z-score >3.5, and have associated risk factors for aortic dissection or are planning pregnancy.	IIa	C
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with TS who are ≥15 years of age, have an ascending ASI >25 mm/m^2, an AHI >25 mm/m, a z-score >4, and who do not have associated risk factors for aortic dissection.	IIb	C
Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome		
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.	I	C
Treatment with celiprolol should be considered in patients with vEDS.	IIa	B
Recommendations for vascular imaging in Marfan syndrome		
In patients with MFS, TTE is recommended: • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aortic imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.	I	C
Recommendations for medical treatment in Marfan syndrome		
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.	I	A
In patients with MFS, the use of both a BB and an ARB, in maximally tolerated doses (unless contraindicated), should be considered to reduce the rate of aortic dilatation.	IIa	A
Recommendations for pregnancy in women with Marfan syndrome		
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team	I	C
It is recommended that couples in which a partner has or is at risk of HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.	I	C
Intake of BBs during pregnancy is recommended.	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.	I	C
Prophylactic aortic root surgery may be considered in women desiring pregnancy with aortic diameters of 40–45 mm.	IIb	C
Recommendations for physical exercise in patients with Marfan syndrome		
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C
For patients who present with aortic dissection and/or have undergone aortic surgery, post-operative cardiac rehabilitation aiming at improving both physical and mental health should be considered.	IIa	B
Recommendations for imaging follow-up in Loeys–Dietz syndrome		
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth, is recommended.	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.	I	C
Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease		
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate for aortic root/ascending aorta enlargement is recommended.	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.	I	C
Prophylactic aortic root surgery should be considered with a diameter ≥45 mm, or lower in cases with other risk factors.	IIa	C

Continued

Recommendations for bicuspid aortic valve-associated aortopathy management		
Surgery for bicuspid aortopathy of the root phenotype is recommended when the maximum aortic diameter is ≥50 mm.	I	B
Screening by TTE in FDRs of BAV patients with root phenotype aortopathy and/or isolated aortic regurgitation is recommended.	I	C
In patients with low surgical risk, surgery for bicuspid aortopathy of ascending phenotype should be considered when the maximum aortic diameter is >52 mm.	IIa	B
Recommendations for evaluation and medical treatment of patients with coarctation of the aorta		
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).	I	B
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases		
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
In patients with stable PVD who are symptomatic in at least one territory and without high bleeding risk, treatment with a combination of rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.	IIa	A

AAA, abdominal aortic aneurysm; AAD, acute aortic dissection; AAS, acute aortic syndrome; AHI, aortic height index; ARB, angiotensin receptor blocker; ASI, aortic size index; BAV, bicuspid aortic valve; BB, beta-blocker; b.i.d., twice daily; BP, blood pressure; BTK, below-the-knee; BSA, body surface area; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CLTI, chronic limb-threatening ischaemia; CMR, cardiovascular magnetic resonance; CS, carotid artery stenosis; CV, cardiovascular; CVRFs, cardiovascular risk factors; DM, diabetes mellitus; DTA, descending thoracic aorta; DUS, duplex ultrasound; ECST, European Carotid Surgery Trial; FDR, first-degree relative; FL, false lumen; GSV, great saphenous vein; HBET, home-based exercise training; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; IC, intermittent claudication; i.v., intravenous; LDL-C, low-density lipoprotein cholesterol; MFS, Marfan syndrome; NASCET, North American Symptomatic Carotid Endarterectomy Trial; OAC, oral anticoagulation; o.d., once daily; OMT, optimal medical treatment; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; PVD, polyvascular disease; QoL, quality of life; RAS, renal artery stenosis; SAPT, single antiplatelet therapy; SET, supervised exercise training; TAA, thoracic aortic aneurysm; TAAD, type A aortic dissection; TBAD, type B aortic dissection; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TS, Turner syndrome; TTE, transthoracic echocardiography; vEDS, vascular Ehlers–Danlos syndrome.

Table 4 Revised recommendations

Recommendations in 2017 (PAD) and 2014 (Aortic)	Class	Level	Recommendations in 2024	Class	Level
Recommendations for abdominal aortic aneurysm screening					
Screening for AAA with DUS					
Is recommended in all men >65 years of age.	I	A	Is recommended in men aged ≥65 years with a history of smoking to reduce the risk of death from ruptured AAA.	I	A
(i) May be considered in women >65 years of age with history of current/past smoking.	IIb	C	May be considered in men aged ≥75 years (irrespective of smoking history) or in women aged ≥75 years who are current smokers, hypertensive, or both.	IIb	C
(ii) Is not recommended in female non-smokers without familial history.	III	C			
Family AAA screening with DUS					
Targeted screening for AAA with ultrasound should be considered in first-degree siblings of a patient with AAA.	IIa	B	Is recommended for FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.	I	C
Opportunistic AAA screening with DUS					
Targeted screening for AAA with ultrasound should be considered in first-degree siblings of patients with AAA.	IIa	B	Should be considered in men ≥65 years and in women aged ≥75 years during TTE.	IIa	B
Recommendations for antihypertensive therapy in patients with peripheral and aortic disease					
In patients with PAD and hypertension, it is recommended to control blood pressure at <140/90 mmHg	I	A	In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.	I	A
ACEIs or ARBs should be considered as first-line therapy in patients with PAD and hypertension.	IIa	B	ACEIs/ARBs may be considered in all patients with PAD, regardless of BP levels, in the absence of contraindications.	IIb	B
Recommendations for lipid-lowering therapy for patients with peripheral arterial and aortic diseases					
In patients with PAD, it is recommended to reduce LDL-C to <1.8 mmol/L (70 mg/dL) or decrease it by >50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).	I	C	An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
Recommendations for carotid artery stenosis assessment					
DUS (as first-line imaging), CTA, and/or MRA are recommended for evaluating the extent and severity of extracranial carotid stenosis.	I	B	It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.	I	C

Continued

Recommendations in patients with visceral artery stenosis					
In patients with acute embolic occlusion of the SMA, both endovascular and open surgery therapy should be considered.	IIa	B	In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.	I	B
Recommendations for surveillance of patients with abdominal aorta aneurysm					
In patients with small (30–55 mm) AAA, the following time interval should be considered: • Every 3 years for AAA of 30–39 mm diameter • Every 2 years for AAA of 40–44 mm diameter • Every year for AAA >45 mm diameter.	IIa	B	DUS surveillance should be considered annually in women with AAA of 40–45 mm and in men with AAA of 40–49 mm.	IIa	B
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve					
Surgery should be considered in patients who have isolated aortic arch aneurysm with a maximal diameter ≥55 mm.	IIa	C	Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.	I	B
Aortic valve repair using the reimplantation technique or remodelling with aortic annuloplasty is recommended in young patients with aortic root dilation and tricuspid aortic valves.	I	C	Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.	I	B
Lower thresholds for intervention may be considered according to BSA in patients with small stature or in the case of rapid progression, aortic valve regurgitation, planned pregnancy, and patient's preference.	IIb	C	Ascending aortic or root replacement may be considered at a maximum diameter of ≥50 mm in patients with proximal aorta dilatation who can be offered surgery with low predicted risk and present with any of the following: • Growth of the aortic diameter ≥3 mm per year • Resistant hypertension • Short stature (<1.69 m) • Root phenotype • Aortic length >11 cm • Age <50 years • Desire for pregnancy • Aortic coarctation.	IIb	B
Recommendations for surgery in aortic arch aneurysms					
Aortic arch repair may be considered in patients with aortic arch aneurysm who already have an indication for surgery of an adjacent aneurysm located in the ascending or descending aorta.	IIb	C	In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch replacement should be considered if the dilatation extends into the proximal aortic arch (>50 mm).	IIa	C
Recommendations for follow-up after treatment of aortic aneurysms					
After TEVAR or EVAR, surveillance is recommended after 1, 6, and 12 months and then yearly. Shorter intervals can be proposed in the event of abnormal findings requiring closer surveillance.	I	C	After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
Long-term surveillance of open abdominal aortic repair may be considered at loose (5 year) intervals using colour DUS or CCT imaging.	IIb	C	After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and every 5 years thereafter if findings are stable.	I	A
If neither endoleak nor AAA sac enlargement is documented during first year after EVAR, then colour DUS, with or without contrast agents, should be considered for annual post-operative surveillance, with non-contrast CT imaging every 5 years.	IIa	C	After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.	I	A
Recommendations for diagnostic work-up of acute aortic syndrome					
TTE is recommended as an initial imaging investigation. In stable patients with a suspicion of AAS, the following imaging modalities are recommended (or should be considered according to local availability and expertise):	I	C	In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.	I	C
MRI	I	C	In patients with suspected AAS, CMR should be considered as an alternative imaging technique if CCT is not available.	IIa	C

Continued

TOE	IIa	C	In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendations for medical treatment in acute aortic syndromes					
In all patients with AD, medical therapy, including pain relief and blood pressure control, is recommended.	I	C	Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.	I	B
Recommendations for the management of patients presenting with acute type B aortic dissection					
In complicated TBAD, TEVAR is recommended.	I	C	In patients with complicated acute TBAD, emergency intervention is recommended.	I	B
In complicated TBAD, surgery may be considered.	IIb	C			
In complicated TBAD, TEVAR may be recommended.	IIb	C	In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.	I	B
In complicated TBAD, surgery may be considered.	IIb	C			
Recommendations for the management of intramural haematoma					
In complicated type B IMH, TEVAR should be considered.	IIa	C	In complicated type B IMH, TEVAR is recommended.	I	C
Recommendations for the management of penetrating atherosclerotic ulcer					
In the case of type A PAU, surgery should be considered.	IIa	C	In the case of type A PAU, surgery is recommended.	I	C
In complicated type B PAU, TEVAR should be considered.	IIa	C	In complicated type B PAU, endovascular treatment is recommended.	I	C
Recommendations for traumatic aortic injury					
In cases of TAI with suitable anatomy requiring intervention, TEVAR should be preferred to surgery.	IIa	C	In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.	I	A
Recommendations for genetic testing and aortic screening in aortic disease					
It is recommended to investigate FDRs (siblings and parents) of a subject with TAAD to identify a familial form in which relatives all have a 50% chance of carrying the family mutation/disease.	I	C	Imaging screening of family members of patients with TAD with risk factors for HTAD in whom no (likely) pathogenic variant is identified should be considered starting at age 25, or 10 years below the youngest case, whichever is younger. If the initial screening is normal, continued screening every 5 years until the age of 60 should be considered.	IIa	C
Recommendations for bicuspid aortic valve-associated aortopathy management					
Cardiac MRI or CT is indicated in patients with BAV when the morphology of the aortic root and the ascending aorta cannot be accurately assessed by TTE.	I	C	CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.	I	C
In the case of aortic diameter >50 mm or an increase of >3 mm per year measured by echocardiography, confirmation of the measurement is indicated, using another imaging modality (CT or MRI).	I	C			
In the case of a diameter of the aortic root or the ascending aorta >45 mm or an increase of >3 mm per year measured by echocardiography, annual measurement of aortic diameter is indicated.	I	C	Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.	I	C
In cases of BAV, surgery of the ascending aorta is indicated in the case of: • Aortic root or ascending aortic diameter >50 mm in the presence of other risk factors (coarctation of the aorta, systemic hypertension, family history of dissection, or increase in aortic diameter of >3 mm per year).	I	C	In patients with low surgical risk and ascending phenotype bicuspid aortopathy, surgery should be considered at a maximum diameter ≥50 mm if any of the following is the case: • Age <50 years • Short stature • Ascending aortic length ≥11 cm • Aortic diameter growth rate >3 mm per year • Family history of acute aortic syndrome • Aortic coarctation • Resistant hypertension • Concomitant non-aortic-valve cardiac surgery • Desire for pregnancy	IIa	C

Continued

In cases of BAV, surgery of the ascending aorta is indicated in the case of: • Aortic root or ascending aortic diameter >45 mm when surgical aortic valve replacement is scheduled.	I	C	Surgery for bicuspid aortopathy in patients undergoing aortic valve surgery should be considered at a root or ascending diameter ≥45 mm.	IIa	C
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases					
In patients undergoing CABG, DUS is recommended in patients with a recent (<6 months) history of TIA/stroke.	I	B	Carotid DUS should be considered for stable patients scheduled for CABG with TIA/stroke within the past 6 months without carotid revascularization.	IIa	B

AAA, abdominal aortic aneurysm; AAS, acute aortic syndrome; ACEI, angiotensin-converting enzyme inhibitor; AD, aortic dissection; ARB, angiotensin receptor blocker; BAV, bicuspid aortic valve; BP, blood pressure; BSA, body surface area; CABG, coronary artery bypass grafting; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CMR, cardiovascular magnetic resonance; CT, computed tomography; CTA, computed tomography angiography; DUS, duplex ultrasound; ECG, electrocardiogram; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; LDL-C, low-density lipoprotein cholesterol; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; SBP, systolic blood pressure; SMA, superior mesenteric artery; TAAD, type A aortic dissection; TAD, thoracic aortic disease; TAI, traumatic aortic injury; TBAD, type B aortic dissection; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TIA, transient ischaemic attack; TTE, transthoracic echocardiography.

4. Epidemiology and risk factors

4.1. Epidemiology

Peripheral arterial disease (PAD) is prevalent worldwide and affects 113 million people aged 40 and older, of which 42.6% are in countries with a low-to-middle sociodemographic index. Global prevalence is 1.52%, increases with age (14.91% in those aged 80–84 years), and is higher in females than in males (18.03% vs. 10.56%, in the same age group).[10–13]

PAD prevalence rose by 72% from 1990 to 2019, considering a 45% growth rate in the world population.[10,11,14] The overall global age-standardized prevalence is about 1470 per 100 000 persons (*Figure 2*).[14]

Ischaemic cerebral disease, mainly linked to carotid stenosis (65% of cases), has a prevalence of 77.19 million, marking a 95% increase from 1990 to 2019.[15]

The overall prevalence of aortic disease including aneurysm and dissections is estimated at around 1% to 3% in the general population, with up to 10% prevalence in older age groups. European studies show a decrease in abdominal aortic aneurysm (AAA) prevalence in screened men >65 years of age, at 1.3%–3.3%,[16,17] contrasting with the United States of America's 5% found in screened male smokers.[16,17] Globally, in 2019, there were 172 000 aortic aneurysm-related deaths (82.1% increase from 1990).[10]

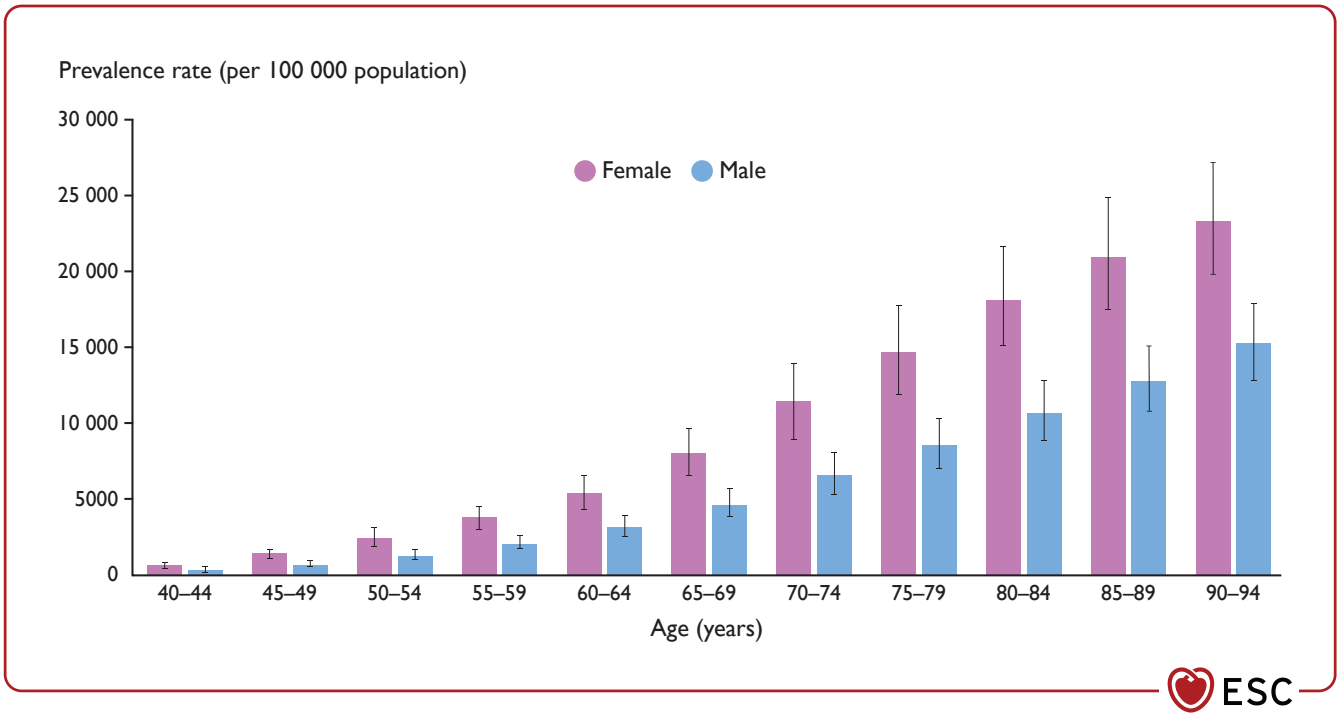

Figure 2 Estimated specific prevalence of peripheral arterial disease, by sex, in people aged 40 years and older. Adapted from[12] under the terms of the Open access Creative Commons CC-BY license.

4.2. Risk factors

Main PAAD risk factors are summarized in *Figure 3*. Traditional risk factors in tools like Framingham, Reynolds, Atherosclerotic Cardiovascular Disease (ASCVD) risk estimator Plus (United States of America), SCORE2 (Systematic Coronary Risk Evaluation 2, age 40–69 years), SCORE2-Diabetes (Systematic Coronary Risk Evaluation 2 - diabetes), and SCORE2-OP (Systematic Coronary Risk Evaluation 2–Older Persons) (Europe)[18] also contribute to PAAD's pathophysiology and development. More details are available in Supplementary data online, *Section 1.1*, and the *2021 ESC Guidelines on CV disease prevention in clinical practice*.[19]

Low-density lipoprotein cholesterol (LDL-C) is a pivotal factor in atherosclerosis,[19] with diabetes and tobacco exposure significantly

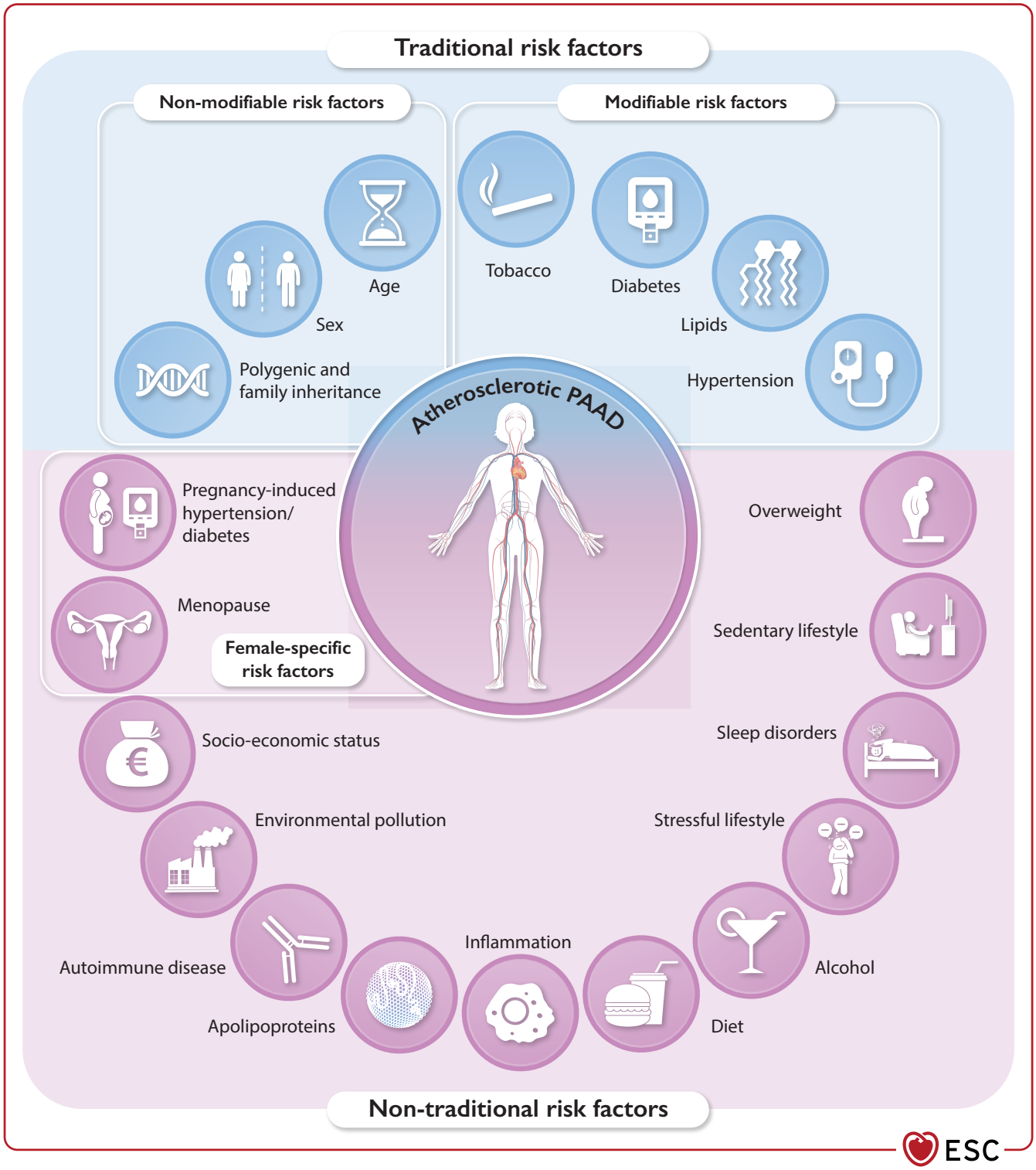

Figure 3 Main risk factors associated with atherosclerosis in peripheral arterial and aortic diseases. PAAD, peripheral arterial and aortic diseases.

amplifying PAD risk by 2–4 times each.[20] Both men and women face a similar risk of PAD, but women have distinct risk factors (*Figure 3*).[21] Hypertension and male sex are major risk factors for AAA, whereas diabetes mellitus lowers its incidence by 25%.[22–24] Thoracic aortic aneurysm (TAA) or dissection share atherosclerotic risk factors, yet monogenic or polygenic diseases like Marfan syndrome (MFS), more prevalent in younger individuals, also contribute.[24,25] Inflammation as a risk factor can be observed in PAAD[26] and the potential for inflammation to be a modifiable risk factor is indicated by research related to colchicine and the effects demonstrated by canakinumab (a monoclonal antibody that reduces inflammation by inhibiting interleukin-1 beta).[27,28]

5. Evaluation of peripheral arteries and aorta

To be consistent with existing literature, the term PAD is used to refer to lower-extremity atherosclerotic arterial disease.

5.1. Clinical history and examination, and laboratory assessment, in patients with peripheral arterial and aortic diseases

Clinical evaluation encompassing history (including family history), review of symptoms, and physical examination are the first steps in diagnosing and assessing patients with PAAD. Pulse palpation, femoral, carotid, and abdominal bruit auscultation, heart auscultation, and observation of the legs and feet need to be part of the vascular examination.

Clinical signs, beyond aiding diagnosis, offer prognostic insights. Carotid bruits double the risk of myocardial infarction (MI) and CV death,[29,30] while a brachial systolic blood pressure (SBP) difference of more than 15 mmHg raises CV death risk by 50%.[31] Hence, bilateral arm blood pressure (BP) measurement is recommended.[32] Lab assessments should include lipid profile (including lipoprotein[a] at least once in a lifetime),[33] fasting glycaemia, glycated haemoglobin (HbA1c), renal function, blood count, coagulation studies, liver function, electrolytes, and inflammatory markers (C-reactive protein [CRP] and erythrocyte sedimentation rate). Additional evaluations, like thyroid function tests, are advised as needed.

5.2. Functional and quality of life assessment in patients with peripheral arterial and aortic diseases

Patients with PAD have decreased walking performance and self-reported physical and mental health-related quality of life (HRQoL).[34–40] Muscle strength and balance are also impaired,[41–45] leading to a faster decline in functional (physical functioning) performance in both symptomatic and asymptomatic patients.[46,47] Depression is associated with greater impairment in functional performance.[48,49] Impaired functional status is related to decreased self-reported HRQoL,[50,51] and predicts further mobility loss and CV mortality.[52,53] Very poor HRQoL has been found in patients with chronic limb-threatening ischaemia (CLTI).[54]

Different questionnaires are available assessing different facets (functional, mental, and social status) of patient-reported outcome measures (PROMs).[34–36,38] The Short-form 36-item health questionnaire (SF-36) (including physical- and mental health-related items) is the most used generic questionnaire in PAD.[35,36,38] The Edinburgh Claudication Questionnaire is a modified version of the initially developed Rose questionnaire and has a sensitivity of 91% and a specificity of 99% in comparison with a physician-based diagnosis.[55,56] The Walking Impairment Questionnaire (WIQ), the Walking Estimated Limitation Calculated by History (WELCH), and the Vascular quality of life (VascuQoL) questionnaire are the most used PAD-specific questionnaires.[34–36,38]

Treadmill testing, using standardized criteria, is the gold standard to assess walking performance.[37,57–62] Patients are asked to walk until maximal pain levels, defining the maximal walking distance (MWD). Patients are also asked to indicate the point at which pain begins, defining the pain-free walking distance (PFWD). Constant-load protocols have poorer reliability than graded protocols.[60–64] Additionally, the six-minute walk test (6MWT) should be performed to assess functional walking performance.[62,65] For muscular lower-limb strength assessment,[66] isokinetic dynamometry has good test–retest reliability.[67] Alternatively, the Short physical performance battery (SPPB) test should be used.[62,64,68,69] The SPPB has good test–retest reliability.[64]

Few data exist on HRQoL, functional assessment, and exercise capacity in patients with aortic diseases.[70,71] Those with acute aortic dissection (AAD), as well as patients who had aortic valve or thoracic aortic surgery, may present with depression and anxiety, leading to mental health issues[72,73] that can also be assessed with the SF-36 questionnaire or the hospital anxiety and depression score (HADS).[72] Patients with MFS have reduced HRQoL and a significant decline over time in physical HRQoL.[74,75] Assessing HRQoL in aortic disease patients is crucial for understanding well-being, disease impact, and treatment effects. This involves PROMs, including surveys, symptom assessment, functional evaluation, psychological well-being (HADS), social and occupational function, and medication/treatment side effects. It also covers healthcare utilization and patient satisfaction, informing care and enhancing aortic disease management.

Recommendation Table 1 — Recommendations for clinical and laboratory, and for functional and quality of life, assessment in patients with peripheral arterial and aortic disease (see also Evidence Table 1)

Recommendations	Class[a]	Level[b]
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of the arterial circulation.[76]	I	B
To assess PAAD, it is recommended to perform thorough clinical, vascular, and CVRFs laboratory evaluation.[77]	I	C
Overall evaluation of functional (physical functioning) performance with objective tests should be considered in patients with symptomatic and asymptomatic chronic PAD.[57,61,63]	IIa	B
Overall evaluation of self-reported (i.e. by questionnaire) physical and mental/social HRQoL should be considered in patients with PAAD.[34–36,38,72]	IIa	B

CVRFs, cardiovascular risk factors; HRQoL, health-related quality of life; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

5.3. Vascular examination of peripheral arteries

The ankle-brachial index (ABI)[78,79] is a low-cost, easy, and largely used tool, used both at rest or after exercise[80–84] for PAD diagnosis and surveillance (*Figure 4*). Both oscillometric and Doppler methods have shown good concordance.[78]

Resting ABI has a 68%–84% sensitivity and an 84%–99% specificity for PAD diagnosis (*Figure 4*).[79] An ABI ≤0.90 confirms PAD diagnosis.[79,85–87] For values >1.40, the term 'non-compressible arteries' should be used.

Ankle–brachial index >1.40, seen in arterial stiffness (diabetes, severe kidney failure, or advanced age), correlates with increased CV events and mortality risk.[88,89] For ABI >1.40, assessing resting toe–brachial index (TBI) is recommended.[79,90–95]

Toe–brachial index addresses medium-calibre artery rigidity[96] measuring pressure on the hallux, second, or third toe using laser Doppler probe or plethysmography.[97,98] Sensitivity and specificity for PAD diagnosis

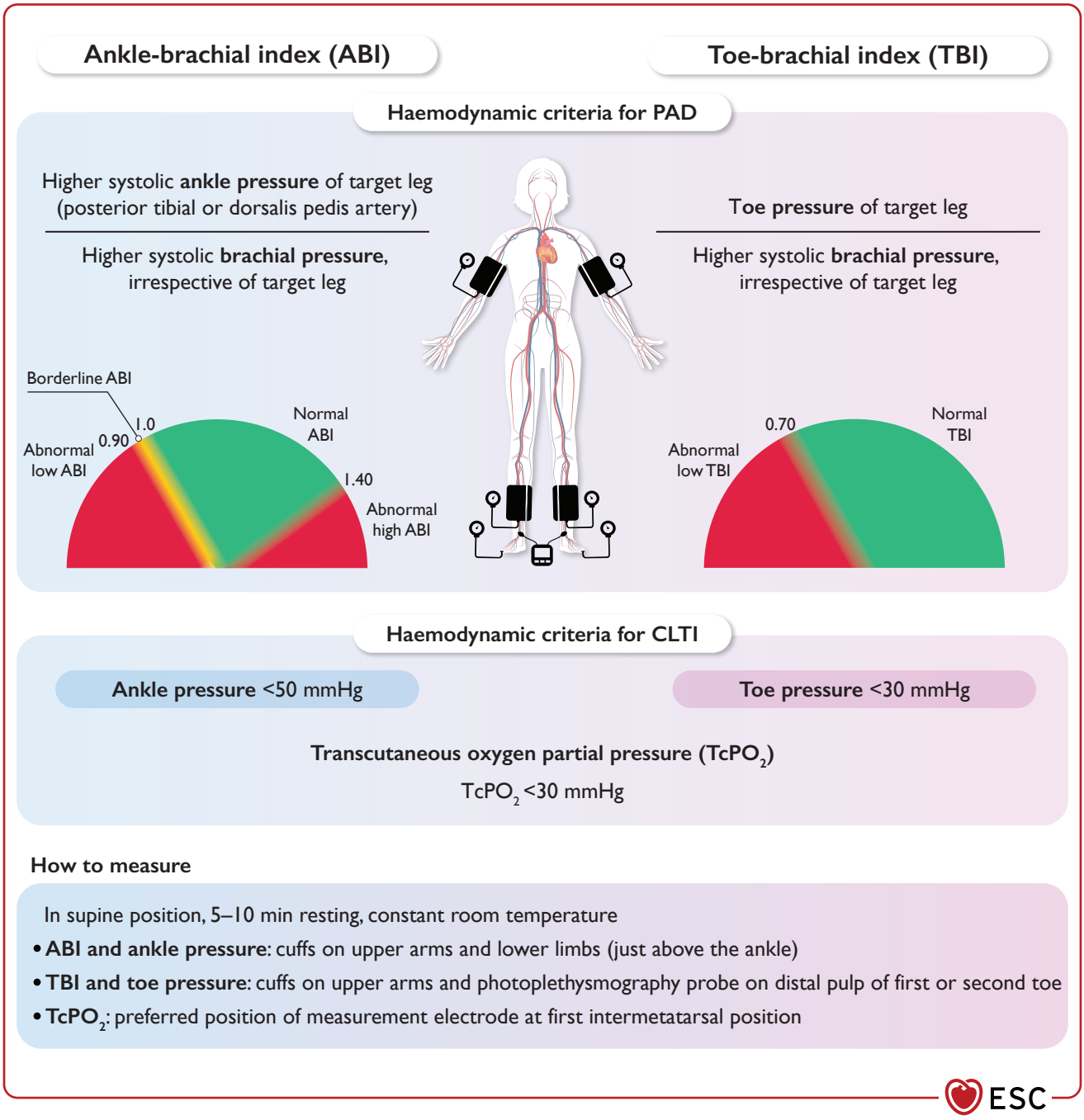

Figure 4 Haemodynamic assessment of peripheral arterial disease. ABI, ankle–brachial index; CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease; TBI, toe–brachial index; $TcPO_2$, transcutaneous oxygen pressure.

range from 45% to 100% and 17% to 100%, respectively.[91] The usual pathological threshold for TBI is ≤0.70 (*Figure 4*).[99]

Used within the Framingham risk score, ABI enables the upgrading of risk estimation in 'low-risk' women and men,[77,88] it allows CV risk assessment in diverse ethnic groups independently of risk factors,[77,89] and is inexpensive and minimally time-consuming.[100] Trained physicians have better reproducibility than inexperienced ones.[101,102]

In patients with exertional limb pain relieved by rest and a resting ABI >0.90, exercise testing with post-exercise ABI measurements or exercise oximetry has been proposed to diagnose lower-limb arterial stenoses.[103–105]

The post-exercise ABI is determined 1 min after the cessation of a standardized treadmill exercise.[106] The physician measures bilateral ankle BP, starting with the symptomatic leg, using the ankle artery used for the reference resting ABI measurement. Brachial SBP should simultaneously be measured to enable calculation of the post-exercise ABI.[104]

Discrepancies in PAD diagnosis exist between exercise criteria, such as a fall in absolute ankle BP >30 mmHg or a drop of >20% in the post-exercise ABI.[104] Recent studies identified numerous false positives in a healthy population when using a post-exercise ABI drop of >20% as the diagnostic threshold, as commonly proposed.[103]

Measurement of transcutaneous oxygen pressure ($TcPO_2$) is a means of evaluating tissue viability and is proposed as a diagnostic criterion of CLTI (*Figure 4*).[107] $TcPO_2$ is affected by local and general factors such as skin thickness, probe temperature, inflammation, and oedema,[108,109] resulting in misleading values.

Resting $TcPO_2$ >30 mmHg is a favourable indicator of wound healing;[110–112] however, resting $TcPO_2$ <10 mmHg is associated with bad prognosis for wound healing and amputation in CLTI patients treated with bone marrow-derived stem cells.[107] When performed at successive levels on an ischaemic limb, $TcPO_2$ measurement may help to determine amputation level.[113–115]

Exercise transcutaneous oximetry has also been proposed.[116,117] This seems of interest to detect proximal (buttock) claudication[105] or unsuspected exercise-induced hypoxaemia[118] in patients with intermittent claudication (IC).[117]

5.3.1. Duplex ultrasound

Duplex ultrasound (DUS) is a first step in the vascular work-up for PAD screening and diagnosis, allowing a dynamic, non-invasive, radiation- and contrast-free examination. It localizes vascular lesions and quantifies their extent and severity through velocity criteria.[119–121] In combination with ABI or TBI, DUS permits determining the haemodynamic relevance of arterial lesions[122,123] and estimation of ABI.[124] DUS has a sensitivity of 88% and specificity of 95% for >50% stenosis detection.[125] Post-exercise DUS can reveal borderline arterial lesions if initial findings are inconclusive.[122,126,127]

Duplex ultrasound distinguishes atherosclerotic (even subclinical disease) from non-atherosclerotic lesions, but its reliability relies on the sonographer's expertise.[122] Cross-sectional imaging is advisable for revascularization planning. ABI and DUS are recommended for PAD patient follow-up post-revascularization.[128]

More recent techniques, such as flow imaging, 3D echography, ultrafast ultrasound, and shear wave elastography, as well as the use of contrast-enhanced ultrasound (CEUS), could further improve DUS performance.[129]

5.3.2. Digital subtraction angiography, computed tomography angiography, and magnetic resonance angiography

Detailed information about these techniques can be found in the Supplementary data online, *Section 1.2* (*Table S1*). Digital subtraction angiography (DSA) remains mostly limited to revascularization procedures. Computed tomography angiography (CTA) offers better spatial resolution than magnetic resonance angiography (MRA) and better calcification visualization; however, it can also overestimate stenosis severity due to the blooming effect. MRA allows arterial wall and lumen assessment as well as tissue and organ perfusion distal to or surrounding the explored arterial territory.

Recommendation Table 2 — Recommendations for diagnostic tests in patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
Measurement of the ABI is recommended as the first-line non-invasive test for screening and diagnosis of PAD, using an ABI ≤0.90 as a diagnostic criterion.[79,90,130,131]	I	B
In the case of non-compressible ankle arteries or ABI >1.40, additional methods such as TP, TBI or Doppler waveform analysis are recommended.[90,91,124,132,133]	I	B

ABI, ankle–brachial index; PAD, peripheral arterial disease; TBI, toe–brachial index; TP, toe pressure.
[a]Class of recommendation.
[b]Level of evidence.

5.4. Evaluation of the aorta

The aorta can be divided into different anatomical regions (from proximal to distal) for reporting purposes. The main anatomical aortic regions are the aortic root, ascending aorta, aortic arch, descending thoracic aorta (DTA), abdominal aorta (AA), infrarenal aorta, and the iliac arteries (*Figure 5*).[134,135]

5.4.1. Aortic measurements

The main imaging techniques used for aortic evaluation are illustrated in *Table 5*.

Evaluating aortic dilation and progression depends on standardized measurements. In echocardiography, aortic diameters should be measured using the leading-to-leading edge method during end-diastole (as systole sees about a 2 mm aortic expansion) in all segments (*Figure 6*).[137,138]

Most studies supporting prophylactic surgery have used this approach. Furthermore, better agreement exists between echo's leading-to-leading edge and cardiovascular computed tomography (CCT)/cardiovascular magnetic resonance (CMR)'s inner-to-inner edge during end-diastole.[137,139,140] However, when the aortic wall thickens (e.g. atheroma, thrombus, intramural haematoma [IMH], or aortitis) or in cases of aortic dissection (AD), also report the outer-to-outer diameter (*Figure 6*).

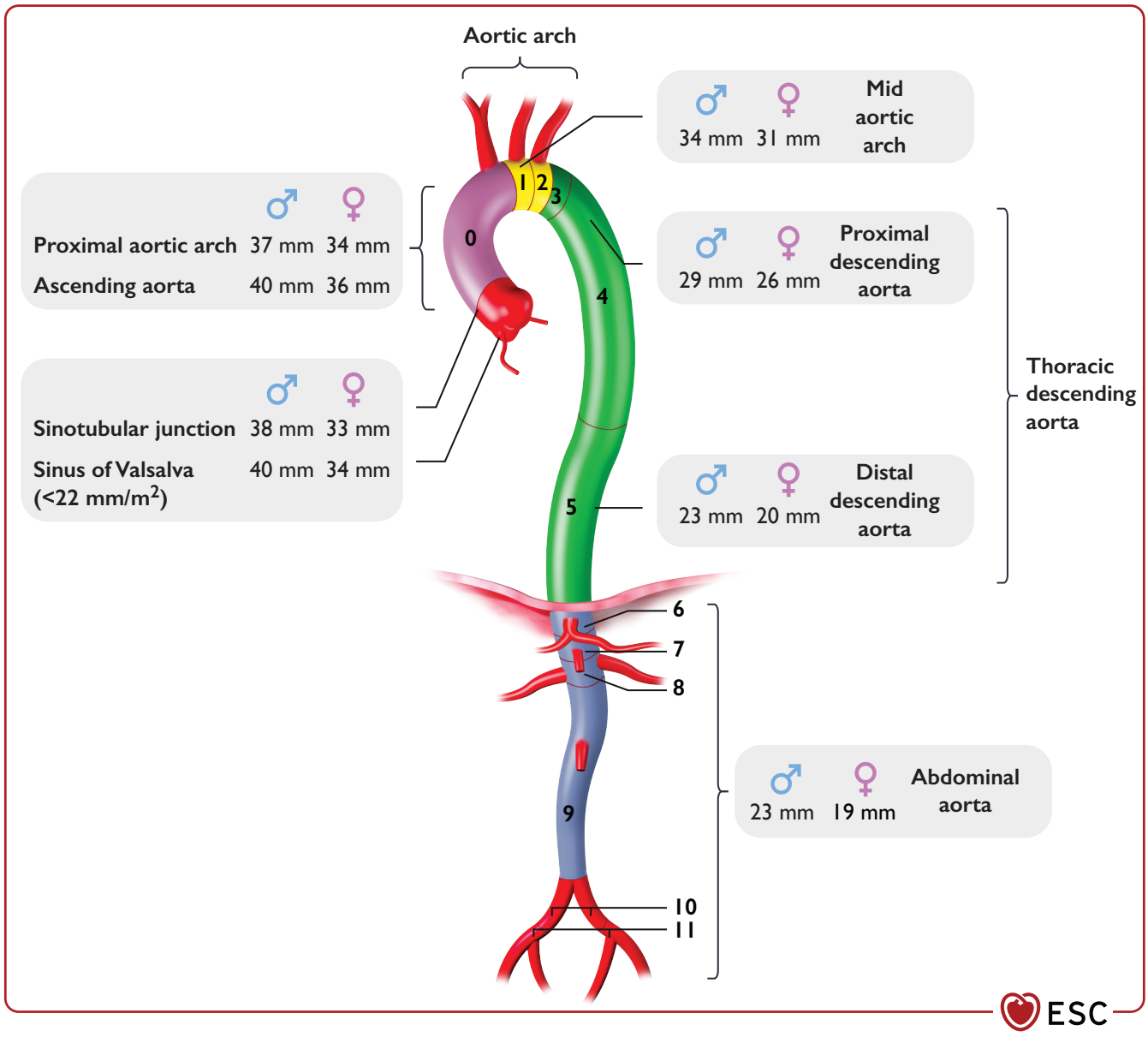

Figure 5 Anatomy and aortic segments and upper normal values for aortic dimensions. Numbers represent the 11 aortic segments based on the Society for Vascular Surgery/Society of Thoracic Surgeons (SVS/STS) classification for surgical and endovascular purposes.[136] Z-scores can be calculated for aortic root and ascending aorta. Calculation of z-scores can be performed following these links: https://www.marfan.fr/accueil/z-score-calculus/ or https://marfan.org/dx/z-score-adults.

Table 5 Main aortic imaging techniques

	TTE/DUS	TOE	CCT	CMR
Availability	++++	+++	++	+
Cost	+	++	+++	++++
Time requirement	+	+++	+++	++++
Radiation	0	0	+++	0
Spatial resolution	1 mm	1 mm	0.6 mm	1–2 mm
Temporal resolution	20 msec	20 msec	80 msec	30 msec
Nephrotoxicity	0	0	+++	+
Accuracy	++	++++	++++	++++
Serial examination	++++	++	++	++++
Aortic wall visualization	++	+++	++++	++++
Aortic valve function	+++	++++	+	++++
RV/LV function	+++	+++	+++[a]	++++
Aortic root assessment	+++	+++	++++	++++
Aortic arch assessment	++	+++	++++	++++
Thoracic aorta assessment	+	++	++++	++++
Abdominal aorta assessment	+++	-	++++	++++

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; LV, left ventricle; RV right ventricle; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.
[a]CCT can be used to evaluate left and right ventricular function only if retrospective gating is used.

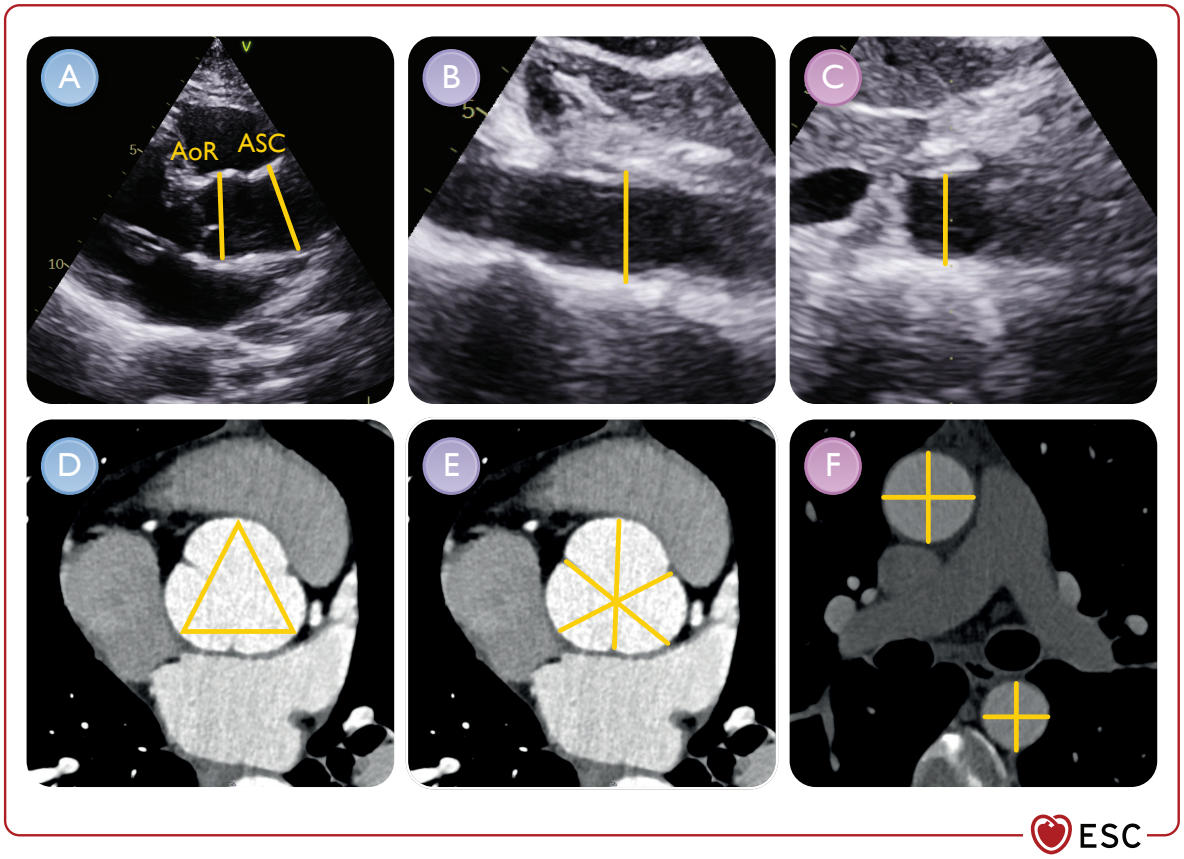

Figure 6 Conventional measurements of the aorta at different levels by echocardiography or duplex ultrasound (*A*, *B*, *C*), cardiovascular computed tomography or cardiovascular magnetic resonance (*D*, *E*, *F*). (*A*) Echocardiographic measurements of the aortic root and ascending aorta using the leading-to-leading edge methodology. (*B*) The outer-to-outer convention in the abdominal aorta in cases with aortic wall disease in a longitudinal view. This method can be used in a non-circular section as an alternative. (*C*) The outer-to-outer antero-posterior diameter of the abdominal aorta in a cross-sectional view. Evaluation of the aortic root using the cusp-to-cusp diameter (*D*) and the cusp-to-commissure convention (*E*); (*F*) measurement of the ascending aorta and the descending aorta with the double-oblique technique. AoR, aortic root; ASC, proximal ascending aorta.

Given the high incidence of atherosclerotic plaques/thrombi in the AA, the outer-to-outer convention should be preferred (also presenting the best agreement with CCT and CMR) (*Figure 6*).[141,142]

Regarding CCT and CMR, measurements must be performed using the inner-to-inner edge method (*Figure 6*) in end-diastole (fewer motion artefacts).[137,143,144]

The aortic root is measured in the parasternal long axis by transthoracic echocardiography (TTE),[137,139,140,145] since the short axis underestimates the diameter due to possible plane obliquity. By CMR or CCT, the cusp-to-cusp diameter best correlates with echocardiography (*Figure 6*). A diameter difference >5 mm (among root diameters within the same imaging modality) indicates root asymmetry, frequent in bicuspid aortic valve (BAV) or genetic aortopathies, which is important to be determined since it generates underestimations.[146] While 3D echocardiography is a potential surveillance alternative in these cases (especially if CMR/CCT is limited for serial follow-up), validation studies are lacking.[147]

In end-diastole, measure the ascending aorta by moving the transducer 1–2 intercostal spaces up in the parasternal long axis. Echocardiography provides information on aortic arch or DTA enlargement, but diagnostic certainty (precise measurement of the diameters) is lacking. CCT or CMR uses the double-oblique technique to measure aortic diameters, reporting antero-posterior and perpendicular dimensions for accurate assessment.[148] It is recommended to report aortic measurements by specific segments based on anatomical landmarks and to relate the largest diameter to a nearby anatomical structure for reference.

Changes in aortic diameter require a ≥3 mm increase in echocardiography, which should be confirmed with CCT/CMR and compared with baseline measurements. For accurate assessment, stick to the same imaging technique, centre, methodology, and side-by-side comparisons.[137,140]

5.4.2. Normal aortic values

When evaluating aortic dimensions and clinical relevance, consider factors like aortic region, anthropometric measurements, patient history, and underlying medical conditions. Factors influencing aortic and peripheral artery size in the normal population include age, sex, ethnicity, body surface area (BSA), and, particularly, height.[149]

Body surface area is the most used method to normalize aortic dimensions based on an individual's body size, thus an ascending thoracic aorta >22 mm/m^2 or a DTA >16 mm/m^2 is considered aortic dilatation.[150–152] However, extremes of low or high body weight pose limitations. In such cases, surgical thresholds may involve indexing aortic diameter by height (an aorta height index >32.1 mm/m is associated with a 12% yearly risk of aortic adverse events [AAE]),[153] aortic cross-sectional area to patient height (a ratio ≥10 cm^2/m implies reduced long-term survival),[154] or aortic length (from the aortic annulus to the innominate artery, considering a length >11 cm a threshold for surgery).[155]

To correlate measured diameter with the expected one based on age, sex, and body surface, use nomograms or z-score calculation formulas, especially in heritable thoracic aortic disease (HTAD). Supplementary data online, *Figure S1* and *Table S2*, presents nomograms developed for echocardiography, applicable also to CCT and CMR.[156,157] Calculation of z-scores can be performed following these links: https://www.marfan.fr/accueil/z-score-calculus/ or https://marfan.org/dx/z-score-adults/; reference values used for their estimation may vary depending on age and other factors. However, z-scores are limited by the fact that not all ethnic groups are equally represented (mostly white) and over- or underweight can lead to an over- or underestimation.[158]

Moreover, with ageing and loss of elastic properties, the aorta tends to enlarge. Aortic growth in adults is about 0.9 mm per 10 years in males and 0.7 mm per 10 years in females, which may be influenced by BP, physical activity, and genetic factors.

Recommendation Table 3 — Recommendations for imaging of the aorta (see also Evidence Table 2)

Recommendations	Class[a]	Level[b]
It is recommended that aortic diameters are measured at pre-specified anatomical landmarks, and the largest diameter of the section be perpendicular to the longitudinal axis.[134,135]	I	C
It is recommended in cases of serial imaging of the aorta over time to use the same imaging modality with the same measurement method.[159]	I	C
It is recommended to consider renal function, pregnancy, age, and history of allergy to contrast media to select the optimal imaging modality with minimal radiation exposure and lowest iatrogenic risk, except for emergency cases.[159–161]	I	C
Indexing aortic diameters to BSA, along with the use of nomograms, z-scores, or other indexing methods, should be considered for more accurate assessment of aortic size, especially for body sizes at the lower end of the normal distribution.[156–158]	IIa	B

BSA, body surface area.
[a]Class of recommendation.
[b]Level of evidence.

5.4.3. Chest X-ray and electrocardiogram

Chest X-ray obtained for other indications in asymptomatic patients or in cases of acute aortic syndrome (AAS) suspicion may detect abnormalities of aortic size/contour that need to be confirmed by another imaging technique. It presents limited sensitivity (64%) and specificity (86%) in the diagnosis of aortic diseases;[162] thus, a normal chest X-ray may not rule out the diagnosis of AAS.[162–164] On the contrary, chest X-ray may identify other causes of chest pain (e.g. pleural effusion or pneumothorax).

Electrocardiogram (ECG) might be useful to rule out other causes of chest pain (e.g. MI) or AAS complications (coronary occlusion/dissection) but it is not useful for AAS diagnosis.

5.4.4. Echocardiography

It is considered the first-line imaging technique in the evaluation of aortic disease, assessing all echocardiographic windows and the aortic valve. It provides key anatomic information (i.e. dilatation, atherosclerotic lesions, or dissection) for the ascending aorta, arch, and AA; however, it is not useful to assess the exact diameters of the aortic arch and DTA (requiring confirmation with CCT/CMR). Also, the distal ascending aorta and proximal arch (blind spot) are inadequately visualized due to left mainstem bronchus interposition.

Transthoracic echocardiography can identify AAS complications (e.g. aortic regurgitation, tamponade, or wall motion abnormalities), but its diagnostic accuracy for AAS is limited (sensitivity: 78%–100% for type A, 31%–55% for type B). Contrast enhancement improves diagnosis.[165]

Transoesophageal echocardiography (TOE) is highly accurate (sensitivity: up to 99%, specificity: 89% for AAS), except with absolute contraindications like oesophageal issues, bleeding, recent gastro-oesophageal surgery, or respiratory distress. TOE is convenient for bedside and intraoperative use but less suitable for long-term surveillance, which requires evaluation with CCT/CMR.

Recommendation Table 4 — Recommendations for thoracic aortic measurements

Recommendations	Class[a]	Level[b]
TTE is recommended as the first-line imaging technique in evaluating thoracic aortic diseases.[159,165]	I	B
It is recommended to report aortic diameters using the leading-to-leading edge convention in end-diastole by echocardiography.[137,139,140,159]	I	C
It is recommended to report aortic diameters using the inner-to-inner edge convention in end-diastole by CCT or CMR.[137,143,144,159]	I	C
It is recommended to report aortic diameters from images obtained with the double-oblique technique (not axial images) by CCT or CMR.[148]	I	C
ECG-triggered CCT is recommended for comprehensive diagnosis, follow-up, and pre-invasive treatment assessment of the entire aorta, particularly the root and ascending aorta.[159]	I	C
CMR is recommended for diagnosis and follow-up of thoracic aortic diseases, especially when chronic follow-up is required.[166–168]	I	C
The aortic root should be measured using the cusp-to-cusp distance. Also, the presence of asymmetry (>5 mm) among distances should be reported.[137,146]	IIa	C
If an increase of ≥3 mm per year in aortic diameters by TTE is observed, confirmation by CCT/CMR should be considered.[137,159]	IIa	C
Chest X-ray may be considered in cases of low clinical probability of AAS; however, a negative exploration should not delay dedicated aortic imaging in high-risk patients.[162–164]	IIb	C

AAS, acute aortic syndrome; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.

5.4.5. Duplex ultrasound imaging of the abdominal aorta

After scanning both transversally and longitudinally, the antero-posterior (AP) diameter in a cross-sectional view of the AA should be measured. Ensure the DUS beam is perpendicular to the AA axis, forming a circular vessel section. If the AA is sinuous or dilated, achieving equal AP and transverse diameters may be challenging. In such instances, calculate the mean ellipse diameter or measure the AA diameter in a clear longitudinal view with a perpendicular diameter (*Figure 6*).[122] The outer-to-outer (*Figure 6*) method is the one recommended by the American Institute of Ultrasound in Medicine, the American College of Cardiology/American Heart Association (ACC/AHA), and the European Society of Cardiology (ESC), since it is more reliable in cases of atherosclerotic plaque or intravascular thrombus and best correlates with CCT and CMR. However, the most effective methodology is under debate and further studies are needed to determine the best convention.[169]

Normal diameters of the AA are reported in *Figure 5* and Supplementary data online, *Section 1.3*.

5.4.6. Cardiovascular computed tomography

Cardiovascular computed tomography, due to its quick acquisition, wide availability, high reproducibility, and suitability for emergency departments, is the primary imaging method for aortic disease diagnosis, prognosis, and therapy planning (sensitivity 100%, specificity 98% for AAS).[170–172] 'Double or triple rule-out' protocols concurrently assess the aorta, pulmonary, and coronary arteries.[173,174]

Electrocardiogram triggering is crucial to prevent motion artefacts (especially in the aortic root and ascending aorta), which can distort measurements or resemble dissection flaps, facilitating coronary artery assessment. The standard protocol comprises non-enhanced scans (for calcification, IMH, or surgical material), contrast-enhanced CCT angiography, and a late scan (to visualize contrast leakage or aortic wall late enhancement suggestive of inflammation or infection).[175]

Iodinated contrast agents carry potential allergic reactions and post-contrast acute kidney injury (PC-AKI) risks.[176] In these cases, opt for contrast-free CCT for accurate aortic diameter measurement (also for CMR-intolerant patients). Moreover, excessive radiation caution is crucial, particularly in young females, when performing CCT for monitoring chronic aortic diseases.[177]

5.4.7. Cardiovascular magnetic resonance

Cardiovascular magnetic resonance comprehensively evaluates the aorta, including shape, diameter, tissue characteristics (inflammation, infection, atheroma, bleeding),[178] lesion extent, side branches, adjacent structures, and mural thrombus. It assesses ventricular and valve function, quantifies flow, and employs cine steady-state free precession (SSFP) or ECG-gated angio-CMR for the aortic root, while non-gated sequences suffice for the rest. Recently, 4D flow sequences[179] have been developed to evaluate complex intravascular flows,[180,181] complex flow parameters (wall shear stress, pulse wave velocity, or kinetic energy), or flow quantification at different levels in one unique acquisition (useful in AD or congenital diseases).[182,183]

Cardiovascular magnetic resonance obviates ionizing radiation and iodinated contrast (3D contrast CMR), making it ideal for young patients, women, and pregnancy. Caution is warranted, especially with non-macrocyclic gadolinium, for estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 (Supplementary data online, *Section 1.2*). CMR is increasingly used in patients with intracardiac devices (pacemakers/implantable cardioverter defibrillators, CMR- and non-CMR-compatible devices) with proper monitoring, but not for those with cochlear implants or intracranial clips.[184,185]

In the acute setting, CMR use is limited because of low availability, difficulties in monitoring unstable patients, and longer acquisition times.[166,186]

5.4.8. Positron emission tomography

Positron emission tomography (PET) usually uses ^{18}F-fluorodeoxyglucose (FDG), allowing non-invasive assessments of metabolic activity

(inflammation/infection) and treatment response.[187,188] Although different tracers have been tested to identify calcification, fibrosis and/or thrombus formation, most PET studies have focused on vasculitis.

The relationship between FDG-PET images and AAA progression is controversial. However, fluorine-18–sodium fluoride (^{18}F–NaF) PET-computed tomography (PET-CT), a marker of active vascular calcification and high-risk plaques, has shown a correlation between increased tracer uptake, AAA growth, and CV events.[189]

PET-CT has shown better diagnostic accuracy in identifying lesions and detecting graft infection or infectious aortic diseases.[190–193] High radiation exposure, high costs, and limited availability are the main limitations of PET.

5.4.9. Intravascular ultrasound

Intravascular ultrasound (IVUS) provides high-resolution imaging for artery and vein diseases, aiding complex aortic disease management by distinguishing true and false lumens and guiding stent placement. It is operator-dependent, costly, and less accessible, but seems to provide better measurements for acute aortic syndromes.[194]

5.4.10. Digital subtraction aortography

Non-invasive imaging modalities have replaced DSA in first-line diagnostic testing, both in suspected AAS or known chronic AD; however, DSA might be useful if findings in non-invasive techniques are ambiguous or incomplete. It is primarily used for the percutaneous treatment of CAD, aortic visceral branches, or for monitoring thoracic endovascular aortic aneurysm repair (TEVAR/EVAR) implantation.

6. Screening for carotid, peripheral arterial, and aortic diseases

6.1. Screening for carotid and peripheral arterial diseases

6.1.1. Lower-extremity peripheral arterial disease

Due to elevated CV risk in chronic PAD, early diagnosis, prevention, and robust cardiovascular risk factor (CVRF) control are essential, even in asymptomatic cases. 'Intermediary CV risk' individuals may be reclassified as 'high or very high risk', prompting adapted prevention. ABI is the preferred first-line test for asymptomatic individuals aged ≥65 years,[14,195] especially women.[196] Screening might also be beneficial at a younger age in case of CVRFs, but data are still lacking. Clinical examination, functional status, and walking capacity assessment are recommended to detect 'masked PAD'.[77]

In diabetes, early PAD (and foot neuropathy) diagnosis is crucial. Effective CVRF management and treatment can prevent CV disease, foot wounds, and amputation.[197] In patients with diabetes and normal resting ABI, TBI measurement should be considered.

The prevalence of popliteal aneurysms (PAs) is high in patients with AAA and subaneurysmal aortic dilatation, warranting screening. PAs are correlated with iliac and femoral artery diameters.[76] In patients needing transfemoral access, screening for iliofemoral artery disease may be considered.[198]

6.1.2. Carotid artery stenosis

Due to the low prevalence of ≥70% asymptomatic carotid artery stenosis (CS) in the general population (0%–3.1%), widespread screening is not recommended since it does not reduce stroke risk and might lead to inappropriate stress and invasive procedures.[199,200] Conversely, screening for significant CS in a highly selected population might be cost-effective, especially if prevalence is ≥20% (*Table 6*).[201] When the degree of asymptomatic CS is ≥70%, the 5 year ipsilateral stroke risk is significantly increased (14.6%) and revascularization may be beneficial.[202] Selective screening aims to prevent CV events, rather than identifying candidates for an intervention.[203]

Table 6 High-risk populations for carotid artery stenosis

Population	Prevalence of carotid stenosis (%)
>60 years + CVRFs (hypertension, CAD, current smoking, first-degree family history of stroke)[210]	Two CVRFs: 14% Three CVRFs: 16% Four CVRFs: 67%
Hypertension + cardiac disease[211]	22%
HD[212]	• In HD patients, prevalence of carotid stenosis is high, and is associated with high peri-operative and long-term stroke or death rates • Carotid stenosis is a predictor of death in patients with long-term dialysis and aged ≥70 years at time of surgery • Lower risk if previous renal transplant.
PAD[213]	23.2%
Severe CAD (before CABG)	• Almost 20%[214] • Carotid bruit and T2DM: increased predictive value[215] • Carotid stenosis = risk factors for peri-operative stroke.[215]
Carotid bruit[216]	31%
Previous neck irradiation[217]	21.7% (70%–99% stenosis)

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVRFs, cardiovascular risk factors; HD, haemodialysis; PAD, peripheral arterial disease; T2DM, type 2 diabetes mellitus.

6.1.3. Multisite artery disease

Multisite artery disease (MAD) is defined as the presence of atherosclerosis in two or more vascular beds.[204] This is a common condition in patients with atherosclerotic diseases. Although associated with worse clinical outcomes, screening for asymptomatic disease in additional vascular sites did not seem to improve outcomes.[77] More recently, screening for coronary calcifications (coronary artery calcium [CAC] score) and screening for carotid and femoral plaques have

been shown to be of potential assistance in CV risk reclassification of 'presumed moderate-risk patients' into a higher-risk category, leading to more aggressive prevention strategies.[205–209]

Recommendation Table 5 — Recommendations for peripheral arterial disease screening (see also Evidence Table 3)

Recommendations	Class[a]	Level[b]
In patients with diabetes or chronic kidney disease, and normal resting ABI, TBI measurement should be considered.	IIa	B
In patients ≥65 years of age with CVRFs, screening for PAD by ABI or TBI should be considered.[77,218,219]	IIa	C
In patients with AAA, femoro-popliteal aneurysm screening with DUS should be considered.[76]	IIa	C
In patients ≥65 years without CVRFs, screening for PAD by ABI or TBI may be considered.[220]	IIb	C
In patients needing intervention with transfemoral access, screening for iliofemoral artery disease may be considered.[198]	IIb	C
In patients with two or more CVRFs, screening for CS may be considered.[201,203,210]	IIb	C

AAA, abdominal aortic aneurysm; ABI, ankle–brachial index; CS, carotid artery stenosis; CVRFs, cardiovascular risk factors; DUS, duplex ultrasound; PAD, peripheral arterial disease; TBI, toe–brachial index.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 6 — Recommendations for abdominal aortic aneurysm screening

Recommendations	Class[a]	Level[b]
Screening for AAA with DUS:		
Is recommended in men aged ≥65 years with a history of smoking to reduce the risk of death from ruptured AAA.[221–224,234]	I	A
May be considered in men aged ≥75 years (irrespective of smoking history) or in women aged ≥75 years who are current smokers, hypertensive, or both.[227,228,235–237]	IIb	C
Family AAA screening with DUS:		
Is recommended for FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.[231]	I	C
Opportunistic AAA screening with DUS:		
Should be considered in symptomatic/asymptomatic PAD patients.[233]	IIa	B
Should be considered in men aged ≥65 years and in women aged ≥75 years during TTE.[232]	IIa	B

AAA, abdominal aortic aneurysm; FDR, first-degree relative; DUS, duplex ultrasound; PAD, peripheral arterial disease; TTE, transthoracic echocardiography.
Smoking is defined as lifetime smoking of >100 cigarettes or equivalent. This threshold is used to distinguish between substantial exposure and occasional use.
[a]Class of recommendation.
[b]Level of evidence.

6.2. Screening for aortic diseases

6.2.1. Screening for abdominal aortic aneurysm

Abdominal aortic aneurysm screening by DUS is effective in reducing rupture-related mortality in populations with high AAA prevalence (especially male smokers aged ≥65 years).[221–224] However, no such effect has been found in a single large study in which AAA prevalence was low (current or former smoking women aged 65–74 years, or with a history of CAD).[225]

Screening for AAA by non-contrast computed tomography (CT) was not found to be effective over 5 years in males aged 65–74 years in a Danish trial.[226] Longer-term follow-up is planned, and as the technique involves ionizing radiation, no recommendation is made in relation to CT at present.

Screening may be considered in populations at intermediate risk, such as men aged >75 years, or women aged >75 years who are hypertensive, smokers, or both, since almost all women in a contemporary population-based study who had ruptured AAA and were aged >75 years were either smokers or hypertensive.[227,228]

Screening for AAA is recommended in first-degree relatives (FDRs) of patients with AAA (especially siblings), as they are at increased risk of AAA when >50 years of age.[229] The risk associated with family history is uncertain, but a population-based study estimated a relative risk of around 2.[230] Screening should be repeated periodically if initial assessment is reassuring and performed at a relatively young age.[231]

Opportunistic screening (during TTE) identified AAA in about 2% of subjects, thus it may be considered in high-prevalence populations (males ≥65 or women ≥75 years of age).[232] Additionally, opportunistic screening detects AAA in patients with symptomatic/asymptomatic PAD (with a 12% cumulative incidence in symptomatic PAD), making it worthwhile in this population.[233]

6.2.2. Screening for thoracic aortic aneurysm

Screening for TAA is described in detail in *Section 10.1* and *Section 10.2*.

7. Optimal medical treatment

Optimal medical treatment (OMT), including lifestyle measures and pharmacological treatment, is recommended for all patients with PAAD (*Figure 7*).

7.1. Lifestyle, exercise, patient education

Apart from genetic-related TAA, hypertension and ASCVD are the main causative factors for PAAD. As lifestyle factors are strongly related to ASCVD,[11] patients with PAAD should strive to maintain a healthy lifestyle. The *2021 ESC Guidelines on cardiovascular prevention*[19] give comprehensive guidance on risk factors for ASCVD and their treatment.

7.1.1. Diet

A Mediterranean diet rich in legumes, dietary fibre, nuts, fruits, and vegetables proves crucial and efficacious for primary and CV prevention in PAAD.[238] It has demonstrated notable reductions in cholesterol and BP,[239–247] and holds potential protective benefits against PAAD development.[248,249] In a large cohort with 17.5 years of follow-up, adherence to a Mediterranean diet was associated with reduced AAA risk in current and ex-smokers.[249,250] Malnutrition and metabolic disorders can complicate post-invasive procedure recovery and nutritional support may improve nutritional status and HRQoL.[251]

7.1.2. Physical activity

Few patients with chronic symptomatic PAD meet the physical activity guidelines[252] for reducing the risk of major adverse cardiac events (MACE).[253,254] Better ambulation, HRQoL, and vascular outcomes have been observed in patients meeting the physical activity time-intensity guidelines.[19,255] Regular physical activity is also relevant in patients with aortic diseases[70,71,256–259] and lowers resting heart rate and BP, thus decreasing the risk of aortic complications.[256,259] Few data exist on the practice of exercise and sports in patients with aortic diseases.[70,71,256–259] Recommendations should be individualized and based on risk stratification.[71]

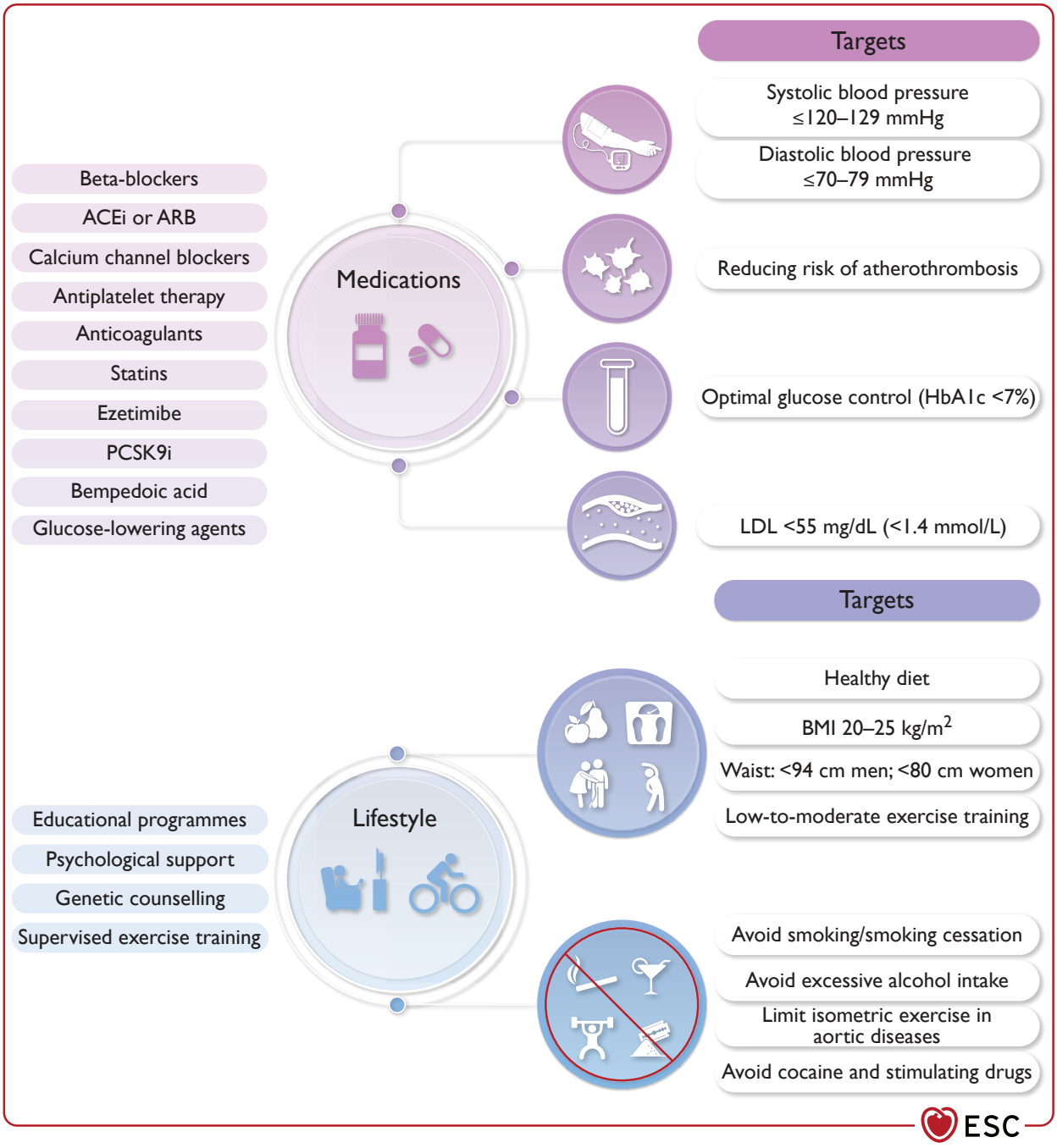

Figure 7 Cardiovascular risk modification and healthy lifestyle interventions and targets in patients with peripheral arterial and aortic diseases. ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BMI, body mass index; LDL, low-density lipoprotein; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; HbA1c, glycated haemoglobin.

7.1.3. Smoking

Patients with PAAD who smoke should strongly be advised to quit (see Supplementary data online, *Section 1.1.5*). Complete smoking cessation and avoiding second-hand smoke or environmental particle air pollution are crucial in patients with PAAD to reduce the risk of death, AD, acute mesenteric ischaemia (AMI), AAA, and PAD.[119,260–267] Smokers should be offered structural follow-up support, including nicotine replacement therapy, varenicline, and bupropion, individually or in combination.[19,268,269] Smoking avoidance also includes cannabis, associated with premature ASCVD.[266]

Vaping and e-cigarette use has surged in the past decade, viewed by some as a healthier option than smoked tobacco, though long-term health effects remain unknown.[270] E-cigarettes may be considered as an aid to quit tobacco smoking, as a recent Cochrane review found that they increase quit rates as compared with nicotine replacement therapy,[271] but their use has been associated with adverse effects on CV, respiratory, immunological, and periodontal health compared with non-users, but with a milder impact than smoked cigarettes.[272–274] However, their use should be brief and preferably not concurrent with traditional cigarettes.[271,275]

The main limitation of the evidence base remains imprecision due to the small number of randomized controlled trials (RCTs), often with low event rates and follow-up limited to 2 years.

7.1.4. Patient education

While detailed explanations of CVRFs might not always inspire lifestyle changes,[276] providing plain language and visual aids is essential for patient understanding.[277] Structured programmes, incorporating psychological and behavioural aspects, are pivotal in fostering desired changes.[276] Engaging patients' families, friends, and support networks significantly contributes to perpetuating these changes (particularly in self-care),[276] and increases treatment compliance and self-efficacy, reducing hospitalization risk and enriching patient HRQoL.[278,279] When caregivers disconnect from healthcare professionals, they should be recognised to receive better support systems.[280,281] Psychosocial interventions are crucial to navigating complexities with resilience.[282]

Advocating active involvement, education, clear communication, and shared decision-making is key for achieving optimal patient outcomes.[276–283]

7.1.5. Risk scoring models in secondary prevention

Recent ESC CV prevention guidelines discuss risk models for developing vascular disease in healthy individuals and ASCVD patients.[19] Several registries enabling risk prediction in ASCVD have been developed: REACH (The REduction of Atherothrombosis for Continued Health)[284] and SMART (Secondary Manifestation of ARTerial disease)[285] which use clinical parameters such as medical history, SBP, and common biomarkers. Addition of carotid ultrasound did not improve the model.[286] A new algorithm combining the SMART and REACH models[287] enables calculation of lifetime risk and treatment effects. The SMART model has recently been updated and validated[288,289] with the SMART-2 algorithm. These tools are available online as clinical risk calculators (see www.u-preveotnt.com) and smartphone apps on the ESC website (https://www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/SMART-Risk-Score).

Recommendation Table 7 — Recommendations for lifestyle, physical activity, and patient education (see also Evidence Table 4)

Recommendations	Class[a]	Level[b]
In patients with PAAD, cessation and abstinence from smoking of any kind is recommended to reduce the risk of AD, MI, death, and limb ischaemia.[119,261–267]	I	A
A healthy diet rich in legumes, dietary fibre, nuts, fruits, and vegetables, with a high flavonoid intake (Mediterranean diet), is recommended for CV disease prevention in patients with PAAD.[239–241,249,290–293]	I	A
Low- to moderate-intensity (or high if tolerated)[c] aerobic activities are recommended in patients with PAD to increase overall and pain-free walking distance.[37,294]	I	A
In patients with PAAD, behavioural counselling to promote healthy diet, smoking cessation, and physical activity is recommended to improve the CV risk profile.[241,249,253,295]	I	B
It is recommended to promote patient and caregivers' education and empowerment through tailored guidance on lifestyle adjustments and the importance of regular physical activity.[276,277,283]	I	C
In patients with PAAD, avoidance of exposure to second-hand smoke and air pollution should be considered.[261]	IIa	C
Physical exercise and sports activities should be considered in patients with aortic diseases based on prior risk stratification (based on the extent of the aneurysm, risk of dissection, and BP control).[71]	IIa	C
Use of web- or app-based secondary prevention risk calculators should be considered in the shared decision-making to improve patient adherence to treatment and lifestyle changes.[288,289]	IIa	C
E-cigarettes may be considered as an aid to quit tobacco smoking, but it is advisable to limit their use and avoid simultaneous use with conventional cigarettes due to unknown long-term effects.[119,271,296,297]	IIb	C

AD, aortic dissection; BP, blood pressure; CV, cardiovascular; MI, myocardial infarction; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]Low intensity refers to an exercising heart rate (HR) of 57%–63% HRmax or a rate of perceived exertion (RPE) on the Borg's scale of 9–11. Moderate intensity refers to an exercising heart rate of 64%–76% HRmax or RPE of 12–13. Vigorous intensity refers to an exercising heart rate of 77%–95% HRmax or RPE of 14–17.[298]

7.2. Principles of pharmacological medical therapy

7.2.1. Antithrombotic therapy

Antithrombotic therapy is crucial for patients with symptomatic PAAD at high CV risk. While trials are fewer than in CAD, recent evidence should guide practice. In the absence of specific indications for chronic oral anticoagulation (OAC) in concomitant CV disease, a single antiplatelet agent is the primary long-term treatment for patients with symptomatic PAAD. Combining it with another antiplatelet agent or low-dose anticoagulants depends on the patient's ischaemic and bleeding risk, as well as therapeutic paths (e.g. endovascular therapy). Recent guidelines[299] propose a tool for bleeding risk assessment in PAD patients (OAC[3] PAD score).

Antithrombotic strategy is detailed in *Sections 8* and *9* for each arterial territory.

7.2.2. Antihypertensive therapy

New 2024 ESC Guidelines on hypertension are currently published and should be reviewed for further details.[300] Patients with hypertension and PAAD are considered to have target organ damage and are at high CV risk.[300]

Different meta-analyses showed that systolic BP treatments reduce CV risk in all ages up to 85 years down to a level of 120–129 mmHg.[301,302] There is no need to increase the BP target in healthy patients up to the age of 85 years.[303,304] To reduce cardiovascular disease (CVD) risk, it is recommended that treated SBP values in most adults be targeted to 120–129 mmHg, provided the treatment is well tolerated. However, in cases where BP-lowering treatment is poorly tolerated and achieving an SBP of 120–129 mmHg is not possible, it is recommended to target an SBP level that is 'as low as reasonably achievable' (ALARA principle).[301,302,305] To avoid overtreatment, out-of-office BP measurements may be helpful when pursuing this target.

If on-treatment SBP is on target, but diastolic blood pressure (DBP) is ≥80 mmHg, intensified treatment may be considered to further reduce the CV risk.[306]

Because the CVD benefit of an on-treatment BP target of 120–129 mmHg may not generalize to some groups, setting personalized and more lenient BP targets (e.g. <140/90 mmHg) has to be considered in patients with pre-treatment orthostatic hypotension, age ≥85 years, clinically significant frailty at any age, or a limited lifespan (<3 years).[301]

Patients with both PAAD and hypertension face a high or very high CV risk. Antihypertensive medications such as diuretics, beta-blockers (BBs), calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) are all appropriate options for managing hypertension in PAAD. These agents can be used as monotherapy or in various combinations (excluding ARBs+ACEIs), considering individual patients' conditions. It is often necessary to implement combination therapy, preferably in the form of a single pill, to effectively achieve the recommended treatment goals. However, ACEIs or ARBs should be considered as first-line antihypertensive therapy to reduce CV events.[300,307–312]

Regardless of BP levels and in the absence of contraindications, ACEIs/ARBs may be considered in all patients with PAD to reduce cardiovascular events.[312,313] A meta-analysis suggests that antihypertensive treatment may improve mean walking distance in patients with PAD.[310]

Beta-blockers can be prescribed, if necessary, to patients with intermittent claudication, since they do not worsen walking capacity or limb events.[314] There is some evidence suggesting a higher amputation rate[315] or increased rate of re-intervention[316] in patients with CLTI treated with ACEIs, although in one smaller study no effect on limb-related outcomes was observed.[317] Thus, they remain a treatment option in hypertensive patients with PAD, especially in those with concomitant CAD.[318] BBs were not associated with worsened clinical outcomes in a retrospective study[319] on CLTI patients, but it seems prudent to avoid excessively low heart rates in these patients.

7.2.2.1. Renovascular hypertension

Angiotensin-converting enzyme inhibitors and ARBs effectively manage unilateral renal artery stenosis (RAS) by blocking the renin–angiotensin system, potentially reducing renal capillary perfusion pressure.[320–322] This transiently lowers glomerular filtration rate (GFR) and raises serum creatinine. For bilateral RAS, regular follow-up assessments of renal function and kidney perfusion are advised.

Angiotensin-converting enzyme inhibitors and ARBs additionally (combined with hydrochlorothiazide and/or CCBs if needed) contribute to CV risk reduction in patients with atherosclerotic disease and reduced eGFR.[307,323,324]

Recommendation Table 8 — Recommendations for antihypertensive therapy in patients with peripheral and aortic disease

Recommendations	Class[a]	Level[b]
In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.[301–305,325]	I	A
In unilateral RAS patients, it is recommended that antihypertensive medication include ACEIs/ARBs.[307,320–323]	I	B
In patients with PAAD and hypertension, ACEIs or ARBs should be considered as first-line antihypertensive therapy.[307,312]	IIa	B
In RAS-related hypertension, the combination of ACEIs/ARBs with diuretics and/or calcium channel blockers should be considered.[324]	IIa	B
An individualized, more lenient BP goal (e.g. <140/90 mmHg) should be considered in:[301] • Age ≥85 years • Residential care • Symptomatic orthostatic hypotension	IIa	C
An individualized, more lenient BP goal (e.g. <140/90 mmHg) may be considered in:[301] • Clinically severe frailty at any age • Limited life expectancy (<3 years)	IIb	C
In patients with bilateral RAS, antihypertensive medication including ACEIs/ARBs may be considered if close patient monitoring (renal function) is feasible.[321]	IIb	B
ACEIs/ARBs may be considered in all patients with PAD, regardless of BP levels, in the absence of contraindications.[312,313]	IIb	B

Continued

In cases where on-treatment SBP is at or below target (120–129 mmHg) but DBP is not at target (≥80 mmHg), intensifying BP-lowering treatment to achieve an on-treatment DBP of 70–79 mmHg may be considered to reduce CVD risk.[306]	IIb	C

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; RAS, renal artery stenosis; SBP, systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.

7.2.3. Lipid-lowering therapy

Patients with symptomatic PAAD are at very high CV risk but are usually inadequately managed compared with patients with CAD.[5,247,326–332] Both LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended to obtain a reduction in CV death, MI, and stroke, and to improve walking distance.[242,333–336]

7.2.3.1. Statins

Statins demonstrate mortality and CV event reduction in RCTs for PAD, CS, and severe aortic arch plaques.[243–245] Even in advanced disease stages, they are linked to lower MACE and mortality.[246]

Statins significantly improve CV outcomes in patients with PAD, reducing major adverse limb events (MALE).[244,327–329,337,338] Meta-analyses show enhanced walking distances.[244,338,339]

For CS, statin pre-treatment lowers recurrent stroke risk post-transient ischaemic attack (TIA).[19,340–343] While lacking RCTs in renovascular or visceral artery disease, statins benefit cardiorenal events and post-RAS stenting prognosis.[344–346]

Mixed evidence suggests statins may mitigate AAA and TAA growth.[347–352] However, since most patients with AAA or TAA present with associated CVRFs, liberal use of lipid-lowering treatment[19] should be considered, using an individualized approach with shared decision-making and considering residual CV risk.[353] Pre-operative statin use links to increased 5 year survival after TEVAR.[19]

Statin use was associated with a mean AAA growth rate reduction and a lower rupture risk.[347–349,352,354]

Some evidence suggests that statins may reduce TAA growth rate and risk of rupture.[350,351,355]

No benefit on AAA or TAA growth rate was shown with fenofibrate therapy.[356,357]

7.2.3.2. Ezetimibe

Ezetimibe combined with statins benefits selected patients with PAAD, particularly when the target LDL-C level is not met.[335] In an IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) subanalysis, involving acute coronary syndrome (ACS) patients with PAD, ezetimibe consistently reduced CV risk, especially in high-risk subgroups.[247,331]

7.2.3.3. Proprotein convertase subtilisin/kexin type 9 inhibitors

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, in addition to statins, reduce CV events in symptomatic atherosclerotic disease patients with LDL-C ≥1.8 mmol/L.[336] Adding them to statins further reduces MACE and MALE risk in patients with PAD and improves walking distance;[333] however, their potential in TAA/AAA is an emerging area of research.[247]

Inclisiran, administered semi-annually, has proved a notable 26% MACE risk reduction in a pooled phase III analysis,[358] but its role in PAAD is not firmly established and ongoing RCTs including PAD participants (e.g. ClinicalTrials.gov NCT05030428) aim to provide insights.

7.2.3.4. Bempedoic acid

Bempedoic acid, acting upstream of statins in cholesterol metabolism, has been shown to reduce cholesterol levels by 17%–28%[359,360] and demonstrated a decrease in the incidence of MACE in statin-intolerant PAD patients.[361] However, its impact on aortic diseases and AAA still requires further research.

7.2.3.5. Hypertriglyceridaemia

Beyond LDL-C, evidence shows insulin resistance, elevated triglycerides, and remnant lipoproteins are associated with ASCVD, particularly in PAD.[362–365] However, in a meta-analysis and an RCT, fibrates showed no benefit over placebo in reducing MACE in patients with PAD for a composite outcome of non-fatal stroke, non-fatal MI, and vascular death.[366] Fibrates showed no benefit over placebo in reducing coronary and cerebrovascular events in patients with PAD in an RCT.[367] While the relationship between triglycerides and aortic diseases is complex and not fully understood, some evidence suggests that triglyceride levels may contribute to the development and progression of aortic diseases.

In contrast, icosapent ethyl (IPE) demonstrated a reduction in mortality and morbidity among individuals with hypertriglyceridaemia in the Reduction of Cardiovascular Events With Icosapent Ethyl–Intervention Trial (REDUCE-IT).[368] Its impact on patients with PAAD is unexplored,[369] although a small pilot RCT suggested an improved ABI in hyperglycaemic haemodialysis patients.[370]

Recommendation Table 9 — Recommendations for lipid-lowering therapy in patients with peripheral arterial and aortic diseases

Recommendations	Class[a]	Level[b]
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.[242,334–336]	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.[19,242,246,300,335]	I	A
Statins are recommended in all patients with PAD.[328,329,337,371]	I	A
If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.[372,373]	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.[247]	I	B
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.[361]	I	B
Statins for the reduction of growth and rupture of AAA should be considered.[347–349,352,354]	IIa	B

Continued

Statins for the reduction of growth and rupture of TAA may be considered.[350,351,355]	IIb	B
In high-risk patients with PAAD and triglycerides >1.5 mmol/L despite lifestyle measures and statin therapy, icosapent ethyl 2 g b.i.d. may be considered in addition to a statin.[368]	IIb	B
Fibrates are not recommended for cholesterol lowering.[367]	III	B

AAA, abdominal aortic aneurysm; b.i.d., twice daily; CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PCSK9, proprotein convertase subtilisin/kexin type 9; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.

7.2.4. Diabetes and pre-diabetes conditions

Screening for diabetes or pre-diabetes is recommended in PAAD. Recent ESC Guidelines on diabetes and CVD[374] provide detailed diagnostic criteria and underscore the importance of diagnosing diabetes in ASCVD patients and vice versa. Both Type 1 (T1DM) and Type 2 (T2DM) diabetes mellitus imply significantly increased risk of PAD, carotid stenosis, and polyvascular disease, depending on disease duration and the status of other CVRFs. Diabetes is present in 30% of patients with IC and 50%–70% of those with CLTI.[375,376] Although the prevalence of PAD in patients with diabetes is 20%–30%, only half of them are symptomatic because of peripheral neuropathy with decreased pain sensitivity.[377] As already detailed in *Section 4*, diabetes implies reduced risk of TAA, AAA, or aortic dissection. However, patients with T2DM and PAAD are in the very high-risk group for stroke, MI, and CV death,[374] and for T1DM, an online risk prediction tool has recently been developed.[377–380]

For non-pregnant PAAD patients, aiming for an HbA1c level of <53 mmol/mol (7%) to avoid significant hypoglycaemia is appropriate. Consider a higher threshold (<69 mmol/mol [8.5%]) for limited life expectancy or when treatment risks outweigh benefits.[374]

In PAAD, it is recommended to aim for tight glycaemic control, preferably with agents with proven CV benefits such as sodium-glucose co-transporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA), adding metformin and other glucose-lowering agents as necessary.[374,381–384]

The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial and Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN-6) investigated subcutaneous GLP-1RAs liraglutide (≤1.8 mg/day) and semaglutide (0.5 or 1.0 mg/week), respectively, vs. placebo in T2DM patients with high CV risk. Overall, 12.7% of patients in LEADER and 14.0% in SUSTAIN-6 presented with PAD at baseline. Although non-statistically significant due to a lack of power, the effects on MACE showed a consistently beneficial trend in PAD: liraglutide (hazard ratio (HR), 0.77; 95% confidence interval (CI), 0.58–1.01) and semaglutide (HR, 0.61; 95% CI, 0.33–1.13).[381]

The (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) investigated the SGLT2i empagliflozin (10 mg or 25 mg per day) vs. placebo in patients with T2DM and high CV risk. Overall, 20.8% of patients presented with PAD at baseline. In these patients, empagliflozin reduced CV death (HR, 0.57; 95% CI, 0.37–0.88) and all-cause mortality (HR, 0.62; 95% CI, 0.44–0.88), and there was a non-significant reduction in limb amputation: 5.5% with empagliflozin vs. 6.3% with placebo (HR, 0.84; 95% CI, 0.54–1.32).[382] In the Canagliflozin Cardiovascular Assessment Study (CANVAS)[385] investigating canagliflozin, there was an increased risk of amputation, but this was not confirmed in the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial investigating canagliflozin in patients with T2DM and chronic kidney disease (CKD).[386] Still, the use of other SLGT2is seems reasonable in PAD patients.

Patients with carotid stenosis were included in trials testing GLP-1RA and SGLT2i, but no analysis on this subpopulation was performed. A meta-analysis of eight trials investigating GLP-1RAs vs. placebo in patients with T2DM reported a reduction in all strokes (HR, 0.84; 95% CI, 0.75–0.93).[387] Among patients with T2DM and prior history of MI or non-fatal stroke, GLP-1RAs reduced the incidence of recurrent MACE (HR, 0.86; 95% CI, 0.8–0.92).[388] SGLT2is do not appear to reduce stroke in patients with T2DM, but patients with a stroke history experienced similar cardiorenal benefits as the rest of the population.[389]

Before the era of GLP-1RAs and SGLT2is, different studies (United Kingdom Prospective Diabetes Study [UKPDS] 34[390] and Hyperinsulinaemia: the Outcomes of its Metabolic Effects [HOME] trials[391]) showed that metformin reduced the risk of MALE and MACE in patients with PAD.[391,392] But a recent study with GLP-1RA dulaglutide found the same risk reduction in MACE between patients with and without baseline metformin, calling into question its add-on value.[384,393] However, there are studies suggesting that metformin may reduce AAA growth (see *Section 9.2.4*).

Recommendation Table 10 — Recommendations for the medical management of patients with peripheral arterial and aortic diseases and diabetes

Recommendations	Class[a]	Level[b]
It is recommended to apply tight glycaemic control (HbA1c <53 mmol/mol [7%]) to reduce microvascular complications in patients with PAAD.[374,394–397]	I	A
SGLT2i with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.[382,386,398–402]	I	A
GLP-1RAs with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.[381,403–407]	I	A
It is recommended to avoid hypoglycaemia in patients with PAAD.[374,408–412]	I	B
It is recommended to individualize HbA1c targets according to comorbidities, diabetes duration, and life expectancy.[408,411]	I	C
It is recommended to prioritize the use of glucose-lowering agents with proven CV benefits,[c,d] followed by agents with proven CV safety,[e] over agents without proven CV benefit or safety.[374]	I	C
If additional glucose control is needed, metformin should be considered in patients with T2DM and PAAD.[374,384,393]	IIa	B

CV, cardiovascular; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HbA1c, glycated haemoglobin; PAAD, peripheral arterial and aortic diseases; SGLT2i, sodium-glucose co-transporter-2 inhibitors; T2DM, type 2 diabetes mellitus.
[a]Class of recommendation.
[b]Level of evidence.
[c]Empagliflozin, canagliflozin, dapagliflozin, sotagliflozin.
[d]Liraglutide, semaglutide subcutaneous, dulaglutide, efpeglenatide.
[e]Metformin, pioglitazone, dipeptidyl peptidase 4 (DPP-4) inhibitor (sitagliptin, alogliptin, linagliptin), glimepiride, gliclazide, insulin glargine, insulin degludec, ertugliflozin, lixisenatide, exenatide (extended release), oral semaglutide.

7.2.5. Other pharmacological therapy

Increased attention is focused on inflammation in ASCVD,[413] supported by the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS),[414] which showed that canakinumab, a monoclonal antibody targeting interleukin (IL)-1β, reduced MACE in high-risk patients with previous MI and increased high-sensitivity (hs)-CRP. Data for patients with PAAD are not reported. Furthermore, low-dose colchicine (0.5 mg/day) has been shown to reduce MACE among those with stable atherosclerosis after recent MI.[415] However, the effect of colchicine and other anti-inflammatory drugs in PAAD remains unproven.[416]

8. Peripheral arterial disease

8.1. Lower-extremity peripheral arterial disease

8.1.1. Peripheral arterial disease syndromes

8.1.1.1. Clinical presentation and diagnosis

Atheromatous lower-extremity PAD is a chronic disease with different clinical manifestations. PAD may be symptomatic or asymptomatic and may or may not be associated with limb wounds. Wound healing and amputation risk may be affected by the concomitant presence of PAD, diabetes, and/or infection;[417] therefore, amputation risk assessment should be systematically performed using the Wound, Ischaemia, and foot Infection (WIfI) classification.

PAD presents as:

- Asymptomatic PAD: suspected by lower-limb pulse abolition or imaging studies performed for other purposes and detected by pathological ABI or TBI.[418,419] These patients do not present with IC or atypical effort-related symptoms. However, attention should be paid to those with wounds, with masked effort-related symptoms due to reduced walking capacity (for reasons other than PAD), or reduced pain sensitivity. 'Masked PAD' is defined as PAD without provoked leg pain because of reduced walking capacity for other reasons or reduced pain sensitivity.[420]
- Symptomatic (effort-related) PAD: patients with pathological ABI or TBI, presenting with IC, atypical effort-related symptoms, or chronic lower-limb wounds (diabetic foot or non-healing ulceration/gangrene ≥2 weeks) without critically reduced limb perfusion.[417,421] In these patients, IC is characterized by exertional muscle pain and dysfunction in the supply area of the obstructed arterial segment, which is relieved at rest.[422] Some patients may present with atypical symptoms or with 'masked PAD'.[420,423] In women, the prevalence of IC is lower than in men, while atypical symptoms are more common.[424]
- CLTI represents the more severe chronic PAD presentation and underlies poor limb outcomes without intervention. In addition to common signs of chronic PAD, patients with CLTI present with a critical haemodynamic status (ankle pressure <50 mmHg, toe pressure [TP] <30 mmHg, or $TcPO_2$ <30 mmHg) responsible for ischaemic rest pain, non-healing chronic (>2 weeks of duration) ulceration, or foot gangrene.[425,426]

PAD syndromes can be categorized according to their clinical presentation (*Table 7*).

The 5 year cumulative incidence of clinical deterioration from asymptomatic PAD to IC is 7%, and 21% from IC to CLTI.[427] All patients with PAD are at high risk of MACE, cerebrovascular disease, and MALE (*Figure 8*).[428–430] The 5 year cumulative incidence of CV mortality is 9% in asymptomatic PAD and 13% in symptomatic patients. In comparison with symptomatic PAD, CLTI further increases all-cause mortality risk (relative risk [RR] 2.26) and the risk of MACE (RR 1.73).[431] Health insurance data reveal a major amputation rate of 9% in patients with CLTI and 1% in patients with IC, while considerably higher amputation rates were reported in trials and registries data focusing on patients with CLTI.[432–435] Among patients with PAD, development of MALE is associated with poor prognosis, with a three-fold increase in death and a 200-fold increase in subsequent lower-extremity amputation.[429]

Prevention of MALE is crucial, and the risk of MACE/MALE increases with the increased number of arterial beds involved.

Table 7 Peripheral arterial disease categorized according to clinical presentation

Clinical characteristics of PAD	Rutherford classification		Fontaine classification	
	Category	Signs and symptoms	Stage	Signs and symptoms
Asymptomatic PAD	**0**	Asymptomatic	**I**	Asymptomatic
Symptomatic (effort-related) PAD	**1**	Mild claudication	**IIa**	Non-disabling intermittent claudication
	2	Moderate claudication	**IIb**	Disabling intermittent claudication
	3	Severe claudication		
Chronic limb-threatening Ischaemia	**4**	Ischaemic rest pain	**III**	Ischaemic rest pain
	5	Minor tissue loss	**IV**	Ischaemic ulceration or gangrene
	6	Major tissue loss		

PAD, peripheral arterial disease.

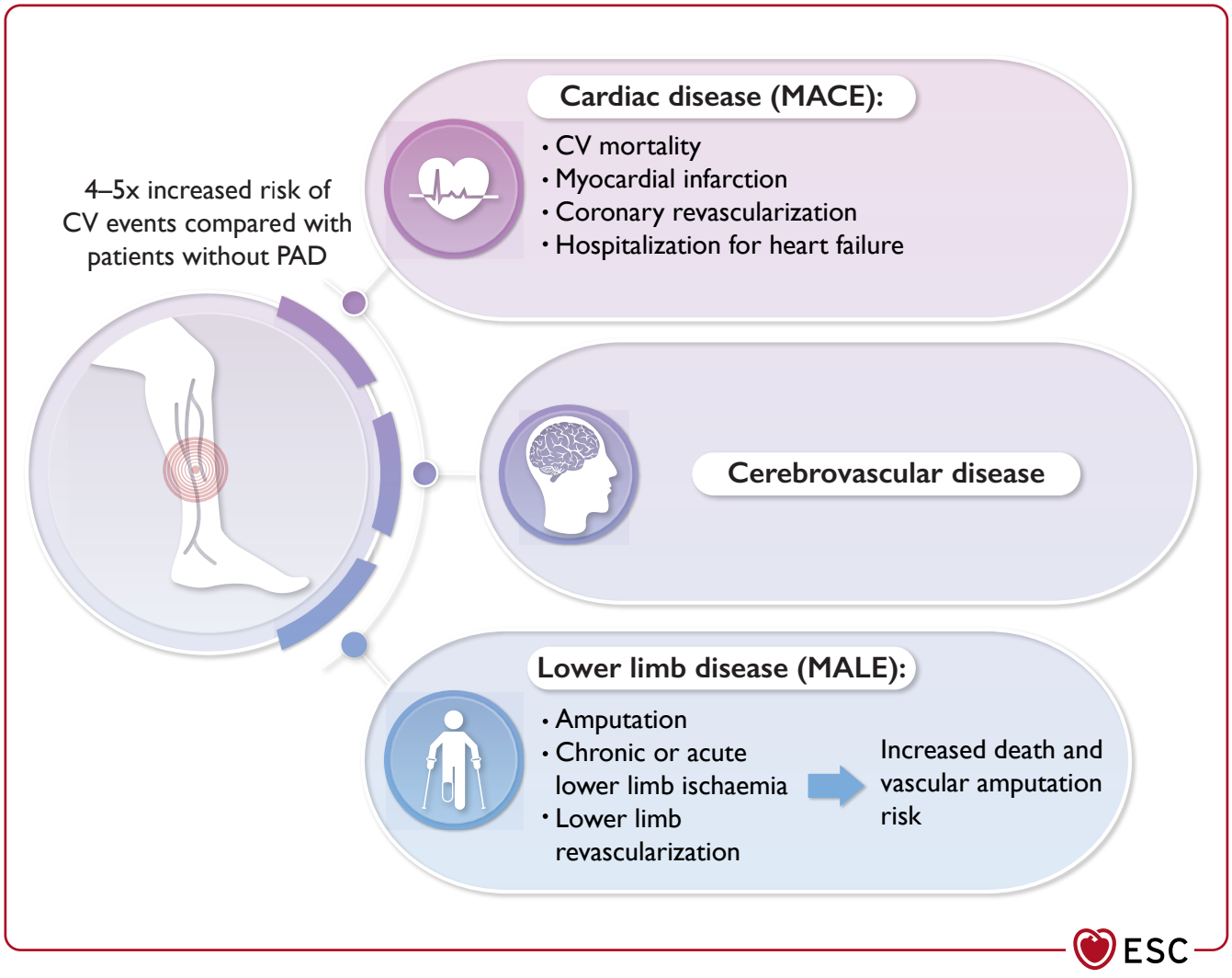

Figure 8 Cardiovascular risk in patients with peripheral arterial disease. CV, cardiovascular; MACE, major adverse cardiac event; MALE, major adverse limb event; PAD, peripheral arterial disease.

8.1.1.1.1. Diagnostic tests. Vascular assessment: ABI, TBI, $TcPO_2$ measurements (refer to *Section 5.3*)

Ankle–brachial index is the proposed initial non-invasive diagnostic test to confirm lower-limb decreased perfusion status[90,436,437] and needs to be reported separately for each leg (see Recommendation Table 2). An ABI ≤0.90 confirms PAD diagnosis.[90,436,437] In cases of an ABI >0.90 and clinical suspicion of PAD, post-exercise ABI measurements should be considered, along with imaging studies (preferably by treadmill). A post-exercise ABI decrease of >20% may serve as a PAD diagnostic criterion.[438,439]

In cases of abnormally high ABI values (ABI >1.4; see Recommendation Table 2) and patients with CLTI and diabetes[440] (see Recommendation Table 11), TP measurements, the calculation of TBI and $TcPO_2$, as well as pulse volume recordings or analysis of distal arterial Doppler waveforms, should be considered,[90,91,132,133,441] and ABI can be estimated from distal Doppler waveforms independent of diabetes and media sclerosis.[124]

Apart from the assessment of limb perfusion, ABI serves as a surrogate marker for CV and all-cause mortality.[88,442,443] A diagnostic PAD algorithm is depicted in *Figure 9*.

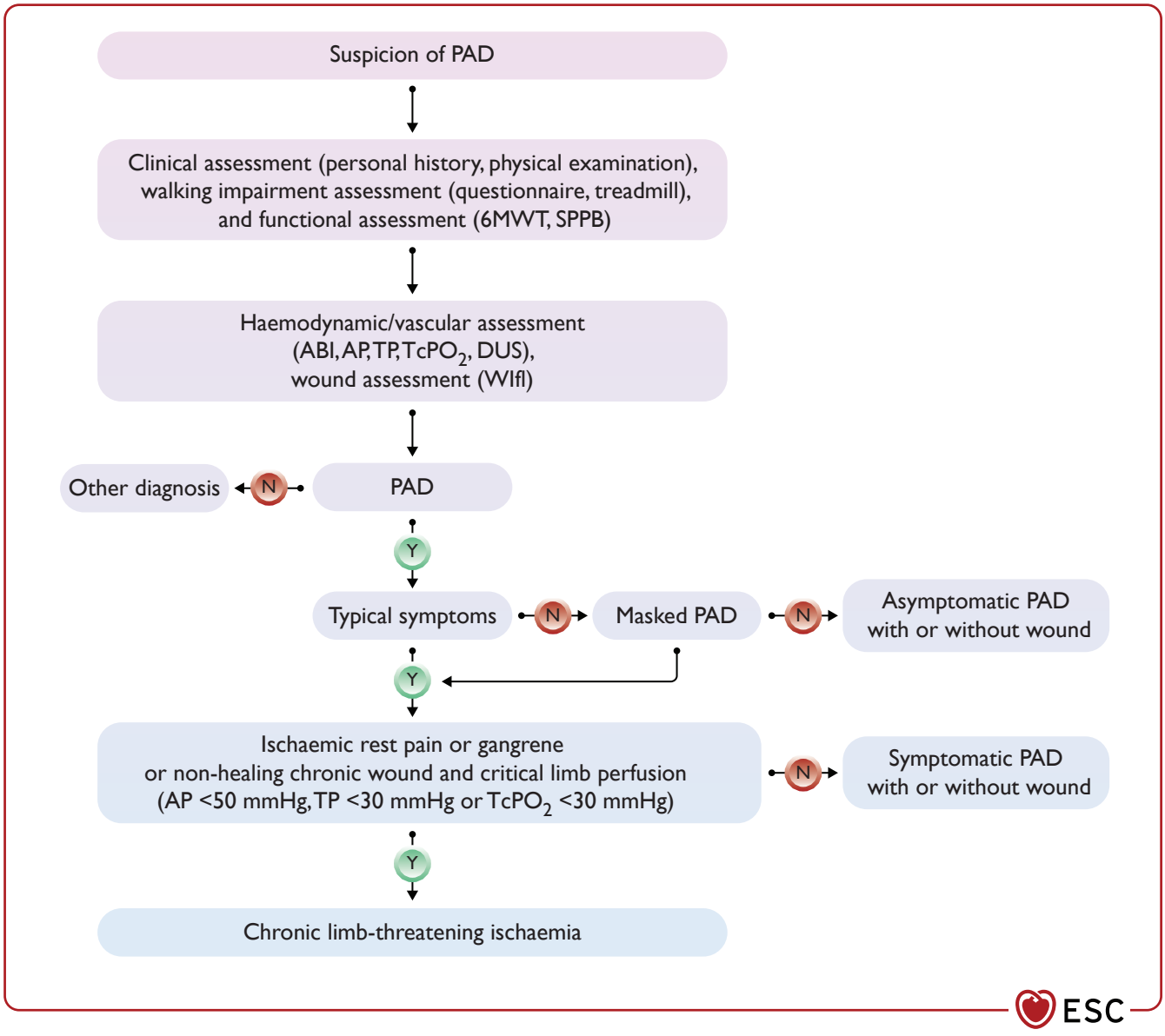

Figure 9 Diagnostic algorithm for peripheral arterial disease. 6MWT, six-minute walk test; ABI, ankle–brachial index; AP, ankle pressure; DUS, duplex ultrasound; PAD, peripheral arterial disease; SPPB, short physical performance battery; $TcPO_2$, transcutaneous oxygen pressure; TP, toe pressure; WIfI, Wound, Ischaemia, and foot Infection classification.

Walking impairment questionnaires, assessment of functional and walking capacity

Determining walking impairment, capacity, and functional status in all patients with PAD is mandatory (refer to *Section 5.2*).

Assessment of amputation risk

In patients with PAD and chronic lower-limb wounds (diabetic foot ulcer, non-healing lower-limb ulceration, or gangrene of ≥2 weeks of duration), even without haemodynamic parameters of critical limb perfusion, the additional presence of comorbidities such as diabetes and/or wound infection may contribute to an increased risk of amputation. The WIfI classification system takes the patients' limb perfusion, wound size, and the extent of foot infection into account to determine the amputation risk (*Table 8*).[417,444–446]

8.1.1.1.2. Imaging methods. Duplex ultrasound is recommended as the first-line imaging method for PAD screening and diagnosis. CTA and/or MRA are recommended as adjuvant imaging. For details refer to Supplementary data online, *Section 1.4*.

Table 8 Assessment of the risk of amputation: the Wound, Ischaemia, and foot Infection classification

Component	Score	Description		
W (Wound)	0	No ulcer (ischaemic rest pain)		
	1	Small, shallow ulcer on distal leg or foot without gangrene		
	2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes		
	3	Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene		
I (Ischaemia)		ABI	Ankle pressure (mmHg)	Toe pressure or $TcPO_2$
	0	≥0.80	>100	≥60
	1	0.60–0.79	70–100	40–59
	2	0.40–0.59	50–70	30–39
	3	<0.40	<50	<30
fI (foot infection)	0	No symptoms/signs of infection		
	1	Local infection involving only skin and subcutaneous tissue		
	2	Local infection involving deeper than skin/subcutaneous tissue		
	3	Systemic inflammatory response syndrome		

	Ischaemia – 0				Ischaemia – 1				Ischaemia – 2				Ischaemia – 3			
W–0	VL	VL	VL	VL	VL	L	L	M	L	L	M	M	M	H	H	H
W–1	VL	VL	VL	VL	L	M	M	M	M	H	H	H	H	H	H	H
W–2	VL	VL	VL	VL	M	M	H	H	H	H	H	H	H	H	H	H
W–3	VL	VL	VL	VL	M	M	M	H	H	H	H	H	H	H	H	H
	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3

Very low (green) = VL = clinical stage 1; low (yellow) = L = clinical stage 2; moderate (orange) = M = clinical stage 3; high (red) = H = clinical stage 4.
ABI, ankle–brachial index; $TcPO_2$, transcutaneous oxygen pressure.
The **W**ound, **I**schaemia and foot **I**nfection (WIfI) classification allows the assessment of the individual risk of amputation in PAD patients: it comprises scores for wound size (**W**), degree of ischaemia (**I**), as assessed by the ABI, ankle pressure, and toe pressure or $TcPO_2$, and extent of foot infection (**fI**) as depicted in the respective table. The combination of all three components results in the amputation risk stratification (***VL*** = very low, ***L*** = low, ***M*** = moderate, ***H*** = high). Table reproduced with permission from.[417]

Recommendation Table 11 — Recommendations for diagnostic tests in patients with peripheral arterial disease and diabetes, renal failure, and wounds

Recommendations	Class[a]	Level[b]
Measuring TP or TBI is recommended in patients with diabetes or renal failure if resting ABI is normal.[90,91,94,440]	I	C
In patients with PAD and chronic wounds, the WIfI classification system should be considered to estimate individual risk of amputation.[417,444–446]	IIa	C

ABI, ankle–brachial index; PAD, peripheral arterial disease; TBI, toe–brachial index; TP, toe pressure; WIfI, Wound, Ischaemia, and foot Infection classification.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 12 — Recommendations for imaging in patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
DUS is recommended as the first-line imaging method to confirm PAD lesions.[122,123,447]	I	C
In symptomatic patients with aorto-iliac or multisegmental/complex disease, CTA and/or MRA are recommended as adjuvant imaging techniques for preparation of revascularization procedures.[448,449]	I	C
Analysis of anatomical imaging tests in conjunction with symptoms and haemodynamic tests prior to an invasive procedure is recommended.[426]	I	C

CTA, computed tomography angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

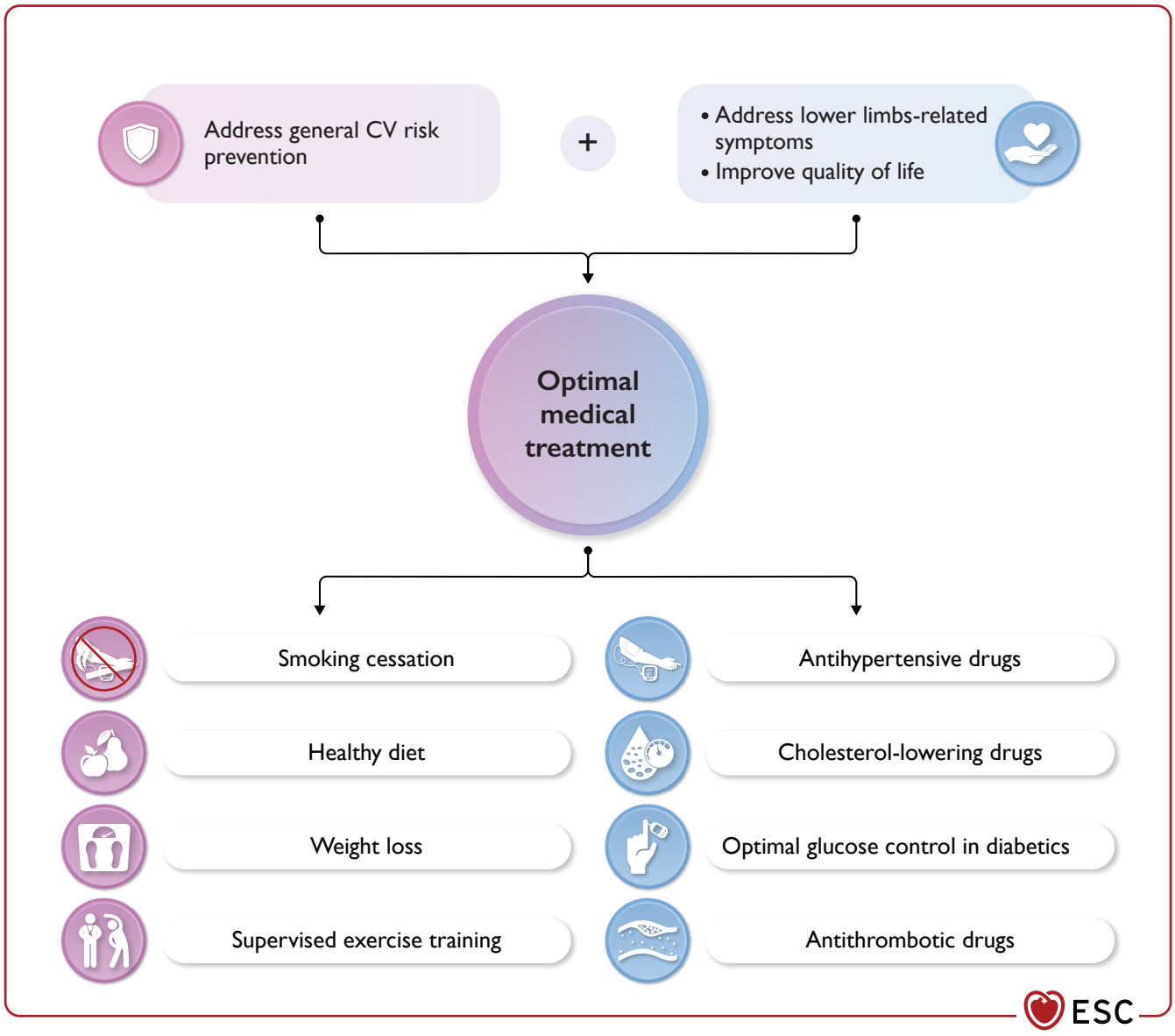

Figure 10 Optimal medical treatment in patients with peripheral arterial disease. CV, cardiovascular.

8.1.1.2. Medical treatment

Patients with PAD should receive comprehensive OMT, including supervised exercise training and lifestyle modification (*Figures 10–12*). A personalized programme of guidelines-guided pharmacotherapy to reduce MACE and MALE should be prescribed and tightly followed.

Patients with PAD are less likely to receive OMT than patients with CAD.[450–452] For general lifestyle and pharmacological therapy see *Section 7*.

8.1.1.2.1. Exercise therapy. A consensus document on exercise and PAD has been published recently.[62] Symptomatic patients should be medically screened before any supervised exercise training (SET) programme initiation.[37,62] In patients with symptomatic PAD, SET is safe and improves treadmill PFWD, MWD, functional walking as measured by six-minute walking distance (6MWD), HRQoL, and cardiorespiratory fitness (*Figure 13*).[294,453–463] Exercise has not been found to improve ABI.[457,458] Ideally, SET should be co-ordinated by vascular physicians, and training sessions supervised by clinical exercise physiologists or physiotherapists.[62] In Europe, SET is usually underused.[464,465]

When SET is not available, home-based exercise training (HBET) should be proposed (*Figure 13*), although it is inferior with regard to improving walking performance.[466–469] HBET is safe and its inferiority is reduced if monitoring is implemented.[469,470] Compared with no exercise, HBET improves walking performance.[471] SET training frequency should be at least three times per week, for 30–60 min, and the programme last for at least 12 weeks.[37,58,59,454,472,473] Patients should exercise to moderate-severe claudication pain to improve walking performance.[37,294,453,454,456–458,474] However, prescribing high-pain exercise may hinder programme uptake and adherence. Additionally, it has been reported that improvements in walking performance may be obtained with less severe claudication pain.[455,460] Therefore, a flexible approach is recommended, considering the patient's needs

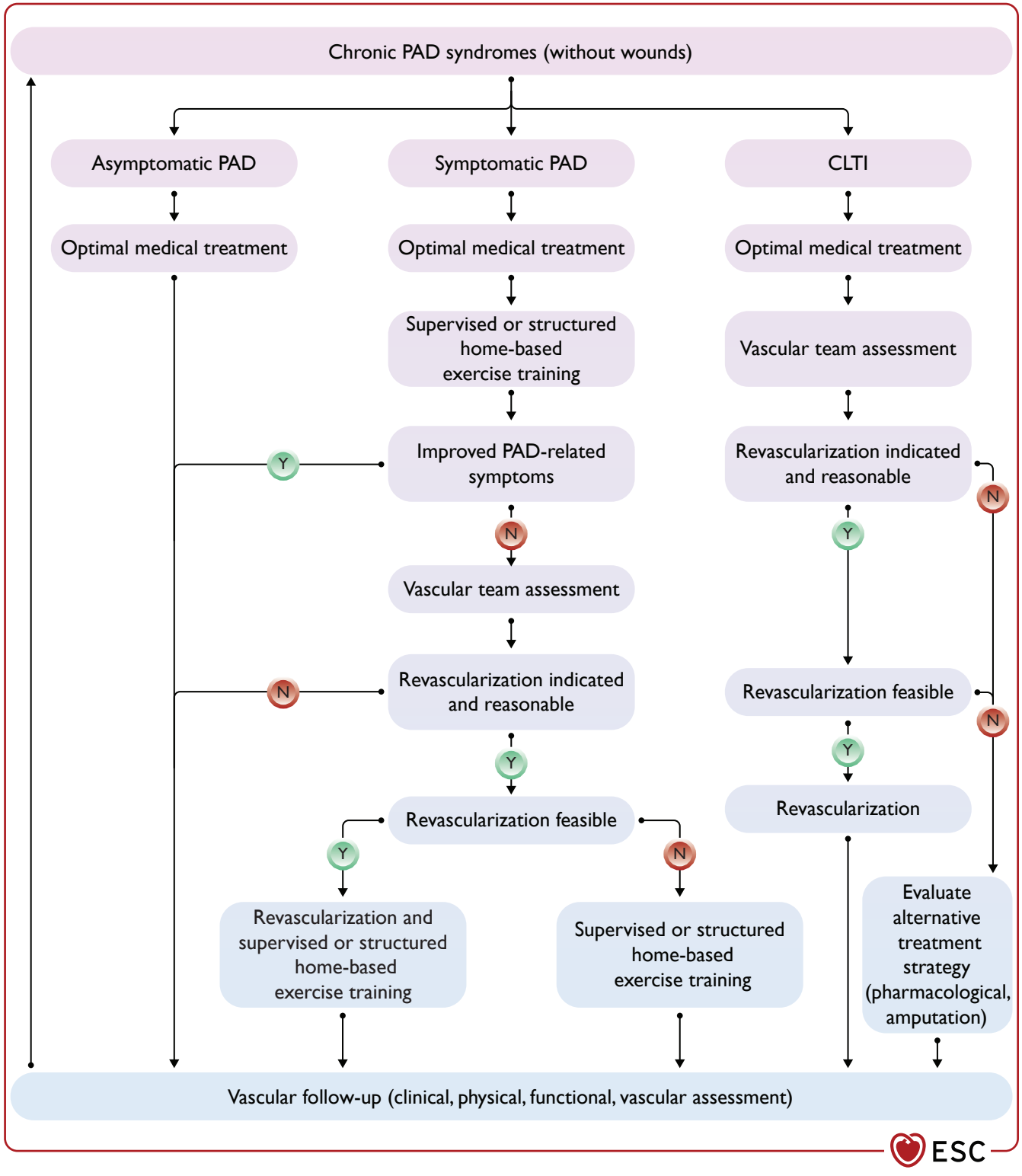

Figure 11 Treatment algorithm in peripheral arterial disease without wounds. CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease.

and preferences.[62] Alternative training modalities, such as strength training, arm cranking, cycling, and combinations of different modes, have proven effective in improving walking performance compared with traditional walking training, with limited evidence for HRQoL.[475] However, this evidence is low due to small sample size and risk of bias.[475] Vigorous intensity exercise training (77%–95% of maximal heart rate or 14–17 on the rate of perceived exertion on Borg's scale) has been shown to induce the best walking and cardiorespiratory fitness improvements.[294,457] Training programmes should begin at low-to-moderate intensity, gradually advancing to vigorous exercise if well tolerated.[62] This approach assesses patient response and minimizes complications.[37,62]

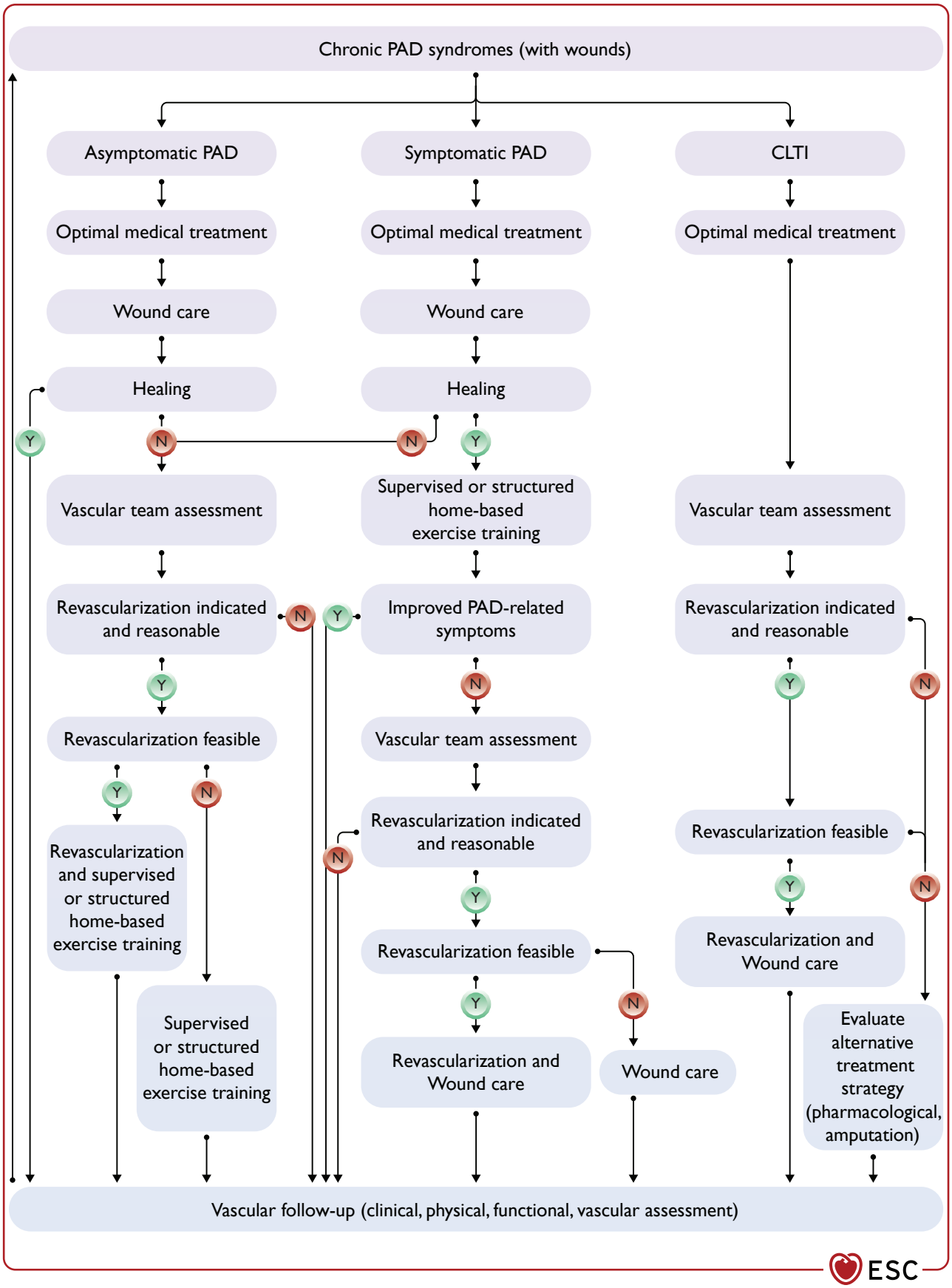

Figure 12 Treatment algorithm in peripheral arterial disease with wounds. CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease.

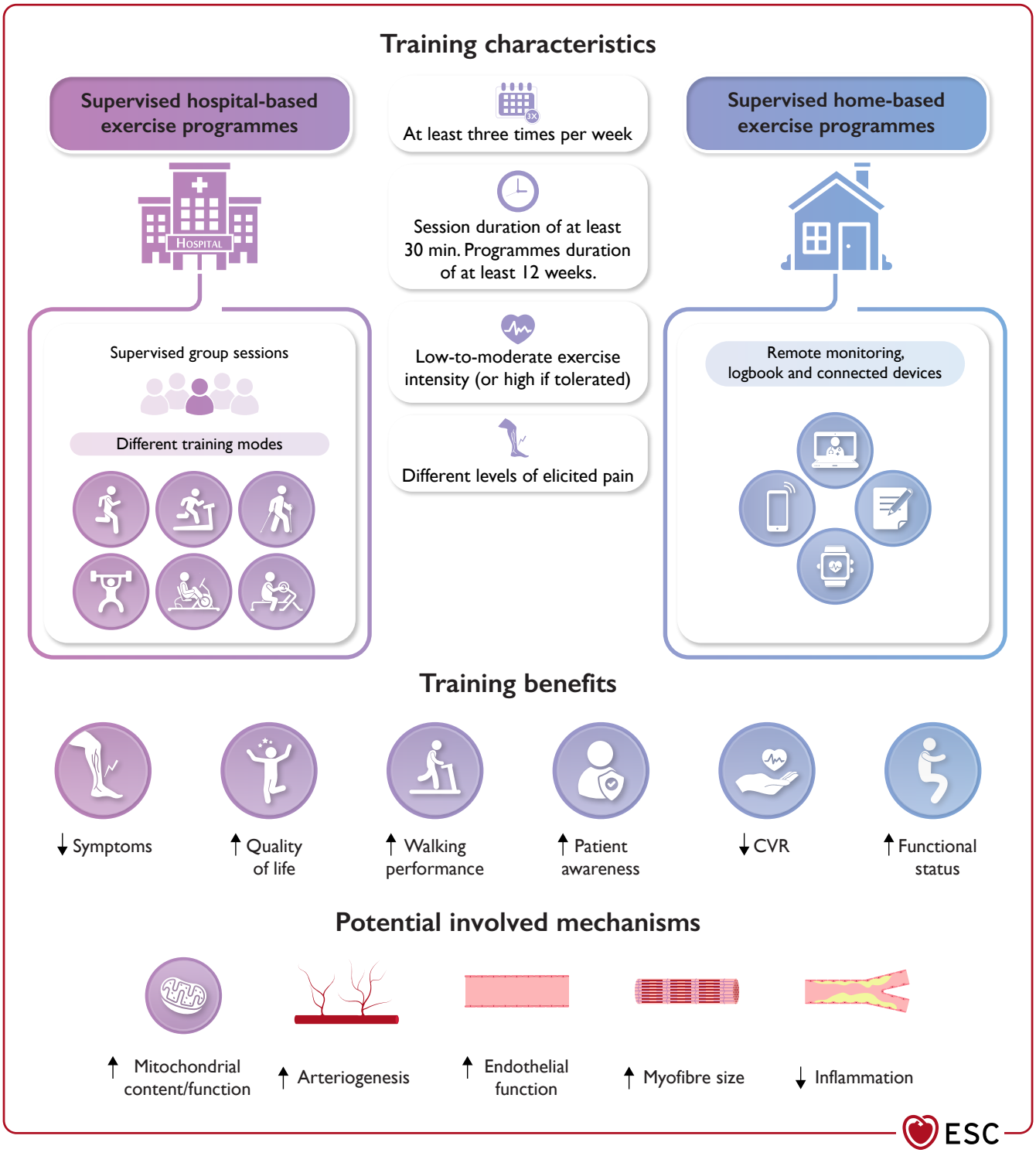

Figure 13 Exercise training characteristics and benefits in patients with peripheral arterial disease. CVR, cardiovascular risk.

Data on the efficacy of exercise therapy in women compared with men are scarce. Women may respond less well than men,[476,477] although discrepancies among studies exist.[478–481]

SET combined with endovascular revascularization significantly improves walking performance, HRQoL, and reduces future revascularization.[482,483]

An exercise therapy algorithm in PAD has been recently described.[62]

Recommendation Table 13 — Recommendations for exercise therapy in patients with peripheral arterial disease (see also Evidence Table 5)

Recommendations	Class[a]	Level[b]
In patients with symptomatic PAD, SET is recommended.[294,453,456–458,462]	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.[482,483]	I	A
When SET is not available or feasible, a structured and monitored (calls, logbooks, connected devices) HBET programme should be considered.[468,469,471]	IIa	A
Walking should be considered as a first-line training modality. When walking exercise is not an option, alternative exercise modes (strength training, arm cranking, cycling, and combinations of different training modes) should also be considered.[475]	IIa	A
Walking training performed at high intensity (77%–95% of maximal heart rate or 14–17 self-perceived exertion on Borg's scale) should be considered to improve walking performance,[294] and high-intensity exercise training (various aerobic training modes) should be considered to improve cardiorespiratory fitness.[294,457]	IIa	A
Training frequency of at least three times per week, training session duration of at least 30 min, and training programme duration of at least 12 weeks should be considered.[472]	IIa	B
In patients with PAD, exercise training to moderate-severe claudication pain may be considered to improve walking performance.[37,454,456,458] However, improvements are also achievable with lesser claudication pain severities (low-mild pain or pain-free).[455,460]	IIb	B
Based on patient's tolerance, a progressive increase (every 1–2 weeks) in exercise training load may be considered.[37,62]	IIb	C

HBET, home-based exercise training; PAD, peripheral arterial disease; SET, supervised exercise training.
[a]Class of recommendation.
[b]Level of evidence.

8.1.1.2.2. Pharmacological treatment. Antithrombotic therapy

Asymptomatic PAD

Although patients with PAD are at very high CV risk,[404,484] a trial evaluating the effect of antiplatelet agents in asymptomatic patients with an ABI ≤0.95 did not show an effect on MACE or revascularization.[485] Another trial on patients with an ABI ≤0.99 and diabetes also failed to show any difference in MACE or amputation.[486] However, these data were not powered to analyse subgroups and do not rule out the possibility that aspirin could provide a benefit in subjects at increased risk of CV events. In a randomized trial evaluating aspirin in the prevention of cancer and CVD in patients with diabetes without known arterial disease, MACE occurred in a significantly lower percentage of participants in the aspirin group than in the placebo group, with more major bleeding events in the aspirin group.[487] The effect of antithrombotics in patients with higher-risk PAD (i.e. ABI <0.90 and other CV risk factors) has not been evaluated in randomized trials. Antithrombotic therapy should not be systematically administered in patients with asymptomatic PAD.

Symptomatic PAD

In patients with symptomatic PAD, antithrombotic therapy improves CV prognosis.[488–492] Clopidogrel may have a modest advantage over aspirin (*Figure 14*).[493,494] In the Examining Use of tiCagreLor In peripheral artery Disease (EUCLID) trial, single antiplatelet therapy (SAPT) with ticagrelor showed no superior benefit in the reduction of MACE or major bleeding compared with clopidogrel.[495–497]

Dual antithrombotic therapy with aspirin and vascular-dose rivaroxaban (2.5 mg b.i.d.) in patients with PAD is more effective than aspirin alone, reducing MACE, MALE, and preventing acute limb ischaemia (ALI), but with increased major bleeding risk.[429,430,498,499] Patients with high-risk limb presentation (CLTI, previous amputation, or revascularization) or high-risk comorbidities (heart failure [HF], diabetes, or polyvascular disease [PVD]) benefit the most.[498]

After endovascular therapy, dual antiplatelet therapy (DAPT) for 1–3 months is supported by rare randomized studies.[500,501] DAPT is not associated with reduced CV mortality or MACE,[501] but seems to improve patency without increasing bleeding (*Figure 15*).[502–504] The combination of aspirin 100 mg and vascular-dose rivaroxaban (2.5 mg b.i.d.), started post-revascularization, showed a moderate but significantly lower incidence of MALE and MACE compared with aspirin alone,[490,505] without an increase in thrombolysis in myocardial infarction (TIMI) major bleedings, but with an increase in International Society on Thrombosis and Haemostasis (ISTH) major bleedings, especially when clopidogrel was given for >1 month.[506]

Patients with CLTI are at high risk of MACE and MALE.[429,431,507] Among CLTI patients, there is no robust evidence favouring a specific antithrombotic strategy for vein graft maintenance. DAPT with clopidogrel and aspirin is not superior to aspirin alone in below-the-knee (BTK) bypass grafts.[508–510] Vitamin K antagonists (VKAs) may be considered for high-risk conduits with low bleeding risk.[509]

Dual antiplatelet therapy could confer benefit for prosthetic conduit (occlusion, revascularization, amputation, or death), without increasing major bleeding.[510] VKAs with an international normalized ratio (INR) of 3–4.5 are slightly beneficial in venous conduits, but with a 1.9-fold and 1.3-fold increase in major and fatal bleedings, respectively.[509] A study suggested that VKAs could be associated with prolonged patency of at-risk prosthetic grafts due to poor run-off.[511]

In patients with another indication for OAC (such as atrial fibrillation [AF] or mechanic valve replacement) and PAD, anticoagulation is warranted.[512] Additional SAPT post-endovascular therapy should be brief.

Recommendation Table 14 — Recommendations for antithrombotic therapy in patients with peripheral arterial disease (see also Evidence Table 6)

Recommendations	Class[a]	Level[b]
Use of antiplatelet therapy with aspirin alone (range 75–160 mg o.d.) or clopidogrel alone (75 mg o.d.) is recommended for the reduction of MACE in patients with symptomatic PAD.[488–490]	I	A
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD, high ischaemic risk,[c] and non-high bleeding risk.[d,429,498,499]	IIa	A

Continued

Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and non-high bleeding risk following lower-limb revascularization.[490,505]	IIa	B
Use of antiplatelet therapy with clopidogrel alone (75 mg o.d.) may be considered over aspirin to reduce MI, stroke, and vascular death.[493,494]	IIb	B
Aspirin (75–100 mg) for primary prevention may be considered in patients with asymptomatic PAD and DM, in the absence of contraindications.[419,487]	IIb	A
DAPT for at least 1 month after revascularization may be considered to reduce limb events.[500,501,503,513,514]	IIb	B
Long-term DAPT in patients with PAD is not recommended.[489]	III	A
Oral anticoagulant monotherapy for PAD (unless for another indication) is not recommended.[515]	III	A
The routine use of ticagrelor in patients with PAD is not recommended.[495]	III	A
It is not recommended to systematically treat patients with asymptomatic PAD without any sign of clinically relevant ASCVD with antiplatelet drugs.[485]	III	B

ASCVD, atherosclerotic cardiovascular disease; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; MACE, major adverse cardiovascular events; MI, myocardial infarction; o.d., once daily; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]High ischaemic risk: previous amputation, critical limb threatening ischaemia, previous revascularization, high-risk comorbidities (heart failure, diabetes, vascular disease in two or more vascular beds), eGFR <60 mL/min/1.73 m^2.[498]
[d]High bleeding risk: dialysis or renal impairment GFR <15 mL/min/1.73 m^2, acute coronary syndrome <30 days, history of intracranial haemorrhage, stroke or TIA, active or clinically significant bleeding.

Pharmacotherapy to decrease walking impairment

Verapamil,[516] statins,[517,518] antiplatelet agents, and prostanoids (prostaglandins I_2 and E_1)[519] can alleviate walking impairment in patients with symptomatic PAD. However, drugs like cilostazol, naftidrofuryl, pentoxifylline, buflomedil, carnitine, and propionyl-L-carnitine are suggested to increase walking distance in patients with IC without impacting CV health.[339,520] Their objective benefit is generally limited, ranging from mild to moderate, with considerable variability.[339] The additional benefit of these drugs alongside antithrombotics, antihypertensives, and statins remains unknown.

Cilostazol, a phosphodiesterase type III inhibitor, improved MWD compared with placebo and pentoxifylline.[520–522] In a Cochrane analysis, 100 mg twice daily increased MWD by 76%,[521] while another review reported a 25% average improvement.[520] Cilostazol also has antiplatelet effects, requiring cautious combination with other anticoagulant and antiplatelet treatments.[522] Notably, it increases bleeding complications.[523]

Naftidrofuryl oxalate, tested for IC,[524] demonstrated a 74% average increase in MWD and improved HRQoL.[524,525] In a systematic review, the average MWD improvement was 60% compared with placebo.[520] However, inconsistent results for other medications, such as prostanoids, pentoxifylline, L-arginine, buflomedil, or *Gingko biloba*, preclude their recommendation for patients with IC.[519,526,527]

8.1.1.2.3. Aorto-iliac lesion revascularization. Aorto-iliac lesions can be treated by either an endovascular or a surgical approach according to the lesion morphology and patient risk. Long-term patency with a low risk of complications can be achieved by balloon angioplasty with or without stenting in external iliac arteries or primary stenting in common iliac arteries.[528] A meta-analysis evaluated outcomes of open surgery vs. an endovascular approach in aorto-iliac lesions (TASC II C-D) and found that short-term morbidity and mortality favours the endovascular approach, but early and mid-term primary patency favours open surgery; however, secondary patency is comparable in all groups.

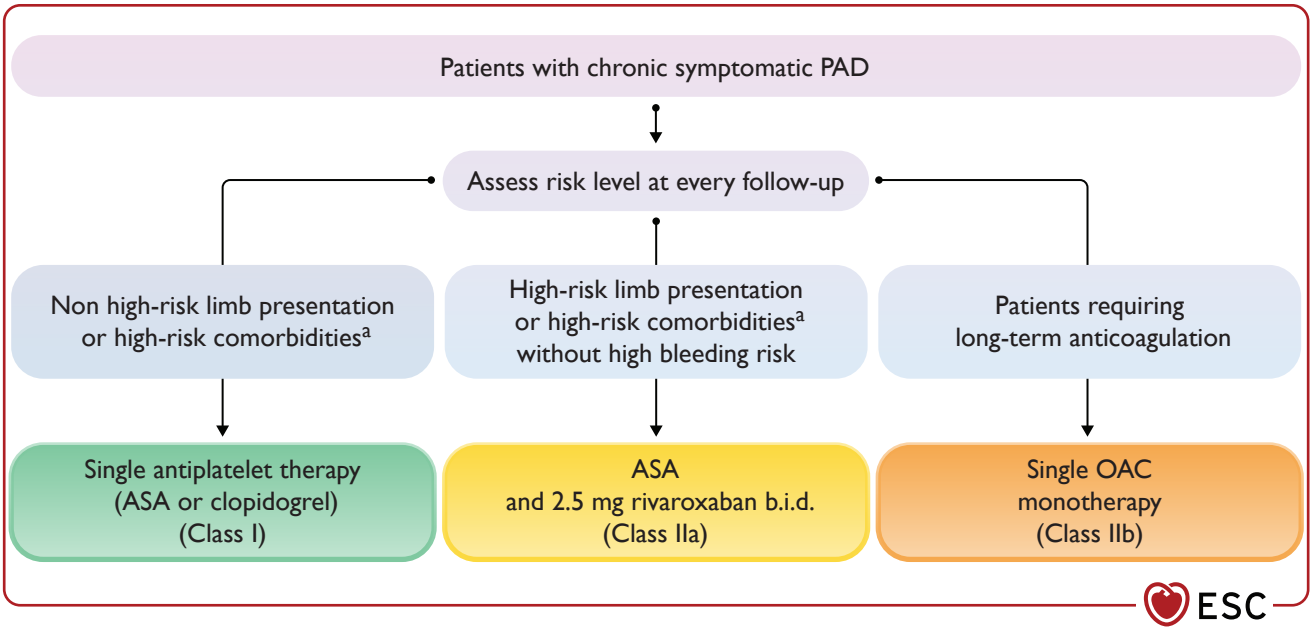

Figure 14 Long-term antithrombotic therapy in patients with symptomatic peripheral arterial disease. b.i.d., twice daily; OAC, oral anticoagulant; PAD, peripheral arterial disease; ASA, aspirin [a]High-risk limb presentation: previous amputation, chronic limb-threatening ischaemia, previous revascularization, high-risk comorbidities: heart failure, diabetes, vascular disease in two or more vascular beds, moderate kidney dysfunction; eGFR <60 mL/min/1.73 m^2.

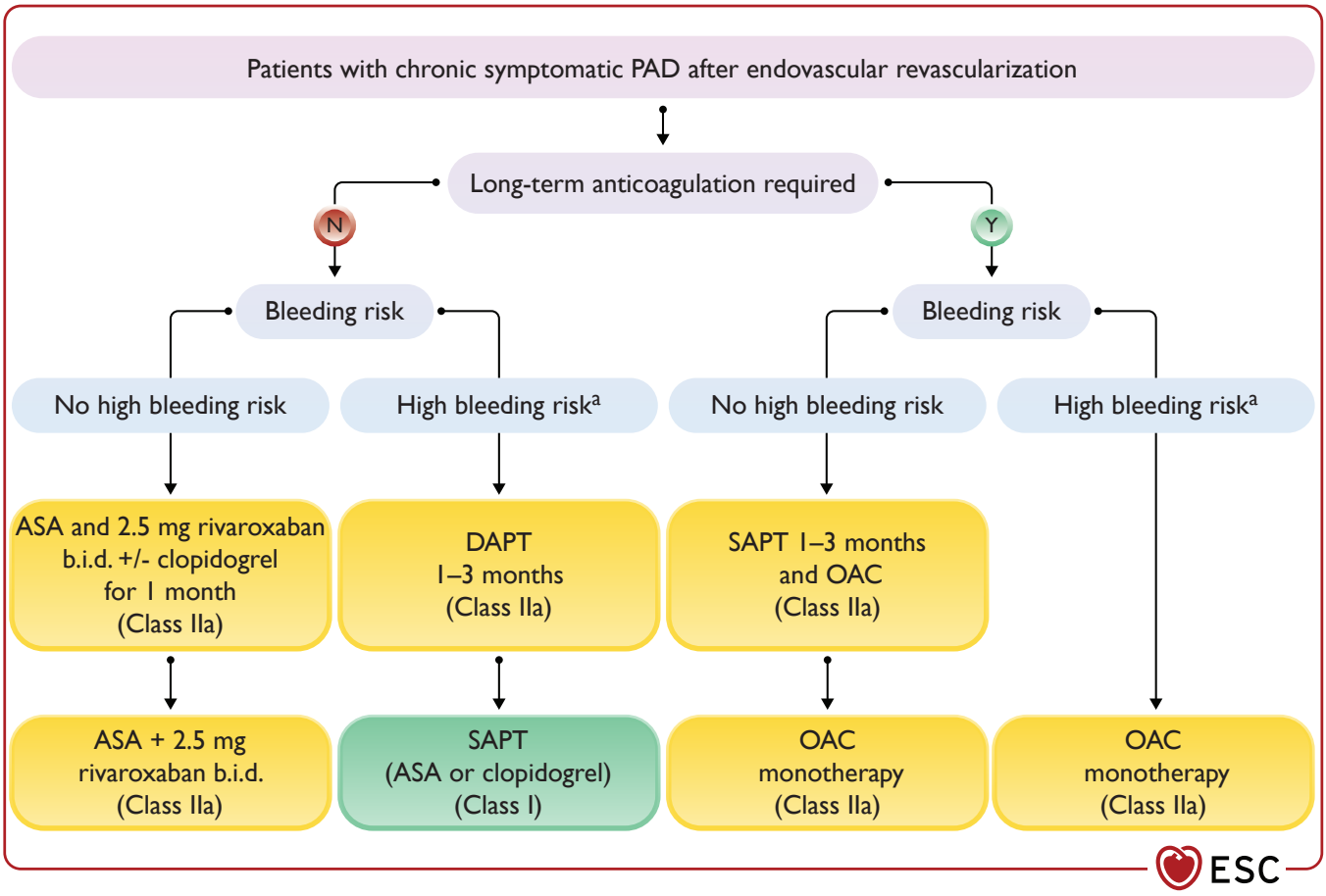

Figure 15 Patients with chronic symptomatic PAD after endovascular revascularization. b.i.d., twice daily; DAPT, dual antiplatelet therapy; OAC, oral anticoagulant; PAD, peripheral arterial disease; ASA, aspirin; SAPT, single antiplatelet therapy [a]High bleeding risk: dialysis or a renal impairment glomerular filtration rate <15 mL/min/1.73 m^2, acute coronary syndrome <30 days, history of intracranial haemorrhage, stroke or TIA, active or clinically significant bleeding.

8.1.1.2.4. Femoro-popliteal lesion revascularization. If revascularization is indicated, endovascular therapy should be the first choice even for complex lesions, especially in surgical high-risk patients.[119,529–531]

Endovascular therapy faces the challenge of sustaining long-term patency and durability in the femoro-popliteal region, particularly post-stent placement in a highly mobile artery. Drug-eluting balloons have improved long-term patency in complex patient cohorts and lesions.[532] With regard to paclitaxel-coated devices, a meta-analysis caused a decline in their usage, especially as the United States Food and Drug Administration (FDA) reacted and restricted their use.[533] Consequently, data from large national databases were evaluated and the mortality signal could not be confirmed. The FDA revised its position, and drug-eluting treatment is now deemed to be a safe and efficient treatment strategy for femoro-popliteal lesions.[534–538]

An open surgical approach in femoro-popliteal lesions should be considered when an autologous vein (e.g. great saphenous vein [GSV]) is available and the patient shows low surgical risk, and in complex lesions after an interdisciplinary team discussion.

8.1.1.2.5. Below-the-knee artery revascularization. In patients with severe IC in whom endovascular femoro-popliteal treatment is performed, BTK arteries can be treated in the same intervention if there is substantially impaired outflow.[539]

Recommendation Table 15 — Recommendations for interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)

Recommendations	Class[a]	Level[b]
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.[119]	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.[119]	I	C
In patients with symptomatic PAD and impaired PAD-related quality of life after a 3 month period of OMT and exercise therapy, revascularization may be considered.[465,540]	IIb	B
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.[541–544]	III	B
In patients with asymptomatic PAD, revascularization is not recommended.[119,529]	III	C

CLTI, chronic limb-threatening ischaemia; OMT, optimal medical treatment; PAD, peripheral arterial disease; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 16 — Recommendations for interventional treatment of patients with symptomatic peripheral arterial disease (per arterial bed)

Recommendations	Class[a]	Level[b]
In femoro-popliteal lesions, drug-eluting treatment should be considered as the first-choice strategy.[534–537]	IIa	A
In iliac lesions, balloon angioplasty with or without stenting in external iliac arteries, or primary stenting in common iliac arteries, should be considered.[545–548]	IIa	B
In femoro-popliteal lesions, if revascularization is indicated, endovascular therapy should be considered.[119,529–531]	IIa	B
In femoro-popliteal lesions, if revascularization is indicated, an open surgical approach should be considered when an autologous vein (e.g. GSV) is available in patients with low surgical risk.[119,529]	IIa	C
In patients with severe IC undergoing endovascular femoro-popliteal revascularization, treatment of BTK arteries may be considered in the same intervention.[549,550]	IIb	C

BTK, below-the-knee; GSV, great saphenous vein; IC, intermittent claudication.
[a]Class of recommendation.
[b]Level of evidence.

8.1.1.3. Follow-up

Asymptomatic and symptomatic PAD are at increased risk of leg symptom worsening[427] and of CV mortality and morbidity.[419,431,551] Follow-up post-revascularization is crucial to ensure perfusion improvement, address CVRFs, optimize pharmacological treatment adherence, identify disease progression, and evaluate mental health and functional capacity. Experienced vascular care physicians should conduct follow-up, although specific protocols are currently undefined.[128,552] Data on asymptomatic PAD follow-up are limited.[553] For symptomatic PAD or post-intervention, annual follow-up are advised, including ABI/TBI measurement and DUS for new or worsening symptoms.

Recommendation Table 17 — Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
It is recommended to regularly, at least once a year, follow up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.[553,554]	I	C

CVRFs, cardiovascular risk factors; DUS, duplex ultrasound; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2. Chronic limb-threatening ischaemia

8.1.2.1. Clinical presentation and diagnosis

Chronic limb-threatening ischaemia describes chronic lower-limb hypoperfusion responsible for ischaemic rest pain, or non-healing ulceration or gangrene (typically in distal segments).[555,556] Ischaemic rest pain primarily affects the patient's forefoot and aggravates in a supine position, while lowering of the affected leg eases ischaemic symptoms.

8.1.2.1.1. Definition. Chronic limb-threatening ischaemia should be considered in the presence of one of the following lower-limb clinical signs or symptoms:

- Ischaemic rest pain
- Non-healing lower-limb wound of ≥2 weeks' duration
- Lower-limb gangrene

The following haemodynamic criteria may be used to guide diagnosis in patients with suspicion of CLTI:

- Ankle pressure <50 mmHg
- TP <30 mmHg
- $TcPO_2$ <30 mmHg

8.1.2.1.2. Initial assessment and risk of amputation. For patients with CLTI, initial diagnostic steps involve clinical examination and limb perfusion assessment through haemodynamic measurements. Regarding haemodynamic assessment in CLTI, standard ABI may be normal or falsely elevated due to non-compressible arteries related to medial sclerosis (common in diabetes or CKD),[557] which can be overcome by estimation of ABI based on Doppler waveforms.[124] Therefore, standard ankle pressure alone may not be reliable in estimating limb loss risk.[441,558] In addition, a large proportion of patients with ulcers may have below-the-ankle lesions.[440] In patients with CLTI, TP, TBI, or $TcPO_2$ should additionally be obtained.[90,441,559]

Particularly in patients with CLTI, the WIfI classification system should be applied. In addition to patients' limb perfusion, the WIfI classification considers the wound size and the extent of foot infection to determine the individual risk of amputation.[417,444–446]

8.1.2.1.3. Imaging. In all patients with CLTI, comprehensive vascular imaging is mandatory to evaluate revascularization options. CLTI commonly affects more than one arterial segment of the lower limbs, involving infra-popliteal arteries (BTK and below-the-ankle arteries) in most cases. While non-invasive imaging (DUS, CTA, MRA) provides reliable results for above-the-knee arteries, imaging of BTK arteries, especially below the ankle, may be hampered by severe calcification.[448,560,561] Therefore, in CLTI additional DSA with dedicated views of the foot should be considered for the assessment of BTK arteries.[560] Even in patients who are not candidates for revascularization, DSA should be obtained to prevent unnecessary amputation or to minimize amputation extent.[560,562]

8.1.2.1.4. Mortality risk assessment. All-cause mortality and event rates of MI are more than two-fold higher in CLTI patients than in unselected patients with an ABI ≤0.90.[431]

In CLTI patients undergoing revascularization, the post-revascularization period is particularly associated with an increased risk of MALE and MACE.[563] The management of patients with CLTI should therefore include an individual peri-procedural risk assessment. Referring to the peri-procedural risk patients can be categorized as average procedural risk (peri-procedural mortality <5% and 2 year survival >50%) or high procedural risk (peri-procedural mortality ≥5% and 2 year survival ≤50%).[564,565]

Besides revascularization, it also needs to be considered that lower-limb amputation is associated with 30 day mortality rates of up to 22%.[566]

Recommendation Table 18 — Recommendations for the management of chronic limb-threatening ischaemia

Recommendations	Class[a]	Level[b]
For limb salvage in patients with CLTI, revascularization is recommended.[564,567]	I	B
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.[417,560]	I	C
In patients with CLTI, imaging of the entire affected limb should be considered.[560]	IIa	C

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.2. Medical treatment

Chronic limb-thretening ischaemia is associated with a high risk of ischaemic events,[429,431] thus management of patients with CLTI must include OMT.

In addition, rest pain, optimal wound care, and infection control should be managed. A vascular team, including at least a vascular physician, a vascular surgeon, and a radiologist, should be involved to prevent amputation.[568] Lower-limb exercise training is contraindicated until ulcers are healed and aggressive offloading should be ensured to allow healing. Depending on infection extent, oral antibiotics may suffice, however, if extensive with systemic signs of inflammation, admission for intravenous (i.v.) antibiotic administration may be required.[569,570]

Good-quality evidence on the advantages of one type of wound dressing over others is lacking, while in selected patients individualized treatments with antimicrobial dressing,[571] silver dressing,[572] collagen dressing,[573] honey- or iodine-based dressings,[574] platelet-rich plasma, or negative pressure therapy[575,576] may accelerate wound healing, shorten hospital stay, and prevent amputations. If deep-seated infection is suspected, X-ray or MRA are required to diagnose osteomyelitis, in which case a longer course of antibiotics may be necessary.[577] Antibiotics for osteomyelitis treatment may be empirical, however, they should be adapted according to (preferably tissue) cultures.[578–581]

Ulcers require assessment of venous aetiology and potential for endovenous therapy, while mixed ulcers require compression therapy after revascularization.[582]

Recommendation Table 19 — Recommendations for medical treatment in patients with chronic limb-threatening ischaemia (see also Evidence Table 7)

Recommendations	Class[a]	Level[b]
It is recommended that patients with CLTI are managed by a vascular team.[568]	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is recommended to allow wound healing.[583,584]	I	C
It is recommended to treat infection with antibiotics.[569,570]	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.[584]	III	C

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.3. Interventional treatment

8.1.2.3.1. Revascularization. In CLTI, revascularization should be attempted to rapidly restore an inline direct blood flow to the foot.[585–588] Three RCTs compared endovascular therapy with open surgery in infra-inguinal arteries. In the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial, no significant difference was found regarding mortality or amputation-free survival at 2 years.[589] However, surgery was associated with a significantly reduced risk of amputation, death, or both after 2 years.[564,589] In the Best Endovascular versus Best Surgical Therapy for Patients with Critical Limb Ischemia (BEST-CLI) trial (median follow-up of 2.7 years), the incidence of MALE or death was lower in patients in which one segment of the GSV was available for surgical revascularization than in patients who underwent endovascular revascularization. In the same trial, outcomes of patients for whom an alternative bypass conduit was needed for surgical revascularization were similar to those of patients who underwent endovascular revascularization.[567]

In the BASIL-2 trial, which included patients requiring infra-popliteal, with or without additional further proximal infra-inguinal, revascularization procedures, endovascular revascularization was associated with better amputation-free survival than surgical revascularization, which was primarily due to fewer deaths in this group.[590] It is important to consider[591] both revascularization options individually in each patient, considering the complexity of the diseased anatomical region.

Multilevel disease

Patients with CLTI commonly present with multilevel disease.[592] Especially for complex lesions, comprehensive patient assessment, including the individual patient's clinical presentation, the lesion morphology, and the peri-procedural risk, needs to be undertaken by a multidisciplinary vascular team to weigh the risks against the benefits of the respective methods of revascularization (endovascular vs. surgical).[590,593–596] A structured approach is essential to achieve rapid and durable restoration of an inline flow to the foot. When possible, the angiosome concept can be considered, targeting the most affected ischaemic area.[597] When CLTI leaves no viable revascularization options, transcatheter arterialization of deep veins may be considered.[598]

Aorto-iliac disease

An endovascular approach is the first choice, commonly employing bare metal or covered stents.[599–603] Surgery is reserved for extensive obstructions and lesions treated unsuccessfully with an endovascular procedure.[604] Hybrid revascularization should be considered in occlusion of the common femoral artery or profunda femoris artery requiring endarterectomy, in addition to inflow and/or outflow disease amenable to endovascular therapy. Hybrid procedures should be encouraged in a one-step modality.[605]

Femoro-popliteal disease

Chronic limb-threatening ischaemia is unlikely to be related to isolated superficial femoral artery lesions; femoro-popliteal involvement in combination with aorto-iliac or infra-popliteal disease is frequently found. In 40% of cases, inflow treatment of femoro-popliteal disease is necessary.[606] The revascularization strategy should be selected according to lesion complexity.[422] If endovascular therapy is chosen, landing zones for potential bypass grafts should be preserved. When bypass surgery is decided, the bypass should be as short as possible, using the saphenous veins.[567]

Infra-popliteal disease

Extended infra-popliteal disease is mainly seen in patients with diabetes[607–610] and CKD,[611,612] often being associated with superficial femoral artery lesions. In short infra-popliteal lesions, endovascular

therapy is the first choice.[593] Drug-eluting balloons[607] and bare metal stent implantation[613] have shown no superiority over plain balloon angioplasty, although drug-eluting stents may be used for relatively short proximal lesions.[614–616]

8.1.2.3.2. Spinal cord stimulation. Spinal cord stimulation (SCS) may be considered in treating patients with CLTI and no viable revascularization options. SCS offers modest pain relief and an 11% reduction in amputation rate compared with conservative management at 1 year. No effect was seen in ulcer healing and benefits should be weighed against the high cost and possible complications.[617] Recent technological advances in neuromodulation may improve the treatment value of this modality.[618]

8.1.2.3.3. Amputation. Minor amputation, usually up to the forefoot, is often needed for necrotic tissue removal with minor impact on patient mobility. Pre-amputation revascularization enhances wound healing. In cases of extensive necrosis or infectious gangrene, primary major amputation without revascularization may be preferable to avoid complications. Secondary amputation is indicated when revascularization fails, re-intervention is not possible, or limb deterioration persists despite a patent graft and optimal management. BTK amputation allows better mobility with a prosthesis. For bedridden patients, above-the-knee amputation may be the preferred choice.

Recommendation Table 20 — Recommendations for interventional treatment of chronic limb-threatening ischaemia

Recommendation	Class[a]	Level[b]
In CLTI patients, it is recommended to perform revascularization as soon as possible.[564]	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.[567,593]	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
An individual risk assessment (weighing the patient's individual procedural risk of endovascular vs. surgical revascularization) by a multidisciplinary vascular team is recommended.	I	C
In CLTI patients with good autologous veins and low surgical risk (<5% peri-operative mortality, >50% 2 year survival), infra-inguinal bypass may be considered.[564,567,590]	IIb	B
In CLTI patients, endovascular treatment may be considered as first-line therapy, especially in patients with increased surgical risk or inadequate autologous veins.[564,567,590]	IIb	B

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.4. Follow-up

In patients with CLTI, the incidence of CV events is increased.[619,620] Follow-up should focus on general clinical CV condition, prevention of revascularization failure, wound healing, and contralateral limb status. After revascularization, at least an annual appointment with a vascular physician expert in CLTI management is warranted. Due to the lack of evidence, recommendations are largely based on consensus and expert opinions.[128]

First-year incidence of vein graft stenosis is 20%;[621] however, if uneventful for 12 months, late issues are scarce.[622] Clinical examination, ABI (or TBI) measurement, and DUS should be performed within 4–6 weeks and thereafter at 3, 6, 12, and 24 months after bypass surgery.[128]

After endovascular treatment, restenosis and occlusion ranges from 5% in the pelvic region to >50% in the infra-popliteal arteries.[623,624] Unlike after surgery, no plateau phase is seen, and the failure rate is constant for at least 5 years. Surveillance includes clinical assessment looking for recurrent symptoms or signs, ABI measurement, and DUS based on the first check-up: if normal, DUS is recommended if symptoms reappear; if abnormal, initial DUS, re-intervention, or closer DUS follow-up on a case-by-case basis are recommended.[128] Post-procedural ankle duplex-based estimated ABI of <0.90 predicts suboptimal wound healing, clinically driven target lesion revascularization (cdTLR), and MALE.[625]

After revascularization, closer follow-up and wound care are recommended until healing. Thereafter, annual appointments with vascular physicians with expertise in CLTI management should be scheduled to check for symptoms, foot condition, ABI, and CVRFs, including availability for TP and $TcPO_2$ if needed. Recurrence of symptoms may also be due to the progression of atherosclerotic disease above or below the bypass or angioplasty site.[427]

Recommendation Table 21 — Recommendations for follow-up in patients with chronic limb-threatening ischaemia

Recommendations	Class[a]	Level[b]
In patients with CLTI, following revascularization it is recommended to follow up patients on a regular basis.[552,626,627]	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.[552,625–628]	I	C

CLTI, chronic limb-threatening ischaemia; CVRFs, cardiovascular risk factors.
[a]Class of recommendation.
[b]Level of evidence.

8.1.3. Acute limb ischaemia

8.1.3.1. Clinical presentation and diagnosis

Acute limb ischaemia is caused by an abrupt decrease in arterial limb perfusion. Potential causes are PAD progression, cardiac/aortic embolization, AD, graft thrombosis, aneurysm thrombosis, popliteal artery entrapment syndrome, trauma, phlegmasia cerulea dolens, ergotism, hypercoagulable states, and iatrogenic complications related to vascular procedures. ALI is a medical emergency and timely recognition is crucial to successful treatment.[629–632] Patients should be rapidly evaluated by a vascular specialist[633] or rapidly transferred to a facility with such resources.

The time constraint is due to the period that skeletal muscle and nerves will tolerate ischaemia—roughly 4–6 h.[634] Lower-extremity symptoms can include both pain and loss of function. The longer and the stronger these symptoms are, the less likely the possibility of limb salvage.

Table 9 Clinical categories of acute limb ischaemia

Grade	Category	Sensory loss	Motor deficit	Arterial Doppler signal	Venous Doppler signal	Capillary refill	Biomarkers	Prognosis
I	Viable	None	None	Yes	Yes	Yes	Not elevated	No immediate threat
IIA	Marginally threatened	None or minimal (toes)	None	No	Yes			Salvageable if promptly treated
IIB	Immediately threatened	More than toes	Mild-moderate	No	Yes			Salvageable if promptly revascularized
III	Irreversible	Profound, anaesthetic	Profound paralysis (rigor)	No	No	No	Massively elevated	Major tissue loss, permanent nerve damage inevitable

Adapted with permission from.[641]

8.1.3.1.1. Clinical examination. The emergency level and the choice of therapeutic strategy depend on the clinical presentation, mainly according to neurological deficits. Clinical assessment must include symptom duration as well as sensory and motor deficit severity to distinguish a threatened from a non-viable extremity. Neurological deficits (sensory loss or especially motor deficit) are signs of limb threat and require emergency imaging and revascularization.[635] Severe sensory deficit and paralysis suggest the limb may be unsalvageable. Clinical ALI categories are presented in *Table 9*.

8.1.3.1.2. Imaging and functional tests. The imaging method depends on availability and aims to diagnose clot presence and assess haemodynamic severity. DSA, CTA, DUS, and contrast-enhanced (CE)-MRA are options based on local expertise, availability, and preference.[636] DUS helps determine treatment urgency when assessing neurological deficit is challenging. Loss of arterial signal suggests limb threat, while a present signal may indicate the limb is not immediately threatened, allowing for ABI measurement. The absence of both arterial and venous Doppler signals, coupled with extensive motor deficit, suggests the limb may be irreversibly damaged (non-salvageable).[637] In addition, biomarkers of muscle damage such as creatinine kinase (CK) or myoglobin may be useful as high levels indicate rhabdomyolysis, risk of amputation,[638] kidney failure, and mortality.[639] In limb ischaemia, CK and myoglobin elevations may be lower in chronic cases, possibly due to ischaemic pre-conditioning and collateral development.[640]

8.1.3.2. Medical treatment

Upon clinical diagnosis, initiate analgesia, anticoagulation, and i.v. fluids. Addressing acidosis and hyperkalaemia may be necessary. Administer i.v. unfractionated heparin (bolus 5000 IU or 70–100 IU per kg body weight, followed by continuous infusion with dose adjustment based on patient response, monitored by activated clotting time or activated partial thromboplastin time) or subcutaneous low molecular weight heparin (e.g. enoxaparin 1 mg per kg twice daily) to prevent further embolization and thrombus propagation.

8.1.3.3. Surgical and interventional treatment

For a salvageable limb, urgent revascularization is essential. Diagnostic imaging, if it will not delay treatment, is recommended to guide therapy. If the limb is deemed unsalvageable, primary amputation or comfort care is indicated.

Different revascularization modalities can be applied, including percutaneous catheter-directed thrombolytic therapy, percutaneous mechanical thrombus extraction or thrombo-aspiration (with or without thrombolytic therapy), or surgical thrombectomy, bypass, and/or arterial repair.[642] Moreover, these modalities can be combined, with the strategy determined by factors such as neurological deficit, ischaemia duration, localization, size, aetiology, comorbidities, type of conduit (artery or graft), and therapy-related risks and outcomes. Current endovascular approaches to ALI boast high technical success rates.[626] To reduce morbidity and mortality, an endovascular-first approach is often preferred, especially in patients with severe comorbidities. Thrombus extraction, thrombo-aspiration, and surgical thrombectomy are indicated in cases of neurological deficit, while catheter-directed thrombolytic therapy is more appropriate in less severe cases without neurological deficit. Modern catheter-based thrombectomy (CDT) is associated with 12-month amputation rates of <10% in Rutherford IIB.[643] A meta-analysis showed that although CDT in the treatment of not immediately threatening ALI showed high angiographic success, the long-term outcomes were relatively poor, with low patency and a substantial risk of major amputation.[644] Systemic thrombolysis has no role in the treatment of patients with ALI.

A meta-analysis showed that CDT and surgery have similar limb salvage rates.[645] Recent analyses indicate benefits of endovascular approaches in terms of mortality at similar amputation rates.[646,647]

A comparison of percutaneous thrombectomy vs. ultrasound-accelerated thrombolysis for the initial management of ALI showed no difference in terms of amputation, bleeding, clinical success, and adverse events, with primary patency at 30 days of 82% and 71%, respectively.[629,648,649]

After thrombus removal, in cases of pre-existing arterial lesions, these should be treated by endovascular therapy or open surgery. If surgical treatment is required, it should be ideally performed in a hybrid room with capacity to allow sufficient completion angiographic imaging and initiation of local lysis if any remaining clot is visualized. Lower-extremity four-compartment fasciotomies should be performed in patients with long-lasting ischaemia to prevent post-reperfusion compartment syndrome.[637] The management of ALI is summarized in *Figure 16*.

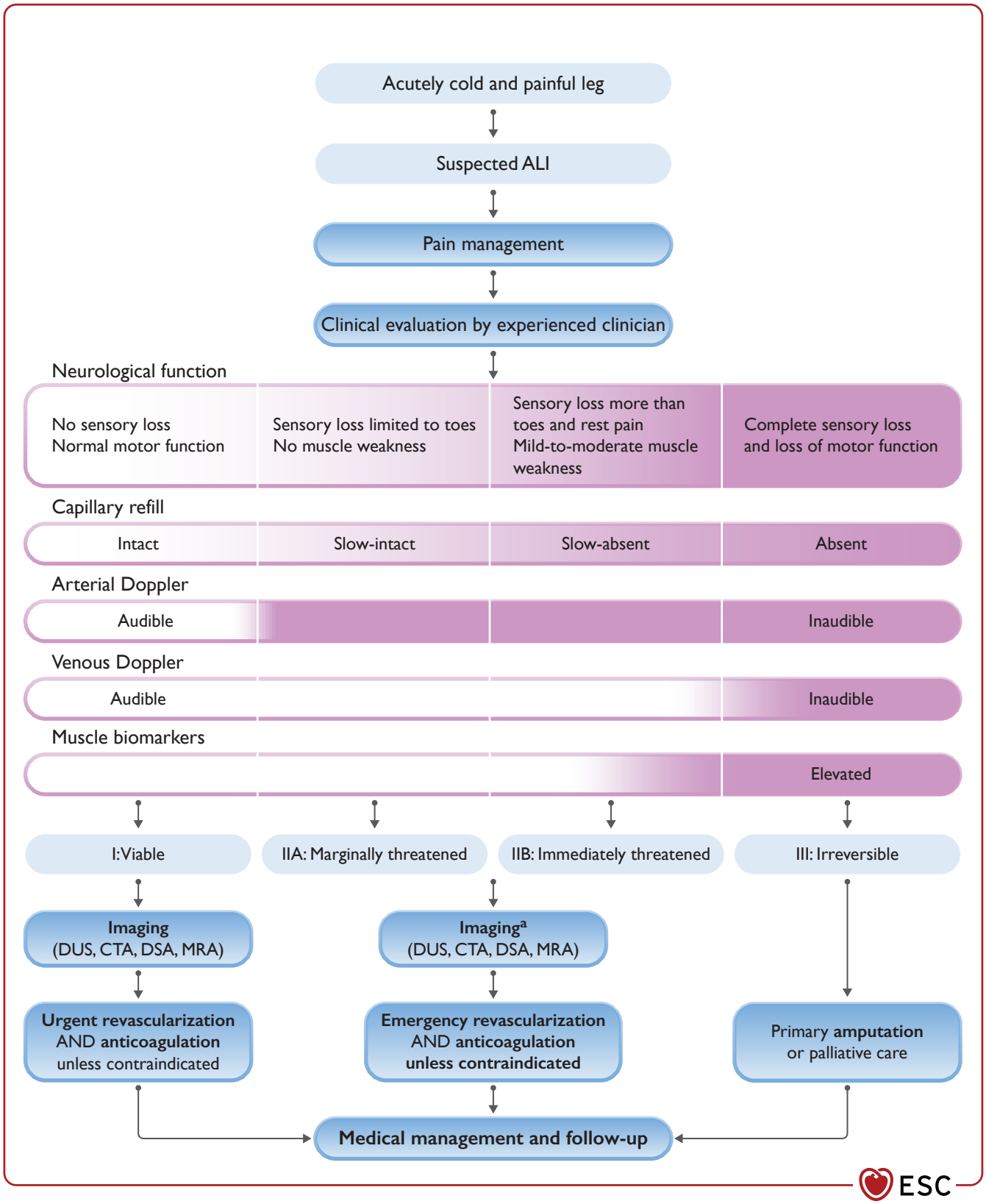

Figure 16 Management of acute limb ischaemia. ALI, acute limb ischaemia; CTA, computed tomography angiography; DSA, digital subtraction angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography. [a]Should not delay treatment.

8.1.3.4. Follow-up

After revascularization or amputation, haemodynamic success should be established, aetiology of ALI investigated, and OMT ensured. Statins improve outcomes after revascularization.[552,630] Since ALI is frequently caused by thrombo-embolism, Holter-ECG, echocardiogram, and aortic imaging are useful to allow initiation of appropriate therapy, in particular anticoagulation.[650] Additionally, consider other prothrombotic syndromes, such as antiphospholipid syndromes and vasculitis, if clinically suspected. While there is only sparse evidence, the inclusion of PAD patients after revascularization into structured follow-up may improve their functional outcomes.[627]

Recommendation Table 22 — Recommendations for the management of patients presenting with acute limb ischaemia (see also Evidence Table 8)

Recommendations	Class[a]	Level[b]
In patients with ALI, it is recommended that an urgent evaluation is performed by a vascular clinician with sufficient experience to assess limb viability and implement appropriate therapy.[635]	I	C
In cases of neurological deficit, urgent revascularization is recommended; diagnostic imaging is recommended to guide treatment, provided it does not delay treatment, or if the need for primary amputation is obvious.[422,635,651,652]	I	C
In the absence of severe neurological deficit, revascularization is recommended within hours of initial imaging in a case-by-case decision.[422,635,652]	I	C
Treatment with analgesics is recommended as soon as possible for pain control.	I	C
It is recommended to monitor for compartment syndrome after revascularization and treat (fasciotomy).[637,652]	I	C
It is recommended to assess clinical and haemodynamic success following revascularization.[627]	I	C
In patients with ALI, it is recommended to obtain a comprehensive medical history and determine the cause of thrombosis and/or embolization.[650]	I	C
In patients with ALI, following revascularization if not on anticoagulation for other reasons, DAPT or rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.[514,653]	IIa	C
Upon confirmation of ALI diagnosis, treatment with heparin may be considered.[635,654–656]	IIb	C

ALI, acute limb ischaemia; b.i.d., twice daily; DAPT, dual antiplatelet therapy; DPI, dual pathway inhibition; o.d., once daily.
[a]Class of recommendation.
[b]Level of evidence.

8.2. Extracranial carotid and vertebral artery disease

8.2.1. Clinical presentation and diagnosis

8.2.1.1. Clinical presentation

Atherosclerotic CS represents one of the major causes of acute ischaemic stroke (20%).[657]

CS may be revealed by a cervical bruit, but also by a TIA or stroke.

8.2.1.2. Diagnosis

Atherosclerotic lesions are primarily located in specific arterial segments, including the carotid bifurcation, siphon, M1 segment of the middle cerebral artery, brachiocephalic trunk, subclavian artery, first and fourth segments of the vertebral artery, or first segment of the basilar artery. Carotid plaques (CP), originating in the intima, offer a better representation of the atherosclerotic process than carotid intima-media thickness (cIMT). CP may be diffuse or focal (protuberant). According to the Mannheim carotid plaque consensus, a CP is defined as a focal structure encroaching into the arterial lumen by ≥0.5 mm or ≥50% of the surrounding vessel.[658] The American Society of Echocardiography (ASE) recently proposed a definition that includes any focal thickening considered atherosclerotic in origin and encroaching into the lumen of any carotid artery segment (protuberant-type plaque) or, in the case of diffuse vessel wall atherosclerosis, when cIMT measures ≥1.5 mm in any carotid artery segment.[659] Plaques can progress to CS, defined as ≥50% narrowing of the extracranial internal carotid artery (ICA), with stenosis severity estimated using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method or its non-invasive equivalent assessed by DUS (*Figure 17*).[122,660] Other methods are described in the Supplementary data online, *Section 1.5*. The European Carotid Surgery Trial (ECST) and the area methods overestimate the severity of the CS and are not recommended.[77]

Carotid DUS is safe, accurate, and reliable if performed by a skilled vascular specialist. It is the first-line imaging modality for screening, diagnosis, and surveillance of extracranial carotid arteries.[77] The degree of stenosis is mostly based on Doppler analysis of blood flow in the common carotid artery (CCA), ICA, and external carotid artery (*Table 10*).[661,662] Vertebral and subclavian arteries must also be checked. In some cases, indirect signs of severe stenosis have to be evaluated by transcranial and/or ophthalmic artery Doppler. Severe arterial calcification can decrease DUS accuracy.[122]

Recommendation Table 23 — Recommendations for carotid artery stenosis assessment

Recommendations	Class[a]	Level[b]
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.[77,122,660]	I	B
It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.[77,663]	I	C
It is not recommended to use the ECST method for ICA stenosis assessment.[77,122,660]	III	C

DUS, duplex ultrasound; ECST, European Carotid Surgery Trial; ICA, internal carotid artery; NASCET, North American Symptomatic Carotid Endarterectomy Trial.
[a]Class of recommendation.
[b]Level of evidence.

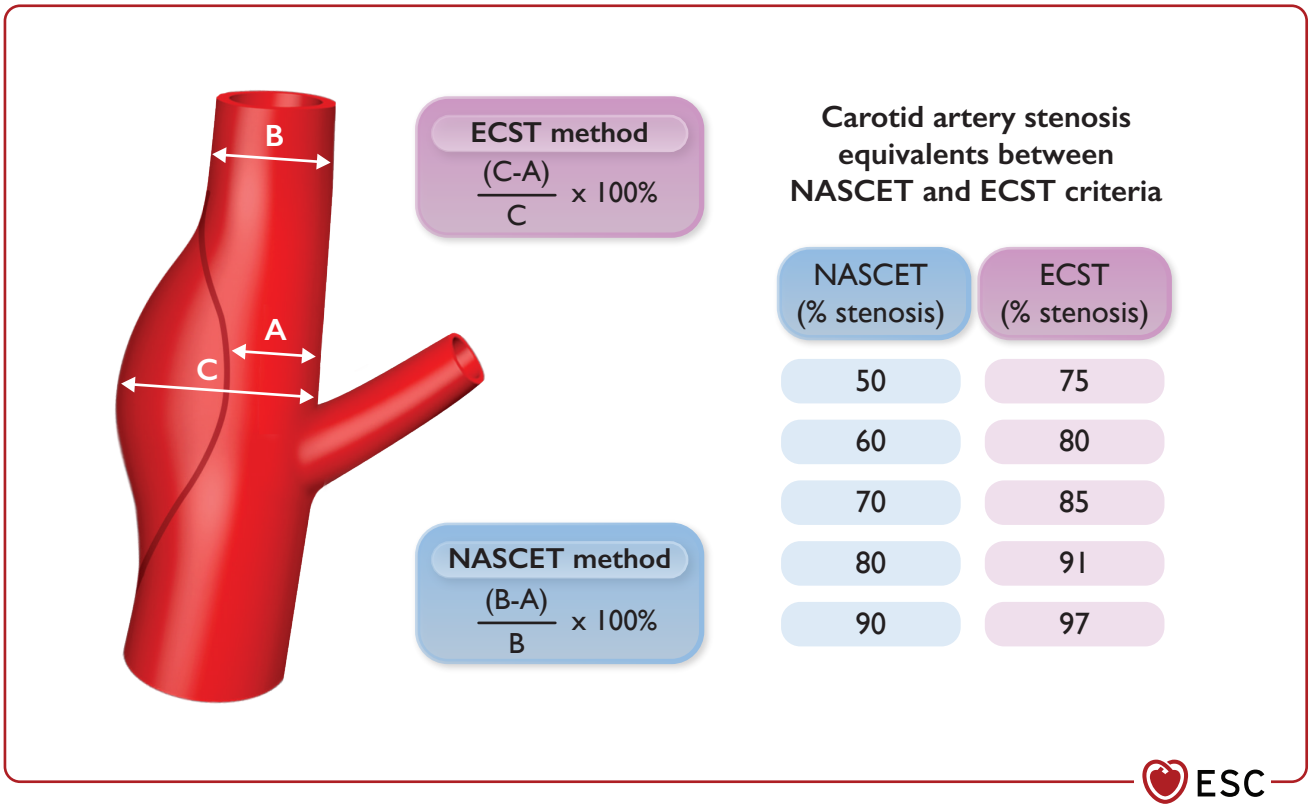

Figure 17 North American Symptomatic Carotid Endarterectomy Trial/European Carotid Surgery Trial methods. ECST, European Carotid Surgery Trial; NASCET, North American Symptomatic Carotid Endarterectomy trial.

Table 10 Peak systolic velocity criteria for grading internal carotid artery stenosis

% stenosis	Reference	50%–69% (moderate stenosis)	≥70% (severe stenosis)
PSV threshold	SRUCC[662] --- Gornik *et al.*[661]	125–230 cm/s --- ≥180 cm/s or ≥125 cm/s + PSV ICA/CCA ≥2	>230 cm/s --- Overestimation with SRUCC criteria but no consensus

CCA, common carotid artery; ICA, internal carotid artery; PSV, peak systolic velocity; SRUCC, Society of Radiologists in Ultrasound.

8.2.2. Asymptomatic carotid artery stenosis

8.2.2.1. Medical treatment

Optimal medical treatment is based on CVRF correction through lifestyle intervention and pharmacological treatment, with the goal of reducing cerebrovascular and global CV events.[19] Concerning hypertension, similar target values as those presented in the general section are recommended for patients with asymptomatic CS.

8.2.2.1.1. Lipid-lowering therapy. See *Section 7*.

8.2.2.1.2. Antihypertensive therapy. See *Section 7*.

8.2.2.1.3. Glucose-lowering therapy. See *Section 7*.

8.2.2.1.4. Antithrombotic therapy. The clinical benefit of antithrombotic treatment in patients with asymptomatic CS remains unproven.[664] The only RCT (the Asymptomatic Cervical Bruit Study [ACB]) addressing the issue enrolled only 188 patients per arm, and failed to show superiority of aspirin vs. placebo in reducing TIA, stroke, MI, or death.[665] In observational studies, SAPT (mainly low-dose aspirin) was associated with reduced risk of MACE, although data were conflicting for moderate stenosis (i.e. 50%–75%);[664] DAPT, combining aspirin and clopidogrel, has no benefit over SAPT.[496,497]

The Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial reported a non-significant decrease in MACE in patients with either history of carotid revascularization or asymptomatic patients with >50% CS and CVRFs allocated to dual antithrombotic therapy (aspirin 100 mg o.d. and rivaroxaban 2.5 mg b.i.d.)

vs. aspirin alone or rivaroxaban 5 mg b.i.d. alone. However, specific data on asymptomatic CS were not reported.

Since these patients present a two times higher risk of MI,[30] lifelong low-dose aspirin should be considered in asymptomatic CS patients at increased risk for CV events (i.e. diabetic patients) and low bleeding risk[497] to reduce stroke and CV risk.[19,299,488,666]

Recommendation Table 24 — Recommendations for antithrombotic treatment in patients with carotid stenosis

Recommendations	Class[a]	Level[b]
Carotid artery disease		
In patients with symptomatic CS, not undergoing carotid endarterectomy or stenting, DAPT with low-dose aspirin and clopidogrel (75 mg) is recommended for the first 21 days or longer, followed by clopidogrel 75 mg or long-term aspirin to reduce the risk of stroke.[667–669]	I	A
In patients with asymptomatic >50% CS, long-term antiplatelet therapy (commonly low-dose aspirin) should be considered if bleeding risk is low.[488,497,670,671]	IIa	C

CS, carotid artery stenosis; DAPT, dual antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

8.2.2.2. Interventional treatment

8.2.2.2.1. Open surgery vs. medical therapy. The rationale for carotid endarterectomy (CEA) in asymptomatic CS stems from two trials that were published some time ago. The Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial 1 (ACST-1) compared CEA with medical therapy in asymptomatic patients with 60%–99% CS.[672–674] In ACAS, 5 year rates of ipsilateral stroke/death under CEA vs. medical therapy were 5.1% vs. 11.0%. ACST-1 reported 5 year rates of any stroke of 6.4% vs. 11.8%, respectively. In a combined analysis of both trials, CEA conferred less benefit in women at 5 years.[675] At 10 years, however, ACST-1[674] reported that females benefit following CEA (absolute risk reduction [ARR] 5.8%) to the same extent as men (ARR 5.5%).

Medical treatment has advanced following the recruitment of patients in these trials.[672–676] A 60%–70% decline in annual stroke rates was also observed in medically treated patients in both trials over 1995 to 2010.[676] This reduction was attributed to better medical treatment and lower smoking incidence. The Stent Protected Angioplasty versus Carotid Endarterectomy study (SPACE-2) compared OMT alone against OMT plus CEA/carotid artery stenting (CAS) in asymptomatic patients with CS ≥70% according to ECST criteria. Due to slow recruitment, the study was underpowered. The 1 year rate of the major secondary endpoint was 2.5% after CEA, 3.0% after CAS, and 0.9% after OMT.[677] Incidence of any stroke or death from any cause within 30 days or any ipsilateral ischaemic stroke within 5 years (primary efficacy endpoint) was 2.5% with CEA plus OMT, 4.4% with CAS plus OMT, and 3.1% with OMT alone. Results from the Carotid Revascularization Endarterectomy vs. Stenting Trial 2 (CREST-2) are awaited to clarify whether intervention is beneficial in the treatment of asymptomatic CS compared with modern OMT.

Table 11 High-risk features associated with increased risk of stroke in patients with asymptomatic internal carotid artery stenosis on optimal medical treatment

Clinical[a]	Contralateral TIA/stroke[681,682]
Cerebral imaging	Ipsilateral silent infarction[683–685]
Ultrasound/CT imaging	Stenosis progression (>20%)[340,684,685] Spontaneous embolization on transcranial Doppler (HITS)[341,686] Impaired cerebral vascular reserve[687,688] Large plaques[689,690] Echolucent plaques[136,691] Increased juxta-luminal black (hypoechogenic) area[689,690]
MRA[b]	Intraplaque haemorrhage[692,693] Lipid-rich necrotic core[694,695]

CT, computed tomography; HITS, high-intensity transient signal; MRA, magnetic resonance angiography; TIA, transient ischaemic attack.
[a]Age is not a predictor of poorer outcome.
[b]More than 40 mm^2 on digital analysis.

The ARR in stroke favouring surgery over OMT was only 4.6% at 10 years in ACST-1, indicating that 95% of asymptomatic patients ultimately underwent unnecessary interventions.[674,678]

A recent meta-analysis confirmed the role of modern OMT in reducing major stroke, combined stroke, and mortality in asymptomatic patients, suggesting that OMT has the potential to reduce the requirement for surgical intervention in patients with asymptomatic carotis stenosis.[679]

In conclusion, for invasive treatment of asymptomatic carotid stenosis, the overall risk reduction is low compared with OMT. Current data are not available to assess subgroups that may still benefit from intervention. However, there is a need to target revascularization in a subgroup of patients with clinical and/or imaging features that increase the risk for stroke on OMT (*Table 11*).[678,680]

Importantly, ACST-1 found no evidence that age >75 years at baseline was associated with any ipsilateral stroke reduction at 5–10 years.[676–678,696] Neither the ACAS nor ACST-1 studies found any evidence that stenosis severity or contralateral occlusion increased late stroke risk.[672,674,697] In a recent meta-analysis, increasing stenosis was associated with late ipsilateral stroke only in the presence of concomitant high-risk features.[698] The general algorithm of CS management is presented in *Figure 18*.[552]

8.2.2.2.2. Carotid revascularization: surgery vs. stenting. In a recent meta-analysis update on RCTs in asymptomatic patients comparing CEA vs. CAS, including altogether 7092 patients, CAS was associated with significantly higher rates of 30 day 'any' stroke and 30 day death/any stroke, while CEA was associated with significantly higher rates of 30 day MI. No significant differences were seen in 30 day death, 30 day disabling stroke, 30 day death/disabling stroke, or 30 day death/any stroke/MI when CAS was compared with CEA.[699] In the largest RCT, ACST-2, post-operative death and major stroke were similar (1.0%) between groups.[700,701]

No significant difference was found in the 5 and 10 year incidence of ipsilateral stroke and any stroke between CEA and CAS.[696,702,703] The 5 year non-procedural stroke rate in ACST-2 was 2.5% in each group for fatal/disabling stroke, and 5.3% with CAS vs. 4.5% with CEA for any stroke.[700,701]

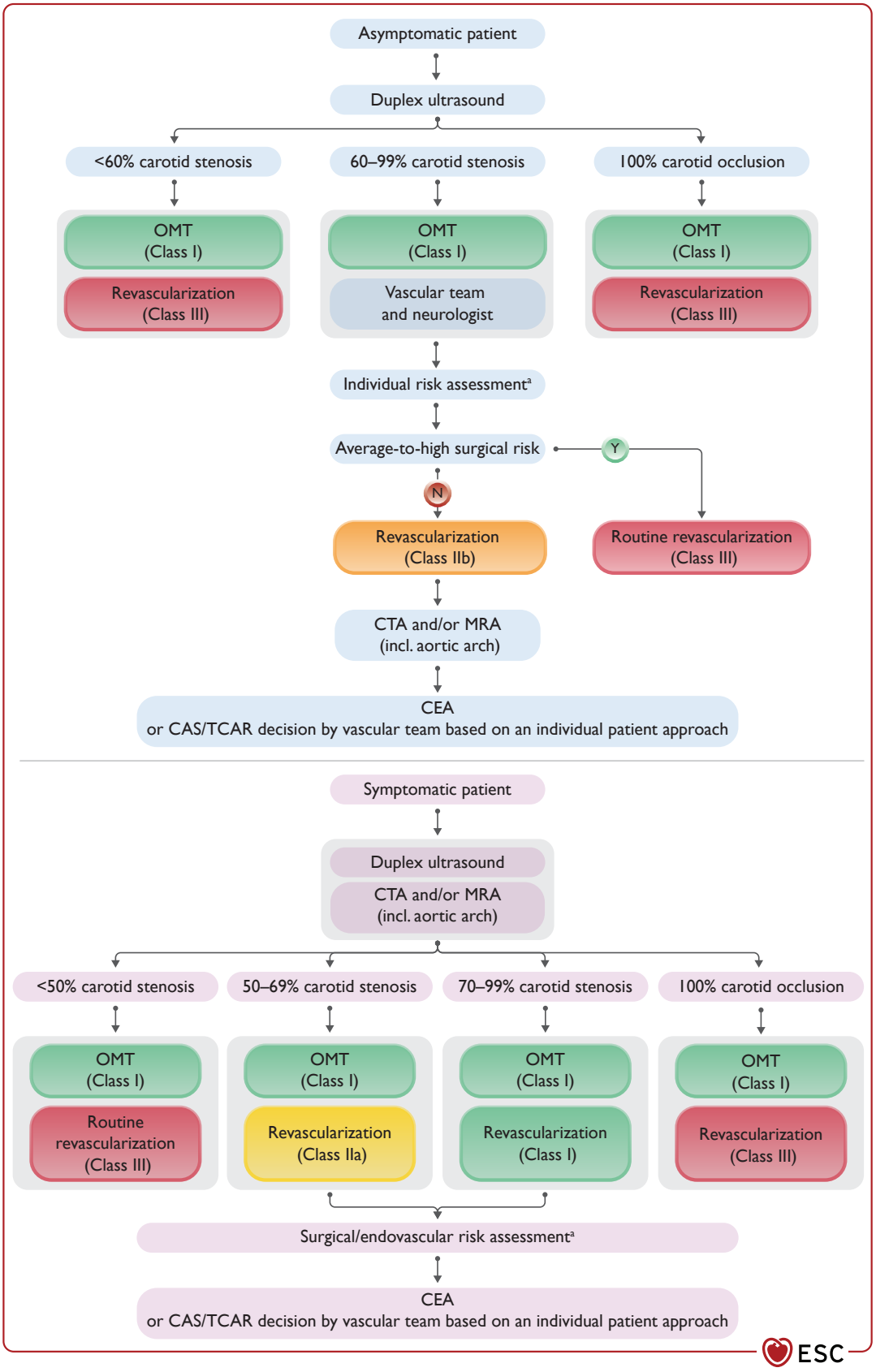

Figure 18 Algorithm of carotid artery stenosis management. CAS, carotid artery stenting; CEA, carotid endarterectomy; CTA, computed tomography angiography; MRA, magnetic resonance angiography; OMT, optimal medical treatment; TCAR, transcarotid artery revascularization; TIA, transient ischaemic attack. [a]Assess presence of high-risk features according to *Table 11*. If surgery/revascularization is considered, assess the overall risk related to surgery according to *Table 12*.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial randomized symptomatic and asymptomatic patients deemed 'high-risk for surgery' to either CEA or CAS (using embolic protection devices).[704] Overall, 71% of SAPPHIRE patients were asymptomatic, and in these patients the 30 day rate of death/stroke after CAS was 5.8% vs. 6.1% after CEA[704]—both beyond the recommended 3%. If these procedural risk levels reflect contemporary practice, most 'high-risk for surgery' asymptomatic patients would be better treated medically.

A small sample size RCT has provided evidence that the use of a double-layer mesh stent can reduce the occurrence of peri-procedural diffusion-weighted imaging (DWI)-detected ischaemic lesion after carotid stents, when compared with conventional stents. At 1 year follow-up the use of a double-layer mesh stent was associated with a significant reduction in the composite endpoint of MACE and in-stent restenosis or occlusion. The clinical benefit of these findings has to be proven.[705,706]

Transcarotid artery revascularization (TCAR) has been introduced recently. Although no RCTs are available, large registry-based analyses report a 99.7% technical success rate and low 30 day complication rates (<3% in 30 day stroke/death and <1% MI).[681]

In a large-scale registry the 1 year rate of stroke or death was 6.4% for TCAR, 5.2% for CEA, and 9.7% for transfemoral carotid artery stenting (TFCAS).[707]

Properly conducted RCTs comparing TCAR with CEA in asymptomatic patients are required to establish the true place of TCAR in carotid revascularization.[708]

Recommendation Table 25 — Recommendations for interventional treatment in patients with asymptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
When ICA revascularization is considered, documented peri-operative stroke/death rates should be <3% and the patient's life expectancy should be considered >5 years after careful consideration of the risks and benefits by a vascular team. [674,709]	IIa	B
In 'average surgical risk' patients over 75 years of age with a CS of 60%–99%, in the presence of high-risk features, CEA, in addition to OMT, should be considered.[674,709]	IIa	B
In 'high surgical risk' patients with a CS of 60%–99%, in the presence of high-risk features, CAS, in addition to OMT, may be considered.[699,701,704]	IIb	B
In 'average surgical risk' patients with a CS of 60%–99%, in the presence of high-risk features, CAS, in addition to OMT, may be considered as an alternative to CEA.[696,701,702,710]	IIb	B
In asymptomatic patients with ICA stenosis, in the absence of high-risk features and with a life expectancy <5 years, routine revascularization is not recommended.[674]	III	A

CAS, carotid artery stenting; CEA, carotid endarterectomy; CS, carotid artery stenosis; ICA, internal carotid artery; OMT, optimal medical treatment.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3. Symptomatic carotid artery stenosis

8.2.3.1. Medical treatment

8.2.3.1.1. Lipid-lowering therapy. See *Section 7*.

8.2.3.1.2. Antihypertensive therapy. See *Section 7*.

8.2.3.1.3. Glucose-lowering therapy. See *Section 7*.

8.2.3.1.4. Antithrombotic therapy. Symptomatic CS is associated with a high risk of early recurrence of cerebrovascular ischaemic events.[667–669,683] DAPT with low-dose aspirin and clopidogrel is recommended for all patients with symptomatic CS for at least 3 months.[669] Those undergoing surgical revascularization can stop clopidogrel after surgery.[711] Those undergoing endovascular revascularization should continue DAPT with clopidogrel and low-dose aspirin for 4 weeks after the procedure.[488,666,711,712] In patients with stroke related to extracranial arterial disease, aspirin was more effective than VKAs in reducing recurrencies.[687,713] Subgroup analysis from the Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes (SOCRATES) trial suggested a lower rate of MACE in patients receiving ticagrelor vs. aspirin;[689] however, this analysis was underpowered to make any conclusions regarding the benefit of ticagrelor.

A combination of aspirin and clopidogrel in the early phase of symptomatic carotid stenosis reduces asymptomatic cerebral embolization and stroke.[692,694,714] It also reduces stroke recurrence after a minor stroke/TIA.[667,668]

Recently, the Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and acetylsalicylic acid for Prevention of Stroke and Death (THALES) trial showed a 17% reduction in the risk of death or stroke when using ticagrelor and aspirin vs. aspirin alone in patients with minor stroke or high-risk TIA;[715] however, bleeding events occurred more frequently in the ticagrelor plus aspirin group.[700,716] Of note, COMPASS data cannot be applied to symptomatic carotid stenosis since these patients were excluded because of intracranial bleeding risk.[499]

Recommendation Table 26 — Recommendations for evaluation and medical treatment in patients with symptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
DAPT is recommended in the early phase of minor strokes in patients with ICA stenosis, if not revascularized, for at least 21 days, considering the bleeding risk.[667,668]	I	A
It is recommended that symptomatic ICA stenosis patients are assessed by a vascular team including a neurologist.[667,668]	I	C
Long-term treatment with SAPT should be considered following ICA revascularization.[667,668]	IIa	C
DAPT may be considered in the early phase of minor stroke in patients with ICA stenosis for up to 90 days, considering the bleeding risk.[667,668]	IIb	B

DAPT, dual antiplatelet therapy (aspirin and clopidogrel); ICA, internal carotid artery; SAPT, single antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3.2. Interventional treatment

8.2.3.2.1. Open surgery. Optimal medical treatment is recommended for all symptomatic patients with CS. In recently symptomatic patients with <50% stenosis, CEA (plus OMT) did not prevent stroke. However, surgery reduced stroke risk in patients with moderate (50%–69%) and severe (70%–99%) stenosis. The benefit from surgery increased with increasing severity of stenosis, except for 'near-occlusion' lesions (95%–99% stenosis with distal ICA collapse or a narrow calibre lumen with 'trickle flow').[660,717–720]

Some features are associated with a higher increase of stroke in symptomatic patients (50%–99% stenosis) medically treated: age (>75 years), symptoms within 14 days, male sex, hemispheric (vs. retinal) symptoms, cortical (vs. lacunar) stroke, increasing comorbidities, irregular stenosis, stenosis severity, contralateral occlusion, tandem intracranial stenosis, and failure to recruit intracranial collaterals.[721]

Large-scale registries suggest that CEA can be performed safely in the first 7 days after TIA/minor stroke.[722–724] However, not all patients benefit from urgent revascularization, and controversy exists over the safety of performing CEA within the first 48 h after symptom onset due to an increased risk of haemorrhagic transformation. Higher-risk patients include those with acute carotid occlusion, a persisting major neurological deficit, an area of middle cerebral artery infarction exceeding one-third, evidence of pre-existing parenchymal haemorrhage, and signs of impaired consciousness.[724,725]

The choice to perform carotid revascularization within 48 h from symptom onset is still debatable.[726]

Table 12 High-risk peri-operative features for carotid endarterectomy

Clinical
Congestive heart failure (NYHA functional class III/IV)
Unstable angina (CCS III/IV)
CAD with LM or >1 vessel with 70% stenosis
Recent MI (<30 days)
Planned open heart surgery (<30 days)
LVEF <30%
Severe pulmonary disease
Severe renal disease
Anatomical
Surgically inaccessible lesions • At or above C2 • Below the clavicle
Ipsilateral neck irradiation
Spinal immobility of the neck
Contralateral carotid artery occlusion (increases risk for stroke)
Contralateral laryngeal palsy
Tracheostomy

CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; LM, left main; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association.

8.2.3.2.2. Endovascular therapy vs. open surgery. Contemporary RCTs comparing CEA with CAS in symptomatic patients reported a significantly higher risk of 30 day 'any stroke' and 'death/stroke' following CAS. This is mainly due to higher rates of minor stroke, which were non-disabling and resolved within 6 months.[711,727]

However, the occurrence of a peri-operative stroke is associated with three-fold poorer long-term survival,[727] similar to a post-procedural MI (which was more frequent after CEA).[728]

In CAS patients, the risk increased in those aged >60 years, especially for those aged >80 years, who are four times more likely to experience a procedural stroke/death. When comparing CAS with CEA, the age-related effect became apparent in patients aged 60–65 years, and CEA is superior to CAS in patients aged >70 years.[729,730]

Elderly CAS patients may experience more peri-operative strokes, mainly minor ipsilateral strokes, possibly due to a higher burden of aortic arch disease. In these cases, operator/institution experience may play a role in determining peri-procedural outcomes. CAS is associated with significantly lower risks for MI, transient cranial nerve injury, and haematoma.[731,732]

Beyond the 30 day peri-operative period, long-term data suggest that outcomes after CAS are similar to those with CEA.[703,733] The predicted magnitude of 30 day risk (according to clinical/anatomical characteristics and operator/centre experience) will thus largely determine whether CEA or CAS is preferable in individual patients.

Post-hoc trial analysis revealed enhanced benefits of CEA when performed within 2 weeks of the ischaemic event,[734] with reduced complications compared with CAS performed within 1 week of stroke/TIA. The Carotid Stenosis Trialists' Collaboration found a higher stroke/death rate (8.3% with CAS vs. 1.3% with CEA) for CAS in patients treated within 1 week of the last symptomatic event.[735] These findings support a preference for early CEA in symptomatic patients. However, these trials, initiated over 30 years ago, lack evaluation of current OMT. Initially designed as an alternative for high surgical risk (HSR) patients,[704,736] carotid stenting's efficacy needs consideration in contemporary practice (*Table 12*).[735]

In conclusion, CEA is still the treatment choice for patients with symptomatic carotid stenosis. However, in patients eligible for carotid revascularization but deemed high surgical risk by a multidisciplinary team, CAS may be preferred over CEA—the patient must be a suitable candidate for CAS, and the complication rate should not surpass 6%.

At present, TCAR results have been analysed in registries only. In these studies, in-hospital stroke/death has been significantly lower after TCAR compared with transfemoral CAS.[707,737] Similar to the previous results established for CEA, symptomatic patients undergoing TCAR demonstrate similar outcomes if the procedure is performed >48 h after the neurological event.[738] However, TCAR has not yet been evaluated in RCTs and has not been compared with CEA or OMT.

8.2.3.2.3. Vertebral arteries. The evidence on the use of lifestyle modifications and medical therapy in cases of symptomatic vertebral artery stenosis is lacking, but their use is reasonable given the overall CV risk in these patients.

Evidence on the use of preventive strategies and antithrombotic agents is lacking, but their use is reasonable in the presence of other CVRFs.

Surgery on extracranial vertebral stenosis (with transposition to CCA, trans-subclavian vertebral endarterectomy, distal venous bypass) can be performed with low stroke/death rates in experienced centres.[739,740] However, with limited expertise in complex vertebral artery reconstructions, open surgery has been mostly replaced by endovascular interventions.

In a combined analysis of the the Vertebral Artery Ischaemia Stenting Trial (VIST), the Vertebral Artery Stenting Trial (VAST), and the Stenting and Aggressive Medical Management for Preventing

Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial,[741] no clear benefit was shown for extracranial vertebral artery stenting.

Randomized controlled trials have not assessed surgical techniques like vertebral artery endarterectomy or transposition. While case series exist, they often lack a control group following a consistent medical treatment protocol.[742] As a result, the effectiveness of these procedures remains uncertain.

Recommendation Table 27 — Recommendations for interventions in patients with symptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
It is recommended to perform CEA of symptomatic 70%–99% ICA stenosis provided a documented 30 day risk of procedural death/stroke is <6%.[660,719]	I	A
If indicated, it is recommended to perform CEA within 14 days in symptomatic ICA stenosis patients.[734]	I	B
OMT is recommended for all symptomatic ICA stenosis patients.[19]	I	A
CEA of symptomatic 50%–69% ICA stenosis should be considered provided a documented 30 day risk of procedural death/stroke is <6%.[660,719]	IIa	A
For symptomatic patients at high risk for CEA with a 70%–99% ICA stenosis, CAS should be considered provided a documented 30 day risk of procedural death/stroke is <6%.[703]	IIa	B
For symptomatic patients <70 years of age with a 70%–99% ICA stenosis, CAS may be considered provided a documented 30 day risk of procedural death/stroke is <6%.[703]	IIb	A
Revascularization is not recommended in patients with ICA lesions <50%.[660,719]	III	A

CAS, carotid artery stenting; CEA, carotid endarterectomy; ICA, internal carotid artery; OMT, optimal medical treatment.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3.3. Follow-up

Peri-operative and post-procedural medical management after carotid revascularization should include OMT. Post-operative hypertension is a risk factor for stroke and TIAs, wound bleeding, and intracranial haemorrhage.[743] Therefore, proper pharmacological BP control is important in optimizing outcomes.[744]

Fluctuations of hypertension and hypotension are not uncommon and should be treated promptly.[744,745]

An intensive lipid-lowering therapy (ILT) aiming at >50% LDL-C reduction and LDL-C <1.4 mmol/L (55 mg/dL) is also recommended.[19]

Antiplatelet therapy should be tailored according to type of intervention. In CEA, the reduction in peri-procedural and long-term ischaemic events under low-dose aspirin has been demonstrated.[746,747] After carotid stenting, DAPT (aspirin and clopidogrel) is recommended, while optimal duration is debated.[748] In the peri-operative period after CAS, DAPT should be prescribed and continued for at least 30 days post-procedure.[77,749,750] Ticagrelor, when included in DAPT following CAS/TCAR, presents a drawback due to its elevated bleeding risk compared with clopidogrel.[751–753]

Duplex ultrasound is the first-line technique to evaluate patients after CEA or CAS. CTA and MRA are alternative methods for determining restenosis.[749,754]

After CEA or CAS, DUS is recommended at baseline (<3 months) and annually thereafter until the patient is stable (i.e. until no restenosis is observed in two consecutive annual scans). Regular surveillance (e.g. every 2 years) can be performed based on the stenosis of the contralateral ICA, risk profile, and patient's life expectancy.[749,754]

For patients combining multiple CVRFs after the procedure, DUS may be beneficial every 6 months until a stable clinical pattern is established, and annually thereafter.[749,754]

Early surveillance, especially within 1–3 months and particularly in cases where intraoperative completion imaging is absent (e.g. after CEA), aids in detecting technical errors and setting a baseline for future comparisons.

Follow-up enables the identification of ipsilateral carotid restenosis and contralateral disease progression, offering a chance for timely intervention to minimize the risk of stroke. Nevertheless, this concept is facing growing challenges due to a reduced and selective role for intervention in asymptomatic patients. A surveillance protocol holds significance when anticipated outcomes are expected to cost-effectively influence a medical or interventional treatment plan.[749,754]

Recommendation Table 28 — Recommendations for follow-up in patients with carotid artery stenosis

Recommendations	Class[a]	Level[b]
Once-yearly follow-up is recommended to check for CVRFs and treatment compliance.[754]	I	A
After ICA stent implantation, DAPT with aspirin and clopidogrel is recommended for at least 1 month.[77,749,750]	I	A
After ICA revascularization, long-term aspirin or clopidogrel is recommended.[746,747]	I	B
During follow-up, it is recommended to assess neurological symptoms, CVRFs, and treatment adherence at least yearly in patients with CS.[754]	I	C
After ICA revascularization, surveillance with DUS is recommended within the first month.[749,754]	I	C

CS, carotid artery stenosis; CVRFs, cardiovascular risk factors; DAPT, dual antiplatelet therapy; DUS, duplex ultrasound; ICA, internal carotid artery.
[a]Class of recommendation.
[b]Level of evidence.

8.3. Other arterial locations

8.3.1. Subclavian artery disease

8.3.1.1. Clinical presentation and diagnosis

Atherosclerotic upper-limb artery disease (UEAD) is most frequently located in the subclavian artery.[755,756] Digital ischaemia is most frequently caused by non-atherosclerotic aetiologies, including thromboembolism, systemic sclerosis, idiopathic, thromboangiitis obliterans, iatrogenic, or cancer.[757] Isolated subclavian stenosis (SS) is often asymptomatic and may be suspected because of an absolute inter-arm SBP difference >10–15 mmHg.[758] In the Multi-Ethnic Study of Atherosclerosis (MESA), prevalence of asymptomatic SS was approximately 4.5% (male: 5.1%, female: 3.9%) in adults and more frequent in patients with PAD (11.4%).[759] In patients attending CV clinics, a

>25 mmHg SBP difference doubles prevalence and independently predicts mortality.[32,758] As obstructive disease progresses, particularly affecting vertebral vessels, the risk of ischaemia or steal symptoms significantly rises. Visual disturbances, syncope, ataxia, vertigo, dysphasia, dysarthria, and facial sensory deficits during arm movements may indicate subclavian steal syndrome, correlating with inter-arm BP difference.[760] Brachiocephalic occlusive disease can lead to stroke or TIA in carotid and vertebral territories, manifesting as exercise-induced fatigue, pain, and arm claudication. Severe cases, especially with distal disease, may result in rest pain and digital ischaemia with necrosis.

Duplex ultrasound assessment of subclavian arteries enables the detection of SS via intrastenotic high-velocity flows (50% stenosis: peak systolic velocity [PSV] ≥230 cm/s, PSV ratio [PSVr] ≥2.2; 70% stenosis PSV ≥340 cm/s and PSVr ≥3.0) or monophasic post-stenotic waveforms.[761] The majority of patients (>90%) with at least 50% proximal SS have either intermittent or continuous flow reversal in the vertebral artery, though not all will be symptomatic.[760,762] When subclavian steal syndrome is suspected, flow reversal should be assessed in the ipsilateral extracranial vertebral artery by hyperaemia testing and if available transcranial Doppler.[762] Severe stenosis or occlusion of the right brachiocephalic trunk is associated with reduced flow velocities in the ipsilateral subclavian artery and the CCA. Abnormal or doubtful DUS should lead to anatomic imaging (CTA/MRA).[763] CTA is excellent for supra-aortic lesions and can provide extravascular information, especially when thoracic outlet syndrome is a differential diagnosis. MRA provides both functional and morphological information useful to distinguish antegrade from retrograde perfusion and to estimate stenosis severity.[764] DSA is performed if endovascular therapy is indicated. PET is useful for the diagnosis of arteritis but not for assessment of atherosclerotic lesions in clinical practice.

8.3.1.2. Treatment strategy (medical and interventional)

Optimal medical treatment is recommended in all patients with symptomatic UEAD to reduce CV risk.[32] Revascularization is indicated in symptomatic patients with TIA/stroke, coronary subclavian steal syndrome, ipsilateral haemodialysis access dysfunction, or impaired HRQoL. Revascularization should be considered in asymptomatic patients with planned coronary artery bypass grafting (CABG) using the internal mammary artery and those with ipsilateral haemodialysis access, as well as asymptomatic patients with significant bilateral SS/occlusion for adequate BP surveillance. For revascularization, both endovascular and surgical procedures are available. There are no RCTs comparing endovascular vs. open repair but individual studies, including the Danish Vascular Registry, indicate similar long-term symptom resolution but higher general complication rates and hospital length of stay for open surgery.[765] The risk of severe complications, including vertebrobasilar stroke, is low with both approaches. The post-procedural stroke rate is reported at 1.3% for endovascular therapy[765] and 0.9%–2.4% after open surgery.[765–767]

Percutaneous angioplasty for subclavian arterial stenosis is often used with stenting. There is no conclusive evidence to determine whether stenting is more effective than balloon angioplasty.[768] Similar results were reported for endovascular therapy of the innominate artery.[769] In heavily calcified ostial lesions, balloon-expandable stents give more radial force than nitinol stents. An endovascular approach is often the default strategy. However, in selected patients with low operative risk, with subclavian artery occlusion or after endovascular therapy failure, surgical subclavian–carotid transposition is safe with excellent long-term patency results (5 year patency 96%).[766] Carotid–subclavian bypass surgery with a prosthetic graft showed long-term benefit with low operative mortality and morbidity, especially in patients with extensive disease or re-occlusion after stenting (5 year patency 97%).[770] Other options are extrathoracic extra-anatomic bypass procedures (axillo-axillary, carotid–axillary, or carotid–carotid bypass);[771,772] however, axillo-axillary bypasses may occlude at 1 year in 14% of cases.[773] The transthoracic approach is an option in patients with multivessel disease involving the aortic arch and several supra-aortic vessels.[767]

While critical hand ischaemia owing to below-the-elbow atherosclerotic occlusive disease is relatively uncommon, interventions are associated with a high rate of success, major amputations are rare, and many can be treated non-operatively.[756] In appropriately selected patients, both endovascular and open interventions have a high rate of success.[755,756]

In symptomatic patients with contraindications for endovascular therapy or open surgery, prostanoid infusion or thoracic sympathectomy may be considered.[774]

8.3.1.3. Follow-up

Patients with UEAD should be followed up to ensure optimal CV prevention. Tighter follow-up is required in symptomatic patients to reassess indication for revascularization as a large proportion of symptoms resolve spontaneously.[775] After revascularization, patients should be followed up to allow early detection and treatment of impending late procedural failure.

Recommendation Table 29 — Recommendations for the management of subclavian artery stenosis (see also Evidence Table 9)

Recommendations	Class[a]	Level[b]
Bilateral arm BP measurement is recommended for all patients with PAAD.[32,758]	I	B
In symptomatic patients with atherosclerotic subclavian artery disease (TIA/stroke, coronary subclavian steal syndrome, ipsilateral haemodialysis access dysfunction, severe ischaemia), both revascularization options (endovascular ± stenting or surgery) should be considered and discussed case by case by a vascular team.[776]	IIa	B
Endovascular revascularization may be considered over surgery, despite similar long-term outcomes, due to lower complication rates.[765]	IIb	B
In patients with atherosclerotic subclavian artery disease, revascularization:		
Should be considered in cases of proximal stenosis in patients undergoing CABG using the ipsilateral internal mammary artery.[777–781]	IIa	C
Should be considered in cases of proximal stenosis in patients who already have the ipsilateral internal mammary artery grafted to coronary arteries with evidence of myocardial ischaemia.[777,778,780]	IIa	C
Should be considered in cases of ipsilateral haemodialysis arteriovenous access.[778]	IIa	C
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.[776]	III	C

BP, blood pressure; CABG, coronary artery bypass grafting; PAAD, peripheral arterial and aortic diseases; TIA, transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.

8.3.2. Renal artery disease

8.3.2.1. Clinical presentation and diagnosis

8.3.2.1.1. Epidemiology. In >90% of cases, RAS is caused by atherosclerosis and typically involves the ostial renal arterial segment (*Table 13*).[782] Above 65 years of age, overall prevalence of ≥60% RAS is 6.8%, with a higher prevalence in men (9.1%) than in women (5.5%).[783] In patients with PAD, RAS prevalence ranges between 7% and 42%, influenced by diagnostic criteria.[784]

8.3.2.1.2. Clinical presentation. Clinical presentation comprises renovascular hypertension, renal function impairment and eventually, flash pulmonary oedema (*Table 13*). RAS reduces the filtration capacity of the affected kidney, which activates the renin–angiotensin–aldosterone pathway, potentially resulting in renovascular hypertension.[782,785] In unilateral RAS, the functioning contralateral kidney may increase sodium excretion to prevent sodium retention and volume overload. In high-grade bilateral RAS or in unilateral RAS without a functioning second kidney, the risk of cardiorenal deterioration is higher than in unilateral disease.[786]

8.3.2.1.3. Diagnosis of renal artery disease. First diagnostic steps include laboratory tests to examine renal function, analysis of office and out-of-office BP recordings (ambulatory BP monitoring or home BP monitoring, as recommended by [upcoming] ESC/European Society of Hypertension [ESH] Guidelines for arterial hypertension), and non-invasive haemodynamic assessment of renal arteries by DUS.[787]

Renal artery PSV >200 cm/s measured by DUS allows the diagnosis of a >50% RAS (sensitivity 95%, specificity 90%).[788] A renal-aortic peak flow velocity ratio (RAR = renal artery PSV/aortic PSV) >3.5 has 84%–91% sensitivity and 95%–97% specificity for the detection of ≥60% RAS.[789] A side-to-side difference of the intrarenal resistance index ≥0.5 between both kidneys may serve as an additional haemodynamic criterion for haemodynamically relevant RAS.[787,790] Other DUS criteria (acceleration time, acceleration index) have lower diagnostic accuracy.[791]

Sensitivity and specificity of contrast-enhanced MRA in the diagnosis of RAS is 88% and 100%, respectively;[789] however, MRA overestimates the degree of RAS by 26%–32%.[789] The advantages of MRA are the possibility of assessing renal parenchymal blood flow and freedom from radiation and iodinated contrast agents.

Spiral multidetector CTA allows renal artery diameter measurements and provides information on vessel wall calcification and mural plaques. RAS diagnosis by CTA presents 64%–100% sensitivity and 92%–98% specificity.[789] CTA drawbacks include radiation exposure, the need for contrast media in patients with impaired renal function, and limited haemodynamic assessment of RAS.

Catheter angiography is the gold standard for diagnosing RAS, enabling additional haemodynamic measures (*Figure 19*).[792] Considering the potential risks of invasive procedures, DUS and other non-invasive modalities (CTA or MRA) should precede catheter angiography and invasive haemodynamic measurements (*Figure 19*).

Renal scintigraphy, plasma renin measurements before and after ACEI provocation, and venous renin measurements are not considered for RAS evaluation.

8.3.2.1.4. Prognosis. Atherosclerotic RAS progresses with respect to the degree of stenosis, while total renal artery occlusions occur less frequently.[793] The presence of significant RAS is a strong predictor for mortality[794] and renovascular disease is an important risk factor for the development of end-stage renal disease (ESRD).[795] The risk of RAS-related ESRD is higher in men than in women and increases with age.[795]

Table 13 Clinical signs suggestive of renal artery disease

Hypertension onset before 30 years of age
Severe hypertension after the age of 55 years, when associated with CKD or heart failure
Hypertension and abdominal bruit
Rapid and persistent worsening of previously controlled hypertension
Resistant hypertension • Three antihypertensive drugs including a diuretic agent or • ≥4 antihypertensive drugs and • Other secondary form unlikely
Hypertensive crisis (i.e. acute renal failure, acute heart failure, hypertensive encephalopathy, or grade 3–4 retinopathy)
New azotaemia or worsening of renal function after treatment with RAAS blockers
Unexplained atrophic kidney or discrepancy in kidney size, or unexplained renal failure
Flash pulmonary oedema

CKD, chronic kidney disease; RAAS, renin–angiotensin–aldosterone system.

8.3.2.2. Treatment strategy (medical and interventional)

8.3.2.2.1. Medical therapy. Optimal medical treatment is recommended in RAS patients.[785] Data on antithrombotic therapy in patients with atherosclerotic RAS are scarce and retrospective.[796] However, the use of an antiplatelet agent is reasonable in atherosclerotic RAS.

No prospective study has specifically examined antithrombotic therapy post-RAS stenting, and information from existing RAS stenting trials is limited.[797] Following the antithrombotic treatment approach in non-coronary arterial beds, it is suggested to use DAPT for at least 1 month after RAS stent implantation.[666]

8.3.2.2.2. Revascularization. Revascularization in atherosclerotic RAS

Prospective RCTs comparing endovascular revascularization with OMT in atherosclerotic RAS favoured renal artery stenting over balloon angioplasty.[792]

However, renal artery stenting showed no superiority over OMT in reducing BP, CV events, renal events, or mortality in unilateral atherosclerotic RAS.[788,798,799] A trial suggested a potential benefit of renal artery angioplasty for BP in bilateral RAS, but subsequent RCTs did not confirm this.[800–802] Data on the benefit of renal artery stenting in sparing antihypertensive drugs are inconsistent.[324,800,801,803,804]

In specific circumstances or RAS aetiologies, revascularization should be considered (*Figure 19*). Open surgical renal artery revascularization appears comparable to endovascular treatment regarding BP and renal function.[805,806] Thus, open surgery can be an alternative approach in cases with a revascularization indication and complex anatomy or failed endovascular repair.

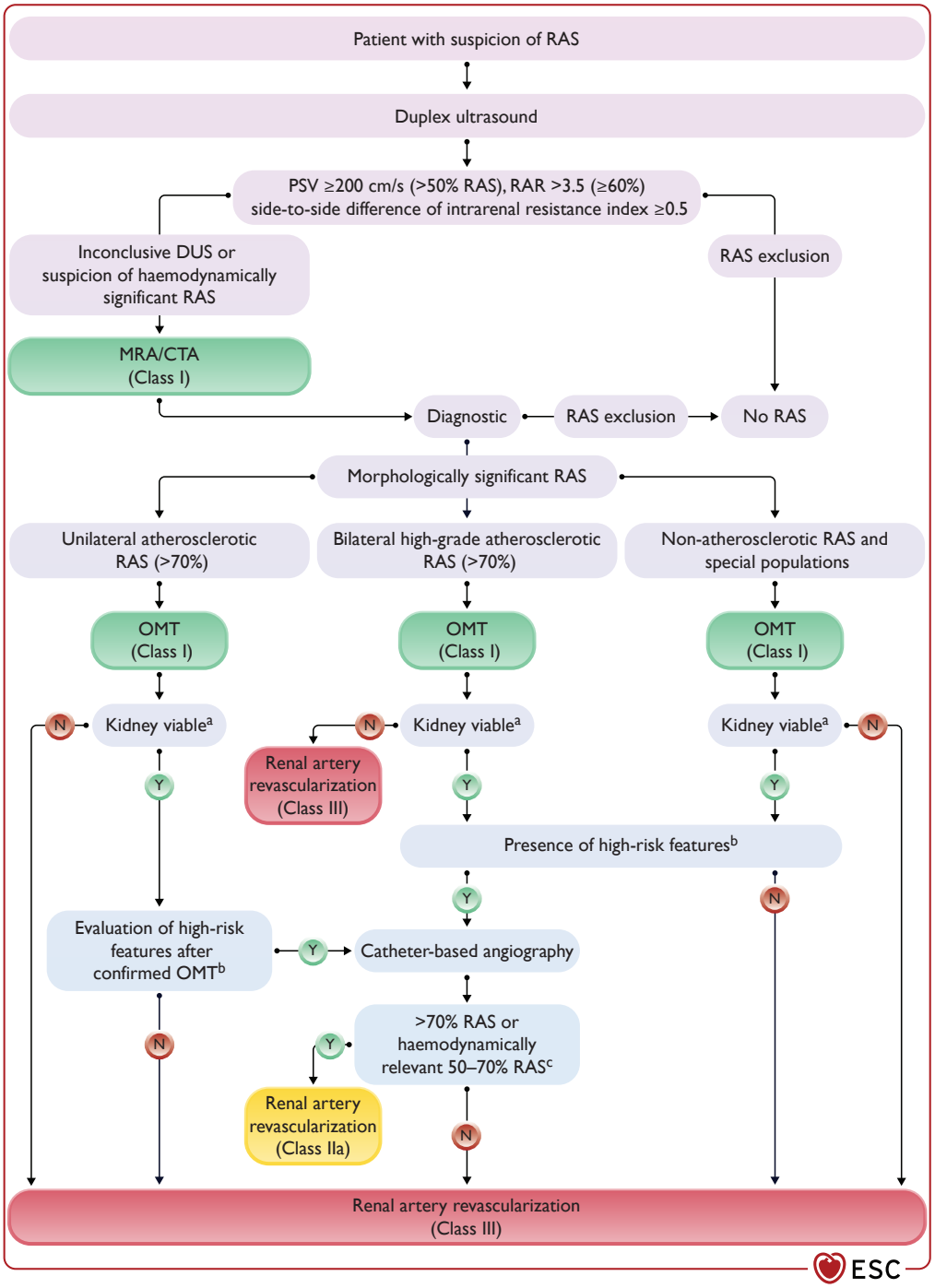

Figure 19 Diagnostic and treatment algorithm for renal artery stenosis. CTA, computed tomography angiography; MRA, magnetic resonance angiography; OMT, optimal medical treatment; Pd/Pa, distal coronary pressure to aortic pressure ratio; PSV, peak systolic velocity; RAR, renal-aortic peak flow velocity ratio; RAS, renal artery stenosis.
[a]see table below

[a]Kidney viability in RAS		
	Signs of viability	Signs of non-viability
Renal size	>8 cm	<7 cm
Renal cortex	Distinct cortex (>0.5 cm)	Loss of corticomedullar differentiation
Proteinuria	Albumin-creatinine ratio <20 mg/mmol	Albumin-creatinine ratio >30 mg/mmol
Renal resistance index	<0.8	>0.8

[b]Rapidly progressive, treatment-resistant arterial hypertension; rapidly declining renal function; flash pulmonary oedema; solitary kidney.
[c]Resting mean pressure gradient >10 mmHg; systolic hyperaemic pressure gradient >20 mmHg; renal PdPa ≤ 0.9 (or 0.8).

8.3.2.3. Follow-up

Following the diagnosis of significant RAS and the implementation of OMT and/or renal artery revascularization, regular follow-up exams are crucial. Monitoring should encompass laboratory tests to assess renal function, analysis of office and out-of-office BP recordings (ambulatory or home BP monitoring per upcoming ESC/ESH Guidelines for arterial hypertension), and renal artery DUS. DUS, comprising renal PSV, RAR, side-to-side difference of the resistance index, and kidney size, is the preferred imaging modality during follow-up.[787]

In conservatively managed RAS patients, follow-up assessment should re-evaluate potential indications for renal artery revascularization (*Figure 19*).

After renal artery stenting, the initial follow-up is recommended at 1 month and subsequently every 12 months or when new signs or symptoms arise.[807] Re-intervention may be considered for in-stent restenosis ≥60% detected by DUS, recurrent signs and symptoms (diastolic BP >90 mmHg on >3 antihypertensive drugs, or a >20% increase in serum creatinine).[787,808]

Recommendation Table 30 — Recommendations for diagnostic strategies for renal artery disease

Recommendations	Class[a]	Level[b]
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.[787,789–791]	I	B
In cases of DUS-based suspicion of RAS or inconclusive DUS, MRA, or CTA are recommended.[789,791]	I	B
In patients with atherosclerotic RAS, it is recommended to assess clinical high-risk features and kidney viability when evaluating renal artery revascularization.[809,810]	I	B

CTA, computed tomography angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography; RAS, renal artery stenosis.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 31 — Recommendations for treatment strategies for renal artery disease (see also Evidence Table 10)

Recommendations	Class[a]	Level[b]
Medical therapy		
In patients with atherosclerotic RAS the use of low-dose aspirin may be considered.[811]	IIb	C
Revascularization		
In patients with atherosclerotic unilateral >70% RAS, concomitant high-risk features, and signs of kidney viability, renal artery revascularization should be considered after OMT has been established.[798,809,810]	IIa	B
In patients with atherosclerotic bilateral (>70%) RAS or RAS in a solitary kidney, concomitant high risk features, and signs of kidney viability, renal artery revascularization should be considered.[800–802]	IIa	B
In patients with hypertension and/or signs of renal dysfunction due to RAS caused by fibromuscular dysplasia, concomitant high-risk features, and signs of kidney viability, revascularization with primary balloon angioplasty and bailout stenting should be considered.[812,813]	IIa	B
In patients with an indication for renal artery revascularization and complex anatomy, or after failed endovascular revascularization, open surgical revascularization should be considered.[805,806]	IIa	B
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.[324,800–804,814]	III	A

Continued

RAS, renal artery stenosis.
[a]Class of recommendation.
[b]Level of evidence.

8.3.3. Visceral artery disease

8.3.3.1. Acute mesenteric ischaemia

Acute mesenteric ischaemia can be caused by arterial embolism or thrombosis *in situ*, non-occlusive mesenteric ischaemia (usually due to superior mesenteric artery [SMA] vasoconstriction), and venous thrombosis. In recent decades, embolism decreased from 46% to 35%, while arterial thrombosis increased from 20% to 35%.[815–817] Acute thrombo-embolic occlusion most frequently affects the SMA. Due to extensive collaterals, it infrequently leads to intestinal infarction.

8.3.3.1.1. Clinical presentation and diagnosis. Clinical examination

Early diagnosis of AMI is based on high clinical suspicion. Embolic AMI typically manifests as sudden onset intense abdominal pain, accompanied by minimal physical findings, bowel emptying (vomiting, diarrhoea), and a common embolic source (primarily AF).[818–820] Emboli may also lodge in other locations, aiding diagnosis. Acute arterial thrombosis tends to occur in areas with pre-existing atherosclerotic disease, resulting in a less dramatic clinical presentation. Patients may have previous symptoms of chronic mesenteric ischaemia (CMI) or other atherosclerotic manifestations.[821]

Laboratory tests are unreliable for the diagnosis of AMI, although elevated levels of l-lactate, leucocytosis, and D-dimer (DD) may exist.[822–825]

Imaging

Computed tomography angiography is the gold standard for diagnosis,[826,827] allowing the detection of thrombi and/or emboli in the SMA trunk or its branches together with the recognition of intestinal ischaemic signs. A plain abdominal X-ray lacks specificity. A normal result does not rule out the diagnosis.[828]

8.3.3.1.2. Treatment strategy. Most patients require immediate revascularization to survive. There are no RCTs comparing surgical vs. endovascular intervention in AMI. Two meta-analyses found endovascular revascularization to be superior to surgical intervention in terms of in-hospital mortality and rates of bowel resection.[829,830] An open surgical approach is most appropriate in centres where endovascular interventions are less available and in patients with peritonitis.[831] Retrograde open mesenteric stenting (ROMS) is an alternative that offers shorter operative time; the SMA is punctured in the open abdomen, followed by stenting.[832]

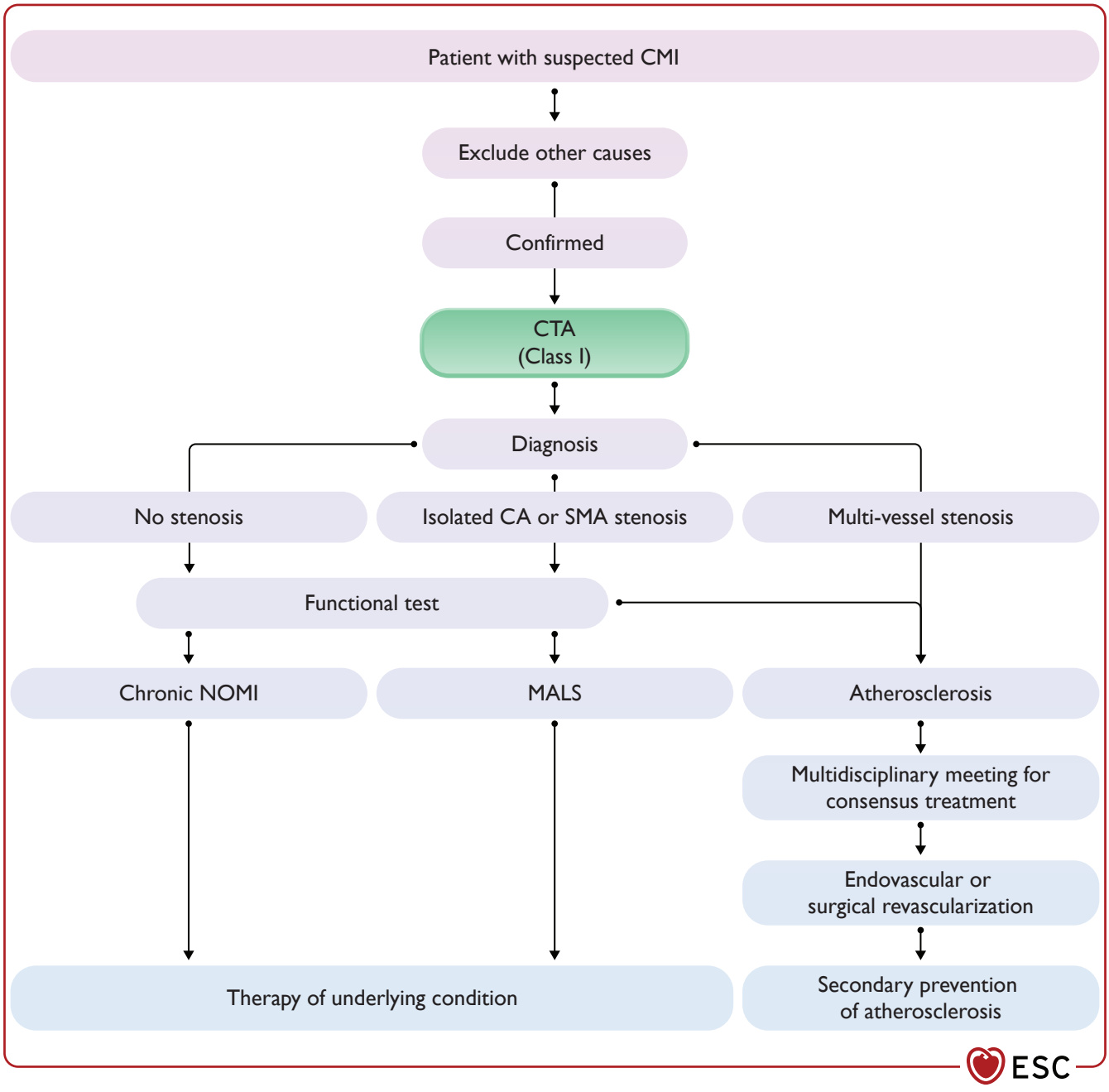

Figure 20 Algorithm of chronic mesenteric ischaemia management. CA, coeliac artery; CMI, chronic mesenteric ischaemia; CTA, computed tomography angiography; MALS, median arcuate ligament syndrome; NOMI, non-occlusive mesenteric ischaemia; SMA, superior mesenteric artery.

8.3.3.1.3. Follow-up. Most patients treated for AMI require lifelong anticoagulant/antiplatelet therapy to prevent recurrence. Patients undergoing revascularization should have surveillance with CTA or DUS within 6 months,[833] as recurrent AMI after mesenteric revascularization accounts for 6%–8% of late deaths.[834] Current Society for Vascular Surgery (SVS) Guidelines recommend DUS at 1, 6, and 12 months after the intervention, and then annually thereafter.[754]

8.3.3.2. Chronic mesenteric artery disease

Occlusive CMI is mostly caused by atherosclerosis and more frequently affects females (65%–72%).[835,836] Symptoms typically manifest when at least two mesenteric vessels are involved due to extensive collaterals. Prevalence of asymptomatic coeliac artery and/or SMA stenosis is 3% in patients under 65 years of age and 18% in those aged >65.[837] However, inadequate anastomoses can result in symptomatic ischaemia even with a single-vessel atherosclerotic occlusion.[838,839]

8.3.3.2.1. Clinical presentation and diagnosis. Clinical examination

Like AMI, early diagnosis of CMI relies on clinical suspicion. Classic symptoms include post-prandial abdominal pain, weight loss, and gastrointestinal disturbances like diarrhoea or constipation. Patients may develop food aversion to avoid pain, but their appetite remains

unaffected, distinguishing them from individuals with malignancies. An abdominal examination might reveal a bruit.

Lactate, lactate dehydrogenase, and/or leucocyte count are unhelpful in CMI diagnosis.[840,841] Functional testing (tonometry, visible light spectroscopy) is applicable in patients with symptomatic mesenteric stenosis and single-vessel disease.[842]

Imaging

Duplex ultrasound is valuable due to its low costs, absence of the need for contrast agents, and no radiation. However, skilled investigators in specialized centres are required for the examination. Despite suggested diagnostic criteria, consensus is lacking.[843,844] Anatomical mapping for treatment planning typically involves CTA or MRA,[845,846] with DSA reserved only for therapeutic purposes (*Figure 20*).

8.3.3.2.2. Treatment strategy. Optimal medical treatment is the basis of CMI management. Prophylactic revascularization is not recommended for asymptomatic CMI. In symptomatic cases, a meta-analysis favoured endovascular over open surgery due to fewer complications and a trend towards lower 30 day mortality.[835] However, open surgery showed superior long-term results, with fewer symptom recurrences and higher 1 and 5 year primary patency rates in two additional meta-analyses.[847,848] Despite the growing use of endovascular therapy, open surgery remains indicated after failed endovascular therapy without the option for repeat intervention, and in cases with extensive occlusions, calcifications, or technical challenges.

8.3.3.2.3. Follow-up. Following CMI revascularization, lifelong medical treatment, including lifestyle changes and OMT for atherosclerosis, is recommended. SVS guidelines propose mesenteric DUS surveillance for recurrent stenosis. A potential follow-up schedule involves controls within 1 month post-procedure, biannually for the first 2 years, and annually thereafter.[849]

Recommendation Table 32 — Recommendations in patients with visceral artery stenosis

Recommendations	Class[a]	Level[b]
In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.[829–831]	I	B
In patients with suspected acute or chronic mesenteric ischaemia, CTA is recommended.[826,827,845,846]	I	C
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C

CTA, computed tomography angiography; SMA, superior mesenteric artery.
[a]Class of recommendation.
[b]Level of evidence.

9. Aorta

9.1. Atheromatous disease of the aorta

9.1.1. General concepts

Atheromatous disease of the aorta has an estimated incidence of 40%–51.3%, being complicated in 7.6% of cases.[850–853] Earlier stages of atherosclerosis, presenting as plaque inflammation, can be present in 48% of asymptomatic individuals.[850] Atherosclerotic plaque classification is based on plaque thickness and the presence of ulceration or mobile components (*Table 14*).[159,171,854] This classification is crucial because severe or complex atherosclerotic plaques in the aortic arch or ascending aorta are strongly linked to cerebrovascular events (odds ratio [OR] 4–9.1 for plaques ≥4 mm).[855–860] Additionally, the annual incidence of stroke recurrence remains high (up to 16%) despite antiplatelet or anticoagulant therapy.[855,861]

9.1.2. Treatment

9.1.2.1. Primary prevention

Asymptomatic non-severe/non-complex aortic plaques (*Table 14*) should not mandate antiplatelet therapy. Nonetheless, in severe/complex plaques, statins should be indicated to decrease plaque progression or CV events,[862] and SAPT with clopidogrel or low-dose aspirin should be considered after risk/benefit evaluation.[493,666,861,863] However, in this scenario, anticoagulation[861] or DAPT (low-dose aspirin and clopidogrel) are not indicated.[666,863] Floating aortic thrombi and complex mobile plaques are rare, with limited large-scale trials on their management. Guidance relies on case reports, observational studies, and expert opinions, yet there is evidence favouring anticoagulation, particularly for symptomatic cases.[864]

9.1.2.2. Secondary prevention

Secondary prevention with antiplatelet therapy after an embolic event is recommended to prevent recurrences.[666,865,866] While the value of DAPT vs. SAPT remains uncertain, recent studies indicate that prolonged DAPT raises bleeding risk without added antithrombotic benefits.[667,863,867] Treatment duration is unclear and must strike a balance between early benefit (notably within 7 days post-emboli) and steady bleeding risk. Statins (LDL target below 1.4 mmol/L [55 mg/dL]) prove effective in preventing strokes regardless of the aetiology.[862,865,868] Additionally, a healthy lifestyle is crucial for improving CV health and reducing complications.

Recommendation Table 33 — Recommendations for primary and secondary prevention in aortic atheromatous plaques

Recommendations	Class[a]	Level[b]
Primary prevention		
In patients with severe/complex aortic atheromatous plaques, statins should be considered to decrease progression and risk of CV events.[862]	IIa	C
SAPT with clopidogrel or low-dose aspirin should be considered in severe/complex plaques.[493,666,861,863]	IIa	C
Anticoagulation[861] or DAPT[863] are not recommended in aortic plaques since they present no benefit and increase bleeding risk.[666]	III	C
Secondary prevention after an embolic event related to aortic atherosclerosis		
In patients with an embolic event and evidence of an aortic arch atheroma, intensive lipid management to an LDL-C target <1.4 mmol/L (<55 mg/dL) is recommended to prevent recurrences.[242,862,865,868]	I	A
In patients with an embolic event and evidence of an aortic arch atheroma, SAPT is recommended to prevent recurrences.[666,865,866]	I	C

CV, cardiovascular; DAPT, dual antiplatelet therapy; LDL-C, low-density lipoprotein cholesterol; SAPT, single antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

Table 14 Grading of atherosclerotic aortic plaques

Grade	Severity (atheroma thickness)	Description
1	Normal	Intimal thickness <2 mm
2	Mild	Intimal thickening of 2 to <3 mm
3	Moderate	Atheroma ≥3 to <4 mm (no mobile/ulcerated components)
4	Severe	Atheroma ≥4 mm (no mobile/ulcerated components)
5	Complex	Grade 2, 3, or 4 atheroma plus mobile/ulcerated components

9.2. Aortic aneurysms

9.2.1. General concepts

9.2.1.1. Definitions

Aortic dilatation, the second most frequent aortic disease after atherosclerosis, is defined as an aortic diameter >2 standard deviations of the predicted mean diameter depending on age, sex, and body size (z-score >2). However, in clinical practice, aortic root dilatation can be suspected in male adults when aortic diameter is >40 mm and in females at >36 mm,[138,149,869] or with an indexed diameter/BSA (aortic size index [ASI]) >22 mm/m^2. In extreme BSA and age values, use of z-scores is recommended (see *Section 5.4* for their calculation).

Arterial aneurysm is defined as a diameter >1.5 times (>50%) larger than the predicted one. This definition, as well as the use of z-scores, introduces the need for normal values and correction for age, sex, and body size. However, correcting for BSA can lead to underestimation in overweight patients,[870] therefore a correction for height (aortic height index [AHI]) is becoming more popular.[153] In terms of clinical risk, both ASI and AHI have been shown to improve risk stratification for AAE.[153,871] Since in many cases of aortic dilatation the surgical indication is established before achieving this aneurysmal diameter, we strongly recommend the use of *significant aortic dilation* specifying the diameter or the indexed diameter value rather than the term 'aneurysm'.

Thoracic aortic aneurysms (TAAs) are more prevalent in men than in women (ratio 4:1);[872] however, the growth rate is greater in women (0.96 ± 1.00 mm per year) than in men (0.45 ± 0.58 mm per year), and thus the risk of AAE.[873]

Aneurysms can be fusiform or saccular based on morphology. Saccular aneurysms relate to infection, penetrating atherosclerotic ulcer (PAU), trauma, or inflammatory diseases, while fusiform aneurysms connect with degenerative and connective tissue conditions. Although evidence about their natural course is limited, saccular aneurysms are considered more malignant in terms of AAE. Based on location, aortic aneurysms are classified into TAA and abdominal aortic aneurysm (AAA) (*Figure 21*). They differ in treating specialists, causes, age at onset, risk factors, and complications. However, this binary classification is artificial due to the prevalence of thoracoabdominal aortic aneurysms (TAAA) and tandem lesions (20%–30% of AAA patients also have TAA),[874,875] emphasizing the importance of comprehensive aortic and vascular assessments at diagnosis. When detecting an aortic aneurysm at any site, it is advisable to conduct a thorough evaluation of the entire aorta initially and during subsequent follow-ups. Specifically, when diagnosing a TAA, it is crucial to assess the aortic valve, particularly in cases of BAV. Data on peripheral aneurysms in TAA, particularly in femoro-popliteal segments, is less clear compared with AAA. However, cerebral aneurysms, notably prevalent in women and those with HTAD, warrant thorough screening, particularly in symptomatic cases.[876–878]

Recommendation Table 34 — Recommendations for initial evaluation of thoracic aortic aneurysm and abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
When an aortic aneurysm is identified at any location, assessment of the entire aorta is recommended at baseline and during follow-up.[874,875]	I	C
When a TAA is identified, assessment of the aortic valve (especially for BAV) is recommended.[879,880]	I	C
When an AAA is identified, evaluation of the presence of aneurysm in the femoro-popliteal arterial segment should be considered.[876–878,881]	IIa	C
Patients with aortic aneurysm are at increased risk of CVD, thus general CV prevention should be considered.[26,882,883]	IIa	C

AAA, abdominal aortic aneurysm; BAV, bicuspid aortic valve; CV, cardiovascular; CVD, cardiovascular disease; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.

9.2.2. Thoracic aortic aneurysms

9.2.2.1. Aetiology, risk factors, and natural history

Thoracic aortic aneurysms occur in 5–10/100 000 person-years,[884] with an approximate predominance of root and/or ascending aorta of ∼60%, arch of ∼10%, and descending aorta of ∼30%.[885,886]

Hypertension is the main risk factor (80%); however, genetics may be involved in 20% of cases.[887] The decision to refer patients for genetic evaluation should consider age, family history, and presence of syndromic features,[25,888] as reported in more detail in *Section 10.1*.

9.2.2.2. Ascending thoracic aorta and arch aneurysms

(1) **Aortic root aneurysms** (including sinuses of Valsalva: annuloaortic ectasia). They can be idiopathic, associated with HTAD (syndromic/non-syndromic), or found in 20%–30% of BAV patients (see *Section 10*).[879,880] Patients are usually younger (30–50 years of age), with aortic regurgitation, and with a 1:1 sex ratio.

(2) **Supra-coronary aortic aneurysms** (above sinuses of Valsalva). Caused by atherosclerosis in relation to hypertension affecting older patients (59–69 years) and males (ratio 3:1),[880] or related to medial degeneration (isolated or associated with aortic valve disease, including BAV) (see *Section 10*). Primary bacterial infection or syphilis are uncommon. Arteritis is rare, but Takayasu's and giant cell arteritis can lead to aneurysm formation.

(3) **Aortic arch aneurysms.** Often accompanying adjacent ascending or descending aorta aneurysms, aortic arch aneurysms present surgical challenges due to potential neurological and CV risks. They are typically linked to atherosclerosis, with cystic medial degeneration primarily affecting ascending aorta-related arch aneurysms. Deceleration injuries or coarctation may extend into the aortic arch.[889]

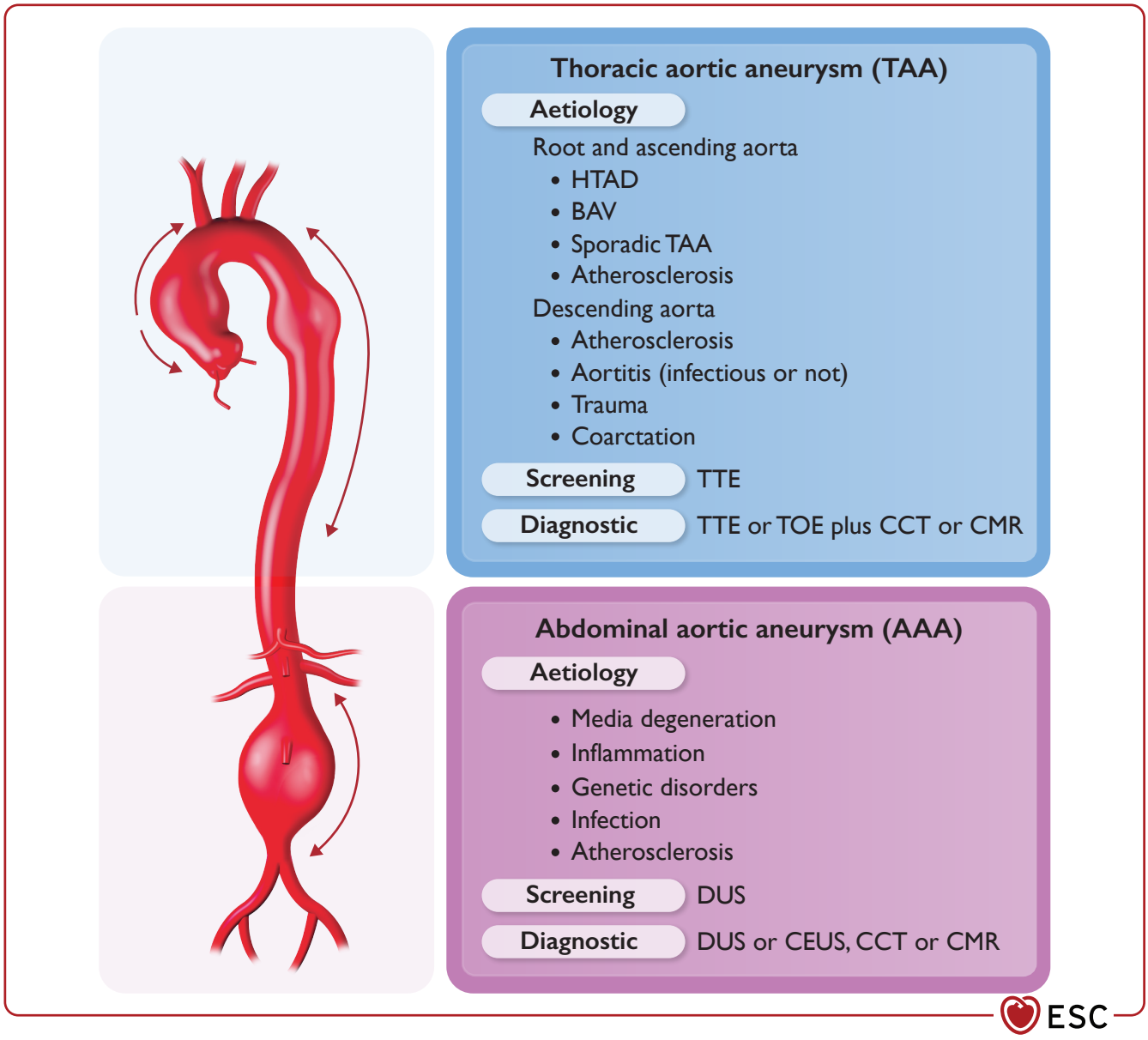

Figure 21 Thoracic and abdominal aortic aneurysms: aetiology, screening and diagnostic methods. AAA, abdominal aortic aneurysm; BAV, bicuspid aortic valve; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced Doppler ultrasound; CMR, cardiovascular magnetic resonance; DUS, Doppler ultrasound; HTAD, heritable thoracic aortic disease; TAA, thoracic aortic aneurysm; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Thoracic aortic aneurysm patients are usually asymptomatic, diagnosed incidentally during unrelated imaging or screenings. Symptoms such as chest pain, aortic regurgitation, and compression-related issues may occur.[890] Patients with aortic root involvement (as seen in HTAD) are more prone to suffer from AAE.[891,892]

Thoracic aortic aneurysm growth rate is variable, associated with aetiology, location, and baseline aortic diameter.[893–895] Degenerative TAAs grow faster in women than men and are associated with a threefold higher risk of AAE.[24,873,896] When the aorta reaches 57.5 mm in size, reported yearly rates of rupture, dissection, and death are 3.6%, 3.7%, and 10.8%, respectively.[897–899]

9.2.2.3. Descending thoracic aorta and thoracoabdominal aorta aneurysms

They can involve different parts of the DTA and may extend to the AA: TAAA. TAAAs are divided into five groups[900] according to the modified TAAA classification scheme (*Figure 22*), which is crucial for risk stratification. By classifying aneurysm extent, surgeons can anticipate procedure complexity, select suitable techniques, and reduce risks during surgical planning.

Most DTA aneurysms and TAAA are degenerative with calcification, although other causes include trauma, infection, inflammation, or genetic factors[901,902] (*Figure 21*). Patients with HTAD rarely develop

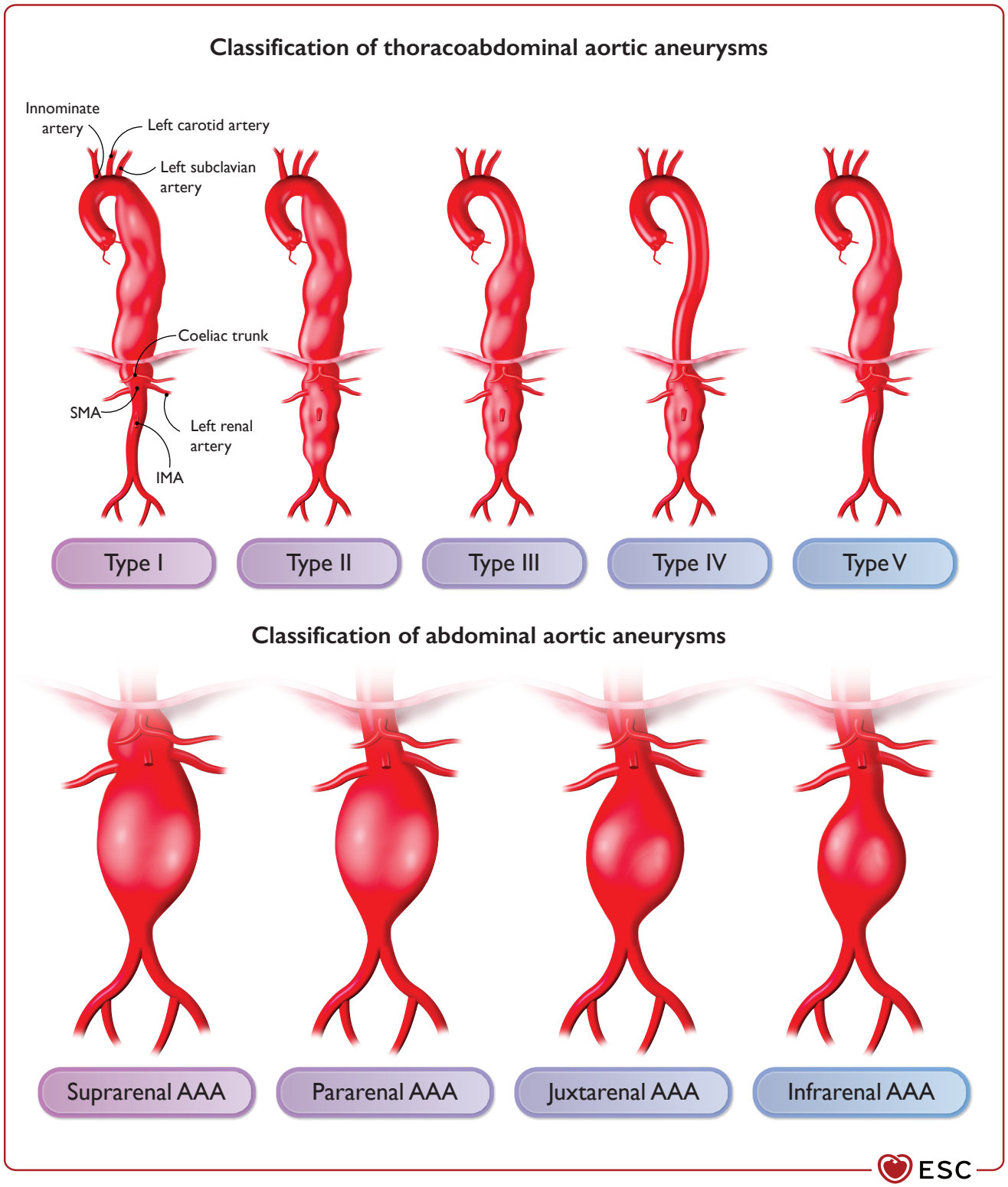

Figure 22 Classification of thoracoabdominal[900] and abdominal aortic aneurysms. AAA, abdominal aortic aneurysm; IMA, inferior mesenteric artery; SMA, superior mesenteric artery.

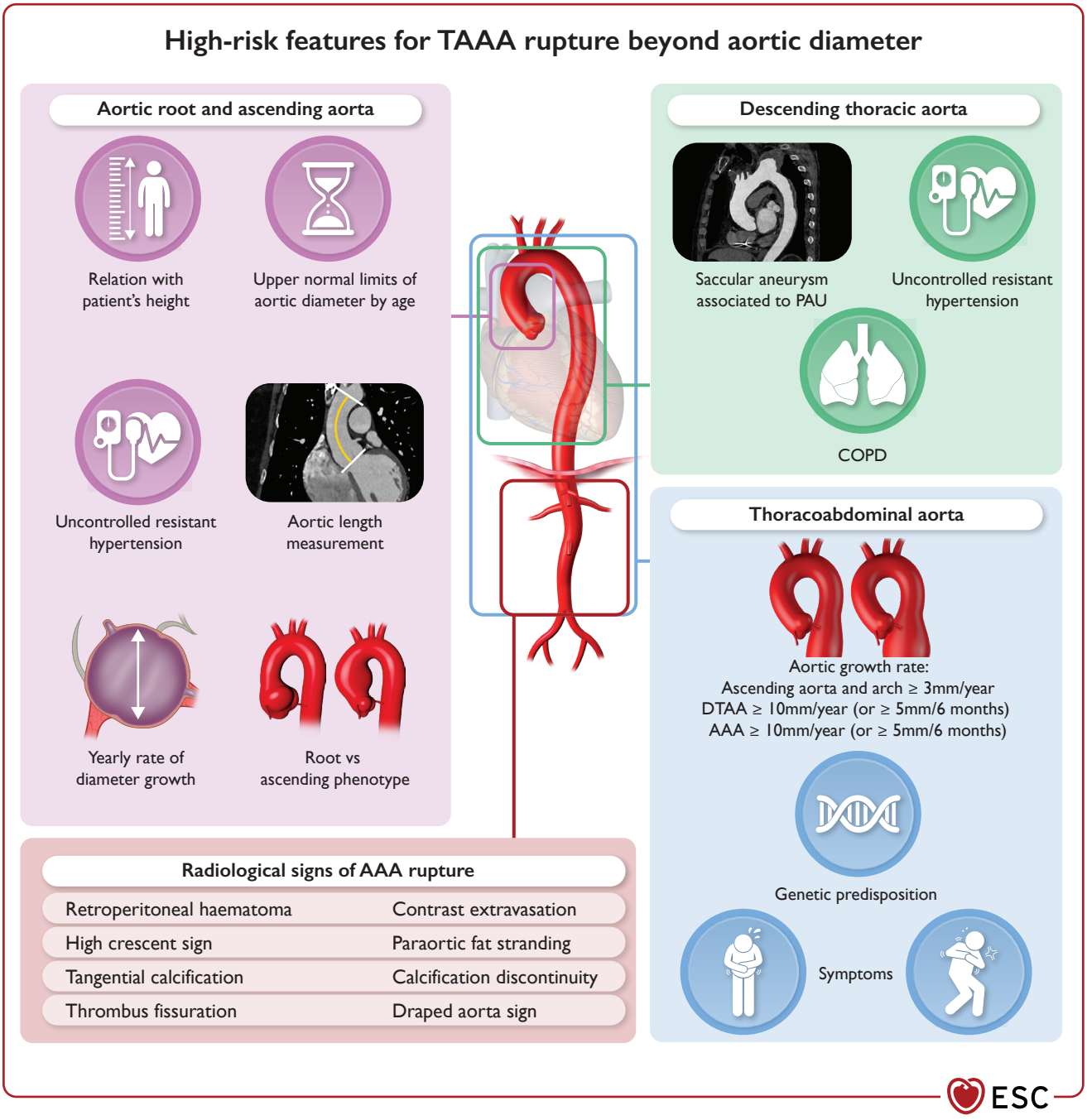

Figure 23 Risk factors for thoracic and abdominal aneurysm rupture. AAA, abdominal aortic aneurysm; COPD, chronic obstructive pulmonary disease; DTAA, descending thoracic aorta aneurysm; PAU, penetrating atherosclerotic ulcer; TAAA, thoracoabdominal aortic aneurysm.[905–908]

thoracoabdominal aortic aneurysms without dissection. Mean age at diagnosis is 59–69, with a male predominance of 2–4:1. Aneurysm growth rate is 1.9–3.4 mm per year,[902,903] but tends to increase notably with diameters over 50 mm or post-proximal aorta surgery in patients with MFS. In this population, debate continues as to whether this reflects a more vulnerable aorta associated to the genetic disease or haemodynamic changes post-surgery.

For untreated DTA aneurysm patients, 5 year survival is about 54%, with aortic rupture as the leading cause of death.[904] Rupture risk factors include HTAD, a diameter over 50 mm, hypertension, smoking, chronic obstructive pulmonary disease (COPD), symptoms, chronic aortic dissection, and age. A significant rise in AAE risk occurs at a 60 mm diameter. Although dissection can occur in smaller aortas, the individual risk is low.[899] High-risk features for rupture are represented in *Figure 23*.

9.2.2.4. Surveillance

Patients with TAA who do not meet surgical criteria require chronic follow-up that includes clinical evaluation and imaging techniques. The best imaging modality depends on aneurysm location: TTE, CCT, or CMR when affecting the aortic root and the ascending aorta; CMR and CCT when involving the distal ascending aorta, the aortic arch, or the DTA.[159,171] Follow-up should be conducted with the same imaging technique and in the same centre.[909] If a TAA is only moderate in size and remains relatively stable over time, CMR rather than CCT is reasonable to minimize radiation exposure.[172,910] Follow-up for aortic aneurysms associated with HTAD is described in *Section 10.1.3.2*.

Figure 24 proposes a follow-up algorithm for patients with TAA. In cases of aortic root or proximal ascending aorta dilatation, after initial diagnosis by TTE the basal diameter and extension must be confirmed by CMR or CCT. If there is agreement between techniques, TTE can be used for follow-up; however, if there is a difference of ≥3 mm, surveillance must be performed by CMR or CCT. After the initial diagnosis, imaging is required at 6–12 months, depending on aetiology and baseline diameter (*Figure 24*); see *Sections 5.4.2* and *9.2.1* about indexed values of aortic dimensions, to ensure stability.[159,911] Subsequently, imaging can be performed annually if there is no expansion/extension or customized according to the underlying condition. If the aorta shows rapid expansion (≥3 mm per year) or approaches the surgery/endovascular repair threshold, a closer evaluation is recommended every 6 months. In contrast, stability in aortic diameters over years could lengthen these intervals (especially in non-genetic aneurysms and those <45 mm). In cases of dilatation of aortic arch or DTA, diameters obtained by TTE are deemed less precise and need confirmation by CMR or CCT. In those types of aneurysms, follow-up frequency will depend on the baseline diameter and aetiology and will follow the same criteria established in the algorithm in *Figure 24* for the 40–49 mm range. However, for the 50–55 mm range, the aorta should be re-imaged every 6 months until the threshold for intervention is reached (see *Sections 9.2.5.3* and *9.2.5.4*).

Recommendation Table 35 — Recommendation for the surveillance of patients with thoracic aortic aneurysms (non-heritable thoracic aortic disease)

Recommendations	Class[a]	Level[b]
In thoracic aortic dilatation, TTE is recommended at diagnosis to assess aortic valve anatomy and function, aortic root, and ascending aorta diameters. Additionally, a global aortic evaluation using all echocardiographic views is recommended.[159]	I	C
CMR or CCT is recommended for surveillance of patients with aneurysm at the distal ascending aorta, aortic arch, DTA, or TAAA.[70,159,172,912–915]	I	C
In thoracic aortic dilatation, CCT or CMR is recommended to confirm TTE measurements, rule out aortic asymmetry, and determine baseline diameters for follow-up.[137,143,144]	I	C
Follow-up imaging with TTE, CCT, or CMR (based on aneurysm location) should be considered annually if there is no expansion/extension or customized according to baseline aortic diameter and the underlying condition.[70,159,172]	IIa	C
TTE is not recommended for the surveillance of aneurysms in the distal ascending aorta, aortic arch, or DTA.[159,171]	III	C

Continued

CCT, Cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DTA, descending thoracic aorta; TAAA, thoracoabdominal aortic aneurysm; TTE, transthoracic echocardiography.
See proposed algorithm in *Figure 24*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.3. Abdominal aortic aneurysms

9.2.3.1. General concepts

An AAA is defined as a focal dilation at least 1.5 times its normal diameter, generally ≥30 mm. Most AAAs are fusiform, and many are lined with laminated thrombi.[916] Their prevalence increases with age, with a 4:1 male/female ratio.[872] They are commonly classified based on their relation to renal arteries (*Figure 22*) because of the complexity of surgical treatment. AAA extends to the common iliac arteries in 25% of cases and in up to 20% of patients is associated with peripheral femoral and/or popliteal artery aneurysm.[876–878]

9.2.3.2. Aetiology, risk factors, and natural history

Smoking, age, male sex, and familial history of aneurysmal disease are major risk factors,[917–921] whereas diabetes is associated with a decreased risk[922,923] and slower growth rate[924] (*Figure 21*, see also *Section 5*). Other aetiologies include inflammation (5%–10% of all AAA),[925] genetic disorders, and infection. The mean growth rate is around 3 mm per year (1–6 mm)[906,926] and depends on sac diameter, presence of genetic disorders, continuous smoking, metabolism (presence of inflammation), and aortic wall calcification.[927–929] Risk of rupture rises exponentially depending on diameter, being higher in women.[930,931]

AAAs are asymptomatic in two-thirds of cases and if they become symptomatic, rupture is the main manifestation. They often represent incidental imaging findings, as the sensitivity of clinical examination—especially palpation of an abdominal mass—is generally poor. Symptoms may include acute abdominal or back pain, and in some cases, hypovolaemic shock. However, contained rupture may present with atypical low flank or abdominal pain (see *Figure 23* for high-risk factors and radiological signs or AAA rupture).[932–935] Independently of risk of rupture, patients with AAA have impaired survival: the 5 year mortality rate is higher (×4 in women, ×2 in men) despite AAA repair, likely due to the presence of cardiovascular disease in other areas.[936]

9.2.3.3. Surveillance

Those with an aortic diameter <25 mm present low risk of developing large AAA in 10 years, whereas a diameter of 25–29 mm deserves reassessment after 4 years.[937,938] DUS is the standard imaging technique for surveillance; however, CCT provides superior visualization of the AA and its branches, especially for pre-operative planning. CMR is reasonable in selected patients (young and female) when a long follow-up is considered, to avoid radiation.

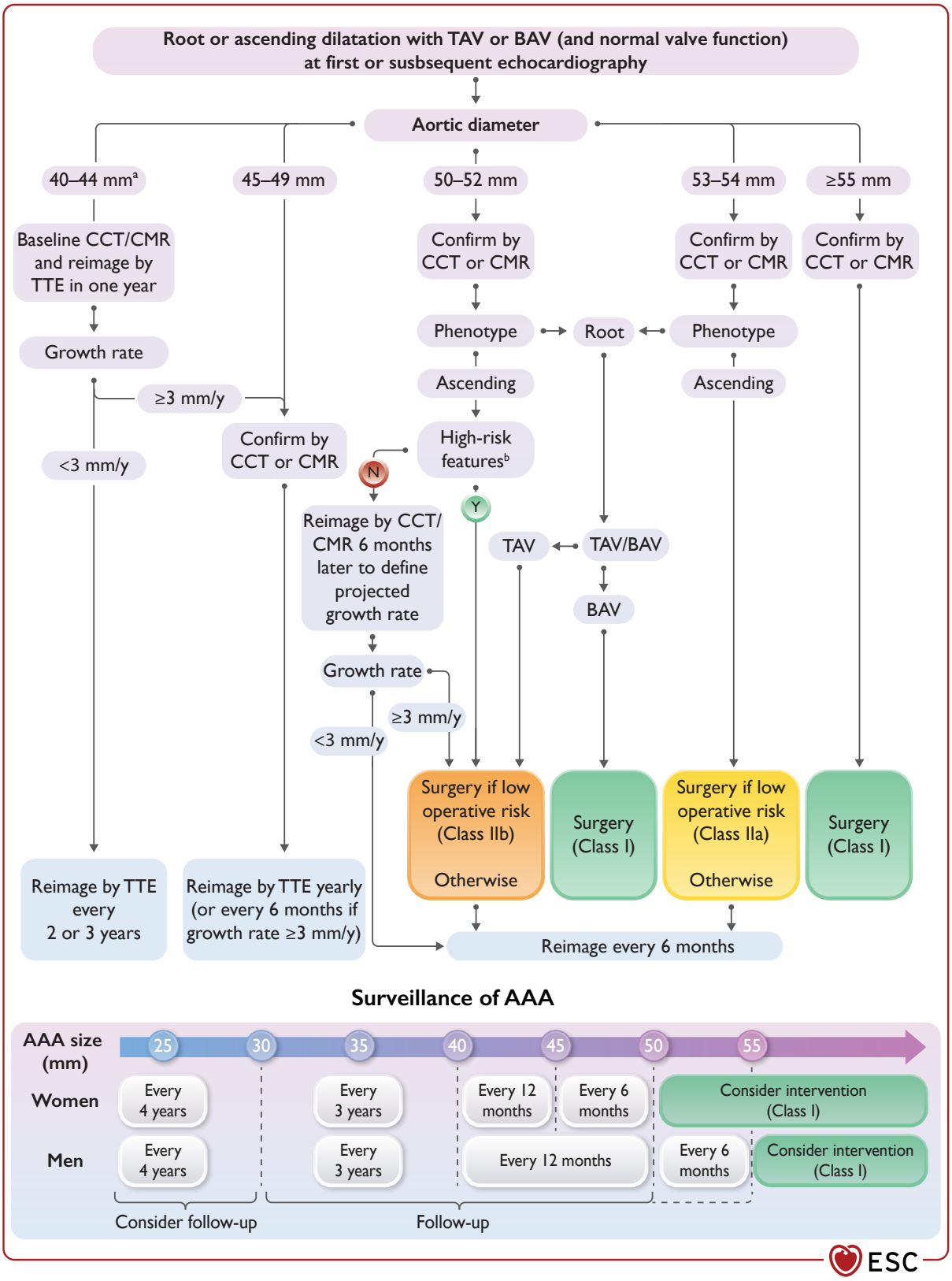

Figure 24 Surveillance of patients with **non-heritable** thoracic aortic disease and abdominal aortic aneurysms. AAA, abdominal aortic aneurysm, BAV, bicuspid aortic valve; CCT, cardiovascular computed tomography; HTAD, heritable thoracic aortic disease; CMR, cardiovascular magnetic resonance; TAV, tricuspid aortic valve; TTE, transthoracic echocardiography. [a]36–44 mm in women. [b]For TAV and BAV: age <50 years; height <1.69 m; ascending length >11 cm; uncontrolled hypertension; and, for BAV: coarctation; family history of acute aortic events.

A meta-analysis advises follow-up intervals for AAAs based on size: 3 years for 30–39 mm, 1 year for 40–44 mm, and 6 months for 45–54 mm in men, with <1% rupture risk.[938] Women have similar growth rates but a four-fold higher rupture risk.[938] A proposed follow-up algorithm is displayed in *Figure 24*. Consider shorter intervals for rapid growth (≥10 mm per year or ≥5 mm per 6 months), in which case repair may be considered.

Recommendation Table 36 — Recommendations for surveillance of patients with abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
DUS surveillance is recommended every 6 months in men with AAA of 50–55 mm and in women with AAA of 45–50 mm.[938]	I	B
CCT or CMR is recommended if DUS does not allow adequate measurement of AAA diameter.[148,939–942]	I	B
DUS is recommended for AAA surveillance.[943]	I	C
DUS surveillance every 3 years should be considered in patients with AAA of 30–<40 mm.[938]	IIa	B
DUS surveillance should be considered annually in women with AAA of 40–<45 mm and in men with AAA of 40–<50 mm.[938]	IIa	B
DUS surveillance should be considered every 4 years in patients with aortic diameter ≥25 mm and <30 mm and life expectancy >2 years.[937,938]	IIa	C

AAA, abdominal aortic aneurysm; CCT, Cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound.
[a]Class of recommendation.
[b]Level of evidence.

9.2.4. Optimal medical treatment of aortic aneurysms

In patients with aortic aneurysms, the role of antithrombotic therapy is uncertain. In complicated aortic atherosclerotic plaques, concomitant CAD is common (OR 2.99) and SAPT should be considered (see Section 9.1). In patients with AAA, results of observational studies are conflicting in relation to aneurysm growth. Low-dose aspirin is not associated with a higher risk of AAA rupture but could worsen prognosis in cases of rupture.[944] In an RCT of patients with AAA (35–44 mm), ticagrelor did not reduce growth rate.[945]

Optimal medical treatment for aortic aneurysms aims to lower CV morbidity, slow growth rate, delay surgery, reduce peri-operative risk, and prevent AAE. Aneurysm patients face elevated CV risk due to common CVRFs, and the 10 year CV event mortality risk (heart attacks or strokes) is 15 times higher than AAE risk, even after repair.[882,883] According to the SMART risk score algorithm, optimal implementation of risk management guidelines would reduce the 10 year risk of MACE from 43% to 14% in patients with AAA.[936] Thus, lifestyle modification, exercise, smoking cessation, and treatment of risk factors are crucial (see *Section 7*).

Risk factors and possible drug treatment to reduce AAA growth and/or the risk of rupture have been thoroughly discussed in a recent review paper.[946] Their meta-analysis suggested a possible effect of ACEIs (but not ARBs) on the risk of rupture, whereas another meta-analysis[947] did not indicate an effect of ACEIs on AAA growth. A reduction of AAA growth by statins is indicated in a recent meta-analysis.[352] Furthermore, reduced AAA growth by the antidiabetic drug metformin has been suggested in several meta-analyses[352,948,949] and there are several ongoing RCTs to explore this. For BP, follow general hypertension guidelines. Aim for BP below 140/90 mmHg, with a target of 120/80 mmHg, if tolerated.[300,302,305] Data on the specific positive effects of beta-blockers and ARBs in TAA and AAA are limited (mostly derived from MFS populations). However, it is reasonable to use BBs and/or ARBs as first-line antihypertensive drugs in TAA and AAA.

Consider moderate/high-intensity statins in TAA patients but skip for those with low CV risk and non-atherosclerotic (HTAD). In AAA, consider statins to reduce aneurysm risks, including growth, rupture, and peri-operative mortality.[330,347,348] Low-dose aspirin is debated but may be reasonable given elevated CV risk factors in TAA and AAA patients.[666,950] Additionally, apply all CVD secondary prevention measures to these patients (see *Section 7*).

Some evidence suggests that fluoroquinolones could be associated with an increased risk for aneurysm progression and dissection,[951–956] but conflicting analyses do not support this association. The cautious use of fluoroquinolones should not be discouraged when there is a clinical indication, even considering concerns regarding aortic aneurysm and dissection (AA/AD). Note that AA/AD risk (both thoracic and abdominal) may increase due to infection itself, regardless of the antibiotic chosen. Infectious disease specialists discourage routine fluoroquinolone use as a first-line antibiotic if equally effective alternatives exist. Hence, do not withhold this therapy in aortic disease cases when clinically necessary. All medical and lifestyle recommendations are summarized in *Figure 7*.

Recommendation Table 37 — Recommendations for medical treatment in patients with thoracic aorta or abdominal aortic aneurysms

Recommendations	Class[a]	Level[b]
In patients with aortic aneurysm (TAA and/or AAA), optimal implementation of CV risk management and medical treatment (see detailed recommendations in dedicated Tables of Recommendations[c]) are recommended to reduce MACE.[936]	I	C
Fluoroquinolones, while generally discouraged for patients with aortic aneurysms, may be considered if there is a compelling clinical indication and no other reasonable alternative.[951–960]	IIb	B

AAA, abdominal aortic aneurysm; CV, cardiovascular; MACE, major adverse cardiovascular events; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.
[c]see Tables of Recommendations 7 to 10.

9.2.5. Surgical management of aortic aneurysms

9.2.5.1. Surgical treatment of aortic root and ascending aorta

In isolated dilatation of the ascending tubular (supra-coronary) aorta, a supra-commissural tubular graft is inserted with the distal anastomosis just before the aortic arch. For aneurysms extending proximally below the sinotubular junction (STJ) with involvement of aortic sinuses, the surgical approach depends on the aortic annulus and valve condition. If the aortic valve cusps are pliable, experienced centres may recommend aortic valve-sparing techniques,[961–965] such as David's procedure (reimplantation) or the Yacoub technique (remodelling).[890,966–968]

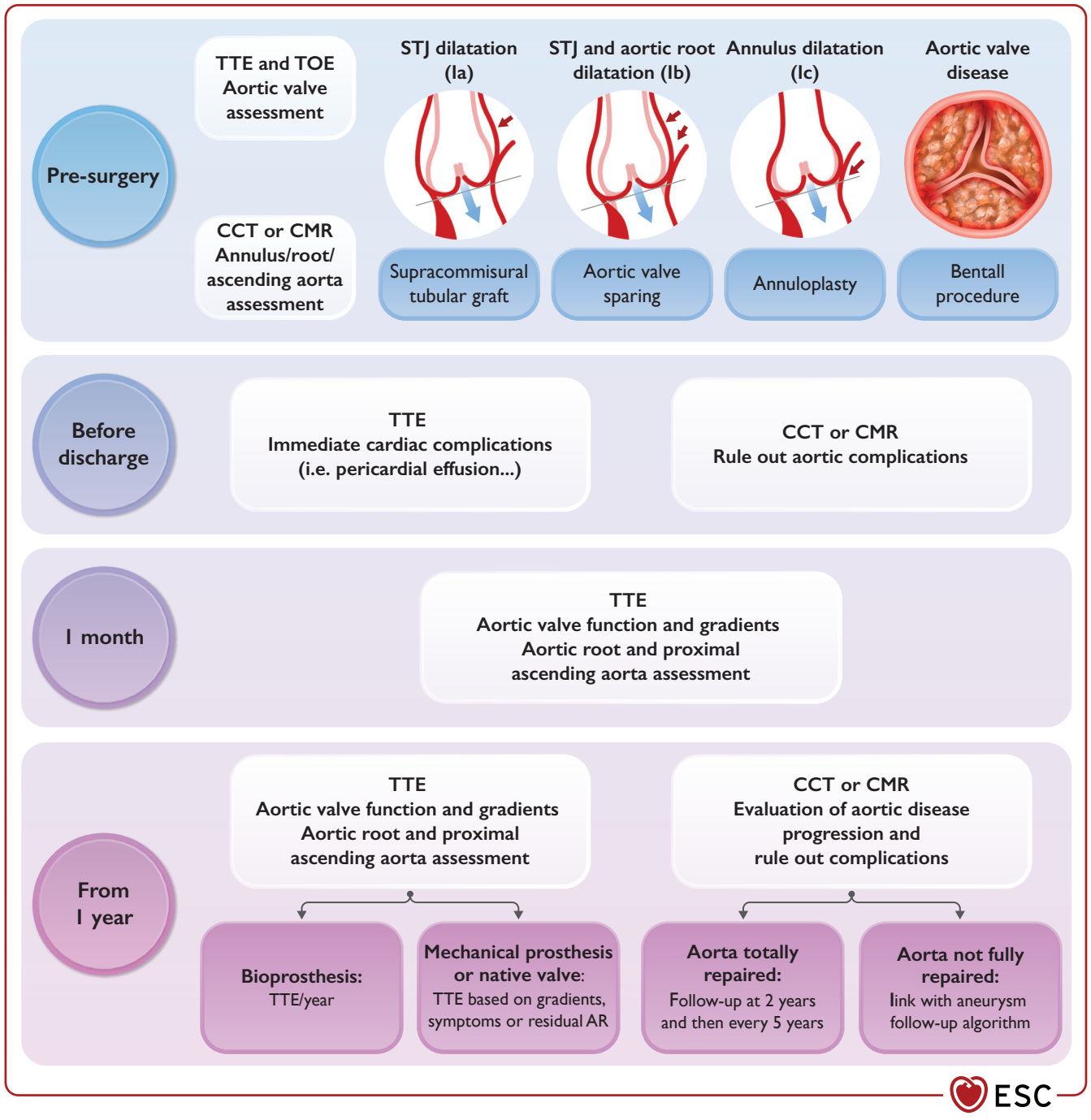

Figure 25 Peri-operative algorithm for the management of patients with surgically treated aortic root and ascending aortic aneurysm. AR, aortic regurgitation; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; STJ, sinotubular junction; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Otherwise, composite replacement of the aortic root and valve with the Bentall procedure is indicated.

Pre-operative evaluation[890] and initial follow-up of patients is defined in *Figure 25*. Patients with a bioprosthetic valve should be monitored by TTE annually. However, in patients with mechanical prosthesis or native aortic valve, clinical evaluation and TTE should be performed as soon as possible if new heart symptoms develop.[969] SAPT with low-dose aspirin (75–100 mg per day) should be considered for the first 3 months after conservative aortic valve surgery if there are no indications for OAC. Lifelong OAC with a VKA is recommended for all patients with a Bentall mechanical prosthesis.[970,971] However, in patients with no baseline indications for OAC, low-dose aspirin (75–100 mg/day) or OAC using a VKA should be considered for the first 3 months after Bentall surgery with a bioprosthesis.[972,973]

Although many risk factors associated with AAE have been described (such as elongation, angulation, and unfavourable biomechanics), aortic diameter is still the main determinant of aortic complications and death.[974–976] AAE rates decreased with prophylactic aortic surgery over a decade,[977] and additionally, surgical risk for ascending aortic/aortic root surgery dropped significantly.[978–980] Now, experienced cardiac surgery centres report <1% mortality with elective surgery.[980,981]

Most acute type A aortic dissections (acute TAAD) occur at diameters below 55 mm. However, the risk exceeds 1% between 50 and 54 mm,[982] with a critical point at 52–53 mm.[153,981,983] Pre-dissection aortic diameter at the tubular level is 25%–30% smaller than post-dissection. Over 60% of non-MFS, non-BAV acute TAAD patients have a non-dilated ascending aorta before dissection.[984,985] Additionally, the 'root phenotype' has been reported to be more malignant than those with ascending phenotype, with higher velocity of progression and AAE risk.[154,891,892,986]

Novel parameters, like ascending aortic length (AAL) and the ascending-arch angle, correlate with acute TAAD risk.[155,976] AAL ≥13 cm links to nearly five-fold higher yearly AAE rates compared with AAL <9 cm, with a threshold of >11 cm as a risk indicator.[155] Indexing aortic diameters to anthropometric parameters has been suggested and a proportional increase in the risk of AAE has been retrospectively demonstrated for increasing diameter indexed to BSA,[904] diameter indexed to patient height,[153] or cross-sectional area indexed to patient height.[154] However, these diameter-based indexing methods share the same limitations in risk prediction as the absolute diameter in the general population,[984,985] whereas they can be advantageous in patients with small body size.[153,154] These additional risk factors (beyond the diameter) are summarized in *Figure 23*.

Recommendation Table 38 — Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve (see also Evidence Table 11)

Recommendations	Class[a]	Level[b]
Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.[172,894,899,904]	I	B
Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.[961–965]	I	B
VKAs are recommended lifelong for all patients with a Bentall procedure with an MHV prosthesis.[970,971]	I	B
In patients with dilatation of the tubular ascending aorta who can be offered surgery with low predicted risk,[c] ascending aortic replacement should be considered at a maximum diameter >52 mm.[153,981,983]	IIa	B
In patients undergoing surgery for tricuspid aortic valve disease who have concomitant dilatation of the aortic root or ascending tubular aorta, and low predicted surgical risk, ascending aorta or root replacement should be considered at a maximum diameter ≥45 mm, otherwise ≥50 mm.[70,987–989]	IIa	B
SAPT with low-dose aspirin (75–100 mg per day) should be considered for the first 3 months after valve-sparing aortic surgery when there are no other baseline indications for OAC.	IIa	C
In patients undergoing non-aortic-valve cardiac surgery who have concomitant dilatation of the ascending aorta or aortic root with a maximum diameter ≥50 mm, concomitant aortic surgery should be considered.[70,990,991]	IIa	C
Ascending aortic or root replacement may be considered at a maximum diameter of ≥50 mm in patients with proximal aorta dilatation who can be offered surgery with low predicted risk[c] and present with any of the following:[153–155,891,892] • Growth of the aortic diameter ≥3 mm per year • Resistant hypertension[d] • Short stature <1.69 m • Root phenotype • Aortic length[e] >11 cm • Age <50 years • Desire for pregnancy • Aortic coarctation	IIb	B

MHV, mechanical heart valve; OAC, oral anticoagulation; SAPT, single antiplatelet therapy; VKA, vitamin K antagonist.
For heritable thoracic aortic disease and bicuspid aortic valve-related thoracic aortic aneurysm refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.
[c]Individual patient's risk <3%.
[d]Hypertension that cannot be adequately controlled despite use of three or more agents recommended by a physician with expertise in the management of hypertension.
[e]Curvilinear distance at aortic centreline between the ventriculo-aortic junction and the origin of the innominate artery.

9.2.5.2. Surgical treatment of aortic arch aneurysms

Surgery for arch aneurysms is challenging, primarily due to risks like hypothermic circulatory arrest and the need for brain protection, resulting in higher mortality and stroke rates. Isolated aortic arch surgery is appropriate for asymptomatic degenerative aortic arch aneurysms ≥55 mm in diameter or symptoms or signs of local compression. Hemi-arch or total arch replacement are frequently required in patients who have an indication for surgery on an adjacent aneurysm of the ascending aorta. In specific cases, supra-aortic vessel transposition via off-pump debranching followed by TEVAR of the arch can be an alternative to traditional surgery, particularly when avoiding hypothermic circulatory arrest is a concern.[992–996] When the disease involves the proximal descending aorta or future need for treatment of the descending aorta is anticipated, the frozen elephant trunk (FET) technique is a good option.[997] Assessment of patency and morphology of the circle of Willis is recommended when treatment involves the aortic arch.[998,999]

Recommendation Table 39 — Recommendations for surgery in aortic arch aneurysms

Recommendations	Class[a]	Level[b]
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.[70,172]	I	C

Continued

In patients with an isolated aortic arch aneurysm who are asymptomatic and have low operative risk, open surgical replacement should be considered at an arch diameter of ≥55 mm.[70,172,899]	IIa	B
In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch replacement should be considered if the dilatation extends into the proximal aortic arch (>50 mm).[70,172,1000]	IIa	C
In patients undergoing open surgical repair of an aortic arch aneurysm, an elephant trunk or frozen elephant trunk procedure should be considered if the aneurysmal disease extends into the proximal descending thoracic aorta.[70,172,997,1001]	IIa	C
In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch or arch replacement may be considered in experienced centres if the dilatation extends into the aortic arch (>45 mm).[70,172,1001]	IIb	C
In patients with an aortic arch aneurysm who meet criteria for intervention but have high surgical risk, a hybrid or endovascular approach may be considered.[70,172]	IIb	C

For heritable thoracic aortic disease refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.5.3. Surgical treatment of the thoracic descending aorta

9.2.5.3.1. General considerations. At 60 mm diameter, a DTA aneurysm has a 10% annual rupture risk, justifying intervention at ≥55 mm.[902,1002] Intervention at a diameter <55 mm may not bring any further survival benefit except for women,[904,1003] patients with connective tissue disorders,[904] or rapid growth (≥10 mm per year or ≥5 mm every 6 months),[1004] (for high-risk factors see *Figure 23*). This threshold may be increased in high surgical risk patients.[1005] It is advisable to centralize complex procedures in centres with expertise in aortic diseases and a multidisciplinary team for effective patient management.

9.2.5.3.2. Open repair. Thoracic endovascular aortic aneurysm repair is recommended as first-choice intervention for DTA aneurysms,[1006–1010] thus open repair is limited to patients with unsuitable anatomy for TEVAR[1011] or connective tissue disorders.[1012] The early mortality benefit of TEVAR seems to decrease after 1 year, and thereafter long-term survival (10 years) seems better with open repair.[1013] Therefore, open repair is advisable for young, healthy patients with unsuitable TEVAR anatomy and prolonged life expectancy, particularly when symptoms from aneurysm rupture or compression arise.

However, open repair involves significant post-operative risks, necessitating thorough pre-operative evaluations for cardiac, pulmonary, renal function, carotid, and peripheral arterial diseases. Risks include stroke, mesenteric and renal ischaemia due to clamping duration,[1014,1015] and paraplegia tied to the extent of aneurysmal disease.[1016,1017] Outside experienced centres, outcomes have shown minimal improvement in recent years, with mortality rates around 10% and spinal cord ischaemia rates at 11%–15%.[1016,1018]

9.2.5.3.3. Endovascular repair. Comparative studies favour TEVAR over open repair, showing lower mortality (6%) and morbidity.[1006,1019,1020] However, TEVAR's survival advantage is balanced by an increased risk of follow-up re-intervention. It reduces spinal cord injury risk (3%).[1021–1024] Left subclavian artery (LSA) coverage during TEVAR for proximal sealing is required in up to 50% of cases.[1025] This is associated with an increased risk of cerebrovascular events, spinal cord ischaemia (SCI), and upper-limb ischaemia,[1026,1027] justifying previous surgical or concomitant endovascular (with branched or fenestrated grafts) revascularization of the LSA in an elective setting.[1026,1028,1029] In cases of inadequate distal zone sealing, safe coverage of the coeliac artery has been proposed when sufficient collateral circulation exists,[1030,1031] but results are controversial.[1032]

9.2.5.4. Surgical treatment of thoracoabdominal aorta aneurysms

9.2.5.4.1. General considerations. Since AAEs increase when TAAA diameter exceeds 60 mm,[902,1002,1033] and there are more technical surgical challenges in TAAA repair (compared with DTA aneurysm or AAA), TAAA repair, in low-moderate surgical risk patients, is proposed if the aortic diameter is ≥60 mm. However, surgical repair should be considered at diameters ≥55 mm if patients present with high-risk features (*Figure 24*) or are at very low risk and under the care of experienced surgeons in a multidisciplinary aorta team.[1004,1033,1034] HTAD, distal location, chronic dissection, and BAV[903] are associated with rapid growth rate and will require closer follow-up.

9.2.5.4.2. Open repair. Open TAAA repair is a complex aortic procedure. Post-operative mortality risk increases with left ventricular (LV) dysfunction, renal insufficiency, and advanced age.[1035–1037] Since organs and tissues distal to the aortic clamp will suffer from prolonged ischaemia, extracorporeal circulation is mandatory to reduce complications,[1011,1038] especially SCI (2.5%–15%).[1011,1039–1044] The mortality rate after open TAAA repair varies between 6% and 8% in high-volume centres[1006,1011,1039] vs. 30% in less experienced centres,[1045,1046] raising the recommendation to perform these complex procedures only in specialized institutions.

9.2.5.4.3. Endovascular repair. Endovascular repair is a promising alternative for treating challenging aortic anatomy like juxta-renal AAA (*Figure 22*).[1047,1048] The use of fenestrated and branched endografts has shown excellent results, allowing perfusion of visceral vessels.[1049–1053] While direct comparison studies with open TAAA repair are lacking,[1054] the increasing adoption of endovascular procedures is notable, especially for high-risk patients, with low post-operative mortality rates (<10%).[1051,1052,1055–1058] A recent meta-analysis confirms these excellent outcomes, endorsing endovascular repair for TAAA.[1059] The incidence of post-operative SCI (around 5%) is similar between endovascular and open repair.[1052,1057,1060,1061] Thus, at mid-term follow-up, endovascular repair is durable with acceptable secondary re-intervention rates, which remain one of the major limitations.[1052,1057,1058,1060,1061] Factors favouring endovascular vs. open repair in TAAA are presented in *Table 15*.

Recommendation Table 40 — Recommendations for the management of patients presenting with descending thoracic aortic and thoracoabdominal aortic aneurysms

Recommendations	Class[a]	Level[b]
In patients with unruptured DTA aneurysm (without HTAD), elective repair is recommended if diameter ≥55 mm.[902,1002]	I	B
In patients without HTAD with unruptured DTA aneurysm, when elective repair is indicated and anatomy is suitable, TEVAR is recommended over open repair.[1006,1019,1020]	I	B
In patients with DTA aneurysm who undergo TEVAR with planned LSA coverage, it is recommended to revascularize the LSA before TEVAR to reduce the risk of SCI and stroke.[1026,1028,1029]	I	B
In patients with unruptured degenerative TAAA, elective repair is recommended when the diameter is ≥60 mm.[902,1002,1033]	I	B
In patients without significant comorbidities and with unruptured DTA aneurysm, when elective repair is indicated and anatomy is unsuitable for TEVAR, open repair should be considered if life expectancy exceeds 2 years.[1013]	IIa	B
In TAAA, surgical repair should be considered at diameters ≥55 mm if patients present with high-risk features, are at very low risk, and are under the care of experienced surgeons in a multidisciplinary aorta team.[1004,1033,1034]	IIa	B
In patients with unruptured degenerative TAAA and suitable anatomy, when elective repair is indicated, endovascular repair using fenestrated and/or branched endografts should be considered in experienced centres.[1051,1052,1055–1059]	IIa	B
In patients with unruptured DTA aneurysm (without HTAD) and high-risk features,[c] elective repair may be considered if the diameter is <55 mm.[904,1003,1004,1033,1034]	IIb	B

Continued

DTA, descending thoracic aorta; HTAD, heritable thoracic aortic disease; LSA, left subclavian artery; SCI, spinal cord ischaemia; TAAA, thoracoabdominal aortic aneurysm; TEVAR, thoracic endovascular aortic aneurysm repair.
For heritable thoracic aortic disease refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 23* for high-risk features.

9.2.5.5. Surgical treatment of abdominal aorta aneurysms

9.2.5.5.1. General considerations. Rupture remains the most feared AAA complication, and is associated with the maximum diameter,[1063] as well as other risk factors (*Figure 23*). Different studies[1064–1071] (including the United Kingdom Small Aneurysm Trial [UKSAT] and American Aneurysm Detection and Management [ADAM] trial) reported no benefits from open or endovascular interventions (despite lower peri-operative complication rates) in asymptomatic AAA patients with a maximal diameter <55 mm in men and <50 mm in women. Evidence that women are more likely to rupture under surveillance and at a smaller aortic diameter justified a lower (50 mm) threshold. Another interesting method to quantify the risk of rupture based on body size, which seems a better predictor in women, has been proposed.[1072] However, in the absence of recent studies, thresholds for intervention have not changed in recent years. Considering the complexity of patient management, it is advisable to centralize complex procedures in centres with a high level of expertise in aortic diseases and a multidisciplinary team.

9.2.5.5.2. Pre-operative cardiovascular evaluation and choice of treatment. Coronary artery disease is the leading cause of early mortality after AAA repair,[937,1073] and is associated with a 5%–10% rate of peri-operative CV complications such as death, MI, or stroke.[1074,1075] Since endovascular repair is associated with lower mortality (<1%) and CV complications,[1076–1079] the need for pre-operative cardiac

Table 15 Overview of factors favouring open vs. endovascular repair in thoracoabdominal aortic aneurysm

Characteristic	Favours open repair	Favours endovascular repair
Biological age and life expectancy	• Younger age • Considerable life expectancy with acceptable quality of life	• Older age • Limited life expectancy
Anatomical considerations	• If aortic and branch anatomy preclude endovascular approach • Poor vascular access	• Suitable proximal and distal landing zones • Favourable visceral and renal configuration • Vascular access obtainable
Pathological	• Chronic dissection	• Acute dissection
Background/causal factor	• Hereditary aortic disease	• Degenerative aortic disease
Cardiopulmonary condition	• Good cardiopulmonary reserve	• Poor cardiopulmonary reserve
Fitness	• No significant comorbidities • Successful rehabilitation likely	• Severe organ impairment (renal, kidney, pulmonary) • Obesity • Limited mobility, unlikely to rehabilitate successfully
Urgency	• Elective repair • Emergency repair without a viable endovascular solution	• Elective repair • Emergency repair with time for custom-made graft or suitable for standard grafts

Adapted from Ouzounian *et al.* with permission.[1062]

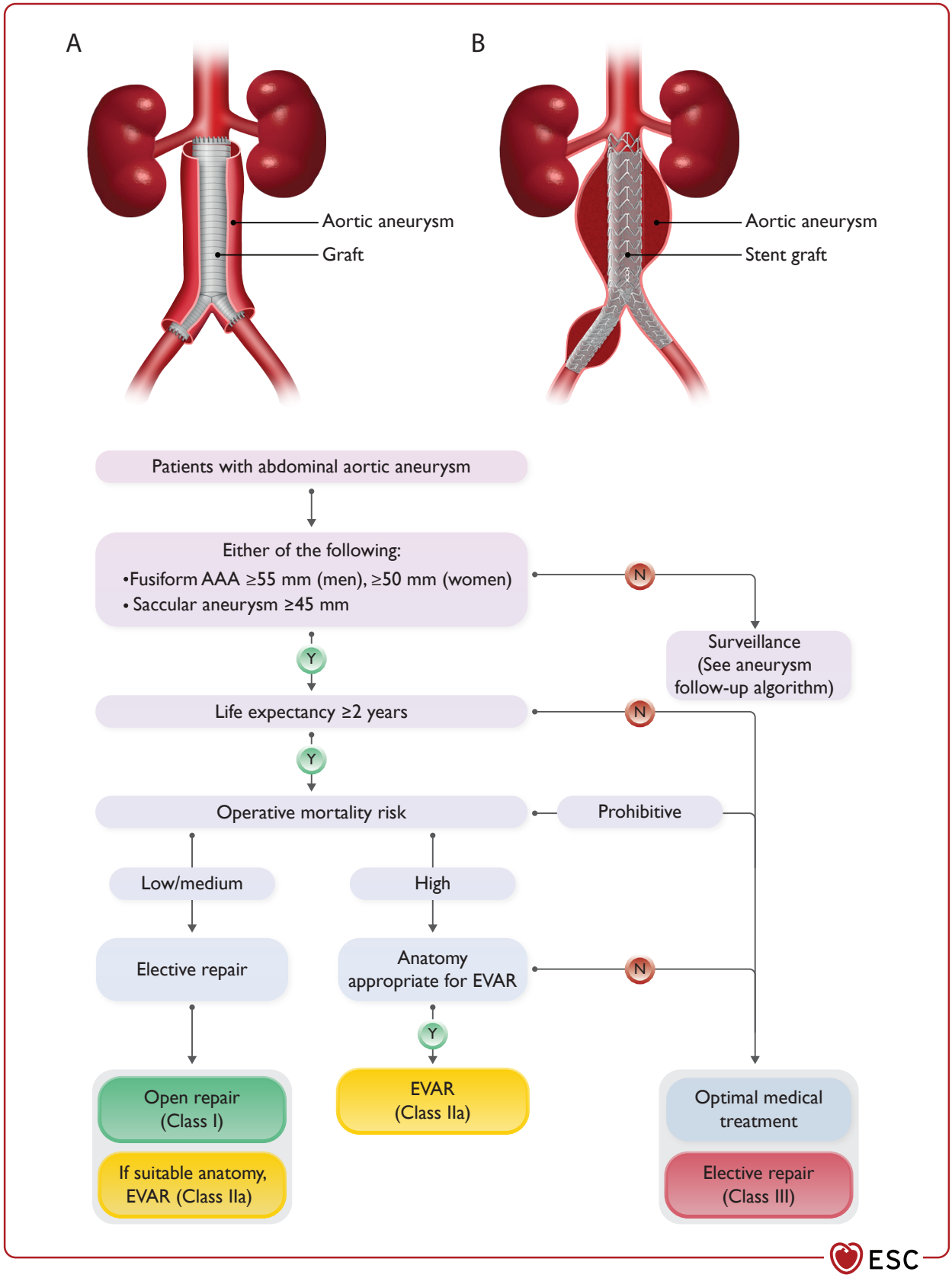

Figure 26 Algorithm for individual decision-making process in the treatment of patients with abdominal aortic aneurysm. (*A*) Illustration of open repair (graft). (*B*) Illustration of endovascular treatment (EVAR). AAA, abdominal aortic aneurysm; EVAR, endovascular aortic aneurysm repair.

work-up will depend on procedure risk, symptoms, and patient-specific CVRFs (see *Sections 4* and *12*, and the *2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery*).[1080] Coronary revascularization before elective aortic surgery in patients with stable cardiac symptoms cannot be recommended, since there is evidence that this strategy does not improve outcomes or reduce the 30 day MI rate.[1080,1081]

A complete vascular evaluation (that includes not only the AA but also the entire aorta: ascending, arch, and descending aorta) is mandatory to determine the best strategy in AAA management, CCT being, by consensus, the optimal pre-operative imaging modality.[1082,1083] When CCT is contraindicated, consider CMR, though calcification assessment is challenging. Pre-operative planning should determine EVAR feasibility by sizing the aorto-iliac system, yet adherence to device-specific instructions remains uncertain.[1084–1090] DUS assessment of the femoro-popliteal segment is advocated since femoro-popliteal aneurysms are commonly associated with AAA.[1091,1092] Additionally, the technique of choice should be discussed between the treating physician and the patient based on the patient's life expectancy and preferences, operator and hospital volumes, and surveillance compliance.[910,1093–1097] Elective AAA repair is not recommended in frail patients or those with life expectancy <2 years.[1098,1099] The individual decision-making process in AAA patients is displayed in *Figure 26*.

Different studies have demonstrated a significant short-term survival benefit for EVAR, but with similar long-term outcomes compared with open repair (up to 15 years)[1100–1103] also reported in females.[1104] However, loss of early benefit is associated with an increased rate of late complications occurring after 8 years, especially late ruptures.[1079] These trials used earlier-generation EVAR devices, so the durability of the latest-generation devices remains uncertain. Recent data, however, suggest a reduced risk of late complications and fewer re-interventions.[1105–1108]

9.2.5.5.3. Open abdominal aorta aneurysm repair. Open AAA repair through mid-line laparotomy (with <30 min clamping time) with a Dacron graft has been the preferred choice for years, despite notable CV morbidity[1078,1100,1109–1113] and a 2%–5% mortality rate.[1110,1111,1113,1114] In ruptured AAA, open repair results are worse than those of elective surgery, with an unchanged complication rate of around 48%.[1115] Thus, endovascular repair is recommended to reduce peri-operative morbidity and mortality.[1116–1118]

Open AAA repair raises incisional hernia risk, particularly in obese patients, suggesting prophylactic mesh use in high-risk cases.[1119–1121]

9.2.5.5.4. Endovascular abdominal aorta aneurysm repair. Endovascular abdominal aorta aneurysm repair reduces peri-operative mortality to <1%, although it implies higher risk of re-intervention in the long term.[1122–1124] Current devices offer features like active fixation, repositioning ability, low-profile design, and polymer-filled rings for improved sealing.[1106,1125–1128] New devices demonstrate similar long-term outcomes with reduced re-intervention risk,[1090] expanding treatment possibilities to 60%–70% of infrarenal AAA cases.[1129,1130]

In cases of juxta- or para-renal AAA (*Figure 22*), both open and endovascular treatment can be proposed in high-volume centres, with similar short- and long-term results. The choice between open surgical repair and endovascular repair depends on various factors, including the patient's anatomy, overall health, and the extent of the aneurysm (see *Table 15*). In cases of complex endovascular treatment, a fenestrated or branch stent endograft should be considered.[1096,1131]

A percutaneous femoral approach is suitable since it provides quicker access, reduced invasiveness, and allows local anaesthesia. Some evidence supports the use of ultrasound-guided percutaneous access for EVAR due to a lower rate of access-related complications and a shorter operation time.[1132–1135]

As patients treated by EVAR are more prone to late complications (endoleaks, migration, or rupture) and re-interventions, lifelong surveillance is currently mandatory.[1096,1136–1140]

Recommendation Table 41 — Recommendations for the management of patients presenting with abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
Elective repair is recommended if AAA diameter is ≥55 mm in men or ≥50 mm in women.[1064–1067]	I	A
In ruptured AAA with suitable anatomy, endovascular repair is recommended over open repair to reduce peri-operative morbidity and mortality.[1116–1118]	I	B
Prior to AAA repair, DUS assessment of the femoro-popliteal segment, to detect concomitant aneurysms, should be considered.[1091,1092]	IIa	B
In patients with AAA with suitable anatomy and reasonable life expectancy (>2 years), EVAR should be considered as the preferred therapy, based on shared decision-making.[910,1096,1141–1143]	IIa	B
In patients with unruptured AAA and aneurysm growth ≥5 mm in 6 months or ≥10 mm per year, repair may be considered.[1064,1065]	IIb	C
Elective repair for patients presenting with a saccular aneurysm ≥45 mm may be considered.[1144]	IIb	C
In patients with AAA and limited life expectancy (<2 years), elective AAA repair is not recommended.[1098,1099]	III	B
Prior to AAA repair, routine evaluation with coronary angiography and systematic revascularization in patients with chronic coronary syndromes is not recommended.[1080,1081]	III	C

AAA, abdominal aortic aneurysm; DUS, duplex ultrasound; EVAR, endovascular aortic aneurysm repair; TAA, thoracic aortic aneurysm.
See also *Figure 23*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.6. Endoleaks

Endoleaks are defined as the persistence of blood flow outside the graft but inside the aneurysm sac, preventing complete thrombosis (*Figure 27*). They are the most common complication, with an incidence up to one-third of either early or late procedures (those appearing after 1 year).[1145] Chronic anticoagulation constitutes a risk factor for re-intervention, late conversion surgery, or mortality.[1146] Endoleaks exposing the aneurysm sac to systemic pressure and expansion will require re-intervention to prevent rupture.

Five types of endoleaks have been described, as detailed in *Figure 27*. Type I and type III require correction with a new (endovascular) procedure. Type II is present in about 25% of patients but may seal

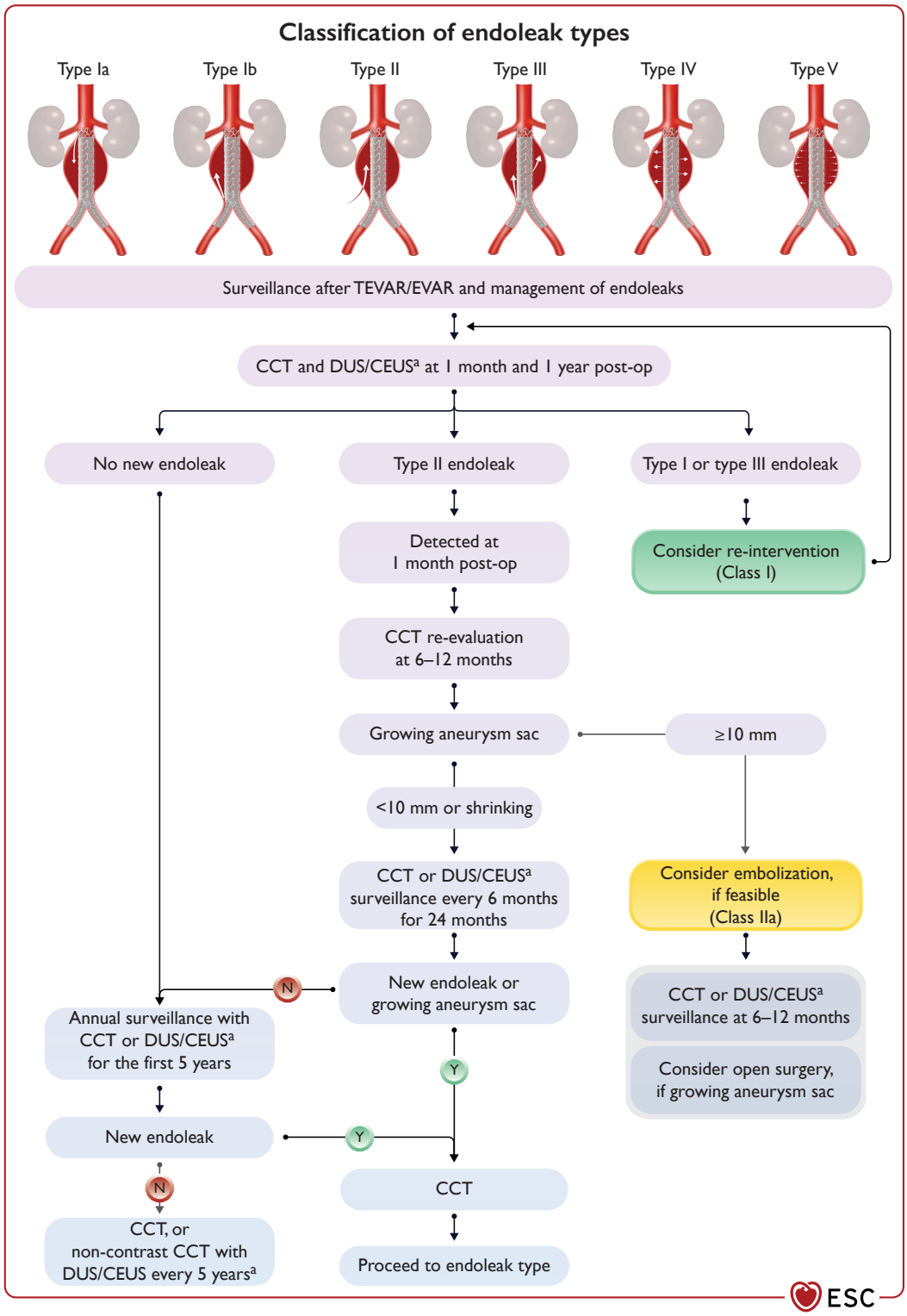

Figure 27 Algorithm for follow-up after thoracic endovascular aortic aneurysm repair, and management of endoleaks and their classification. CEUS, contrast-enhanced ultrasound; CCT, cardiovascular computed tomography; DUS, duplex ultrasound; TEVAR, thoracic endovascular aortic aneurysm repair; EVAR: Endovascular aortic repair. [a]In cases of TEVAR, CCT is the preferred imaging technique since DUS/CEUS does not permit the correct evaluation of the thoracic aorta. In cases of renal failure, non-contrast CCT is a good alternative to monitor aneurysm sac growing and is associated to DUS/CEUS for EVAR monitoring. Endoleaks are classified into five types: Type Ia, proximal attachment site endoleak; Type Ib, distal attachment site endoleak; Type II, backfilling of the aneurysm sac through branch vessels of the aorta; Type III, graft defect or component misalignment; Type IV, leakage through the graft wall attributable to endograft porosity; and Type V; caused by 'endotension', possibly resulting from aortic pressure transmitted through the graft/thrombus to the aneurysm sac. Adapted from Rokosh *et al.* with permission.[1147]

spontaneously in approximately 50% of cases. Risk factors for type II endoleaks include patent collaterals, presence of accessory arteries, and anticoagulation. In cases of significant sac expansion (≥10 mm), re-intervention should be considered, preferably by vessel or sac embolization. Type IV, attributed to device porosity, is rare with modern devices and no intervention is needed. Type V induces sac expansion without any visible endoleak. Treatment may be considered for significant sac growth (≥10 mm) and consists of stent graft relining or definitive endograft explant and open surgical repair.

Cardiovascular computed tomography with(out) contrast, and DUS and/or CEUS, are the main imaging modalities for TEVAR/EVAR follow-up. Imaging within the first 30 days is recommended to assess treatment success and/or complications. For TEVAR, contrast-enhanced CCT is the preferred imaging technique for follow-up and should be performed regularly (shorter or longer intervals are based on the expansion rate). In renally impaired patients, combined follow-up using DUS and non-contrast enhanced CCT is a suitable alternative (see follow-up algorithm, *Figure 27*). For EVAR, CCT and DUS/CEUS are recommended at 1 month following repair. Thereafter, surveillance should be based on the risk of late complications and includes DUS and/or CEUS (*Figure 27*).

Recommendation Table 42 — Recommendations for the management of patients presenting with endoleaks

Recommendations	Class[a]	Level[b]
It is recommended to perform 30 day imaging after TEVAR/EVAR, by CCT and DUS/CEUS, to assess the success of intervention.[1096]	I	B
It is recommended to re-intervene to achieve a seal in patients with type I endoleak after TEVAR/EVAR.[1137,1148]	I	B
It is recommended to re-intervene, principally by endovascular means, to achieve a seal in patients with type III endoleak after TEVAR/EVAR.[1139]	I	B
Re-intervention, principally with an endovascular approach or embolization, should be considered in patients with type II or V endoleak and significant sac expansion ≥10 mm or significantly decreasing proximal or distal seal.[1096,1149]	IIa	C

CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; DUS, Duplex ultrasound; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair.
[a]Class of recommendation.
[b]Level of evidence.

9.2.7. Long-term follow-up after aortic repair

Long-term success in the management of aortic aneurysms depends also on strict post-treatment surveillance, for both secondary prevention of the aortic disease and early identification of post-repair complications.

In endovascularly treated patients, surveillance aims to detect endoleaks, aneurysmal sac dilatation, and graft structural failure or migration.[1150] Surgical treatments, while carrying higher operative risks, often yield more durable results with rarer late complications mostly related to laparotomy.[1151]

After intervention on the thoracic aorta, TTE, TOE, CCT, and CMR are used for follow-up, CCT being the most used and available method for both endovascular and surgical treatments.[1150–1152] After intervention on the AA, CCT, CMR, and DUS/CEUS are used. DUS/CEUS can detect the most common drawbacks of EVAR, except for graft structural issues. For chronic and periodic monitoring, the use of CMR, especially in young women, should be considered (to reduce radiation exposure). However, the choice between these modalities should consider patient factors, potential artefacts, and local imaging expertise and availability. Both for the thoracic and abdominal aorta, due to the lack of studies systematically comparing different surveillance time intervals, recommendations are mostly based on consensus or evidence from single-centre observational studies.[70,1153]

9.2.7.1. Follow-up after thoracic aortic aneurysm treatment

Complications after ascending aorta graft replacement, though rare, include pseudo-aneurysms and graft infections. Pseudo-aneurysms, occurring in roughly 5% of cases, are most common within the first 2 post-operative years, linked to aortic dissection surgery, HTAD, and synthetic glues.[1154] CMR studies systematically following peri-anastomotic haematomas have reported higher rates (15%).[1155] Graft infections can occur in 0.5%–6% of surgical patients with high morbidity and mortality rates, requiring rapid diagnosis. Treatment typically involves surgery and antibiotics, tailored to factors like overall health, infection severity, and underlying conditions.[1156] Residual aortic disease progression depends on the underlying condition, such as HTAD, and requires individualized surveillance.

After TEVAR for DTA aneurysm, late complications are higher than with surgery (up to 38%), leading to re-operation in 24% of cases.[1150] However, over 80% of TEVAR complications arise within the initial post-operative years.[1157] Notably, FET results in fewer stent graft-related complications: 2% stent-induced intimal tear, 3% endoleak, and 7% need for additional TEVAR.[1158]

After surgical treatment of TAAs, the protocol is a first CCT scan at discharge or 1 month, then another in the first post-operative year (at 6, 9, or 12 months), followed by a 2 year scan, and if no issues arise, scans every 5 years thereafter (*Figure 25*).[1062,1159] Stricter lifelong surveillance is recommended after TEVAR: after first imaging at 1 month, yearly controls are recommended for at least the first 5 post-operative years, then less frequently if no complications are detected (*Figure 27*).

Cardiovascular risk profile modification, cardiac rehabilitation, and lifestyle adjustments are an integral part of post-aneurysm repair follow-up (*Figure 7*).[24]

9.2.7.2. Follow-up after abdominal aortic aneurysm treatment

Evidence for follow-up after AAA is more robust than after TAA repair.[70,1096] Post-surgery, anastomotic or para-anastomotic complications are rare (2%–4%).[1160] In contrast, EVAR has higher complication rates (16%–30%), necessitating lifelong surveillance.[1079,1150] EVAR's survival advantage over surgery diminishes after 8 years, with higher aneurysm-related mortality risk for EVAR.[1079] However, most failures are detectable early, and complications seldom occur later in patients with normal early controls.[1161,1162] CCT effectively detects early EVAR abnormalities,[1163] but DUS/CEUS surveillance proves accurate, reducing the need for radiation and nephrotoxic agents, and lowering costs (*Figure 27*).[1164–1167]

Interestingly, a meta-analysis found low compliance of patients to post-operative surveillance without differences in all-cause mortality, aneurysm-related mortality, and re-intervention between compliant and non-compliant patients.[1168] Altogether, the above-mentioned evidence supports stratified methods of surveillance,[1096] with

identification of high-risk situations (e.g. older patients, inadequate sealing, type II endoleaks, no early post-procedural shrinkage of the aneurysmal sac) for which more frequent evaluation should be planned.[1161,1169,1170]

Follow-up of OMT is highly important in AAA patients (*Figure 7*).[24] Statin use after AAA repair (surgical or EVAR) is associated with decreased short- and long-term mortality.[1171] In addition, surveillance for aneurysm development in other arterial locations is recommended.

Recommendation Table 43 — Recommendations for follow-up after treatment of aortic aneurysms (see also Evidence Table 12)

Recommendations	Class[a]	Level[b]
Thoracic aortic aneurysm		
After open repair of TAA, an early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.[c,70,1153,1159]	I	B
After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities[d] are documented.[70,1153,1158]	I	B
After 5 post-operative years without complications, continuing long-term follow-up of TEVAR by CCT every 5 years should be considered.[70,1153,1158]	IIa	B
If growth of the excluded aneurysm is observed, without evidence of type I or III endoleak, repeating CCT every 6–12 months, depending on the growth rate observed, should be considered.[1150]	IIa	C
When frequent controls are required in TAA patients treated either by open or endovascular repair, CMR should be considered instead of CCT after the first year of follow-up. However, the choice between these imaging modalities should be based on individual patient factors, the potential for artefacts, and the local availability and expertise in specific imaging techniques.[1155]	IIa	C
Abdominal aortic aneurysm		
After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and every 5 years thereafter if findings are stable.[1079,1096]	I	A
After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities[d] are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.[70,1079,1100,1163–1165,1167]	I	A
In higher-risk patients, i.e. with inadequate sealing or type II endoleak at first CCT control, more frequent DUS/CEUS imaging should be considered.[e,1096,1161,1164,1165,1167]	IIa	B
In low-risk[f] patients, from 1 year post-operatively after EVAR, repeating DUS/CEUS every 2 years should be considered.[1096]	IIa	B
If any abnormality during DUS/CEUS is found, confirmation should be considered using additional CCT or CMR (based on potential artefacts).[1163,1166]	IIa	B
In post-treatment surveillance, administration of OMT (see 8.1.2.2 and 8.2.4) and assessment of aneurysm development/growth in other arterial segments should be considered.	IIa	C

Continued

AAA, abdominal aortic aneurysm; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CMR, cardiovascular magnetic resonance; DUS, Duplex ultrasound; EVAR, endovascular aortic repair; OMT, optimal medical treatment; TAA, thoracic aortic aneurysm; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]Both at the level of the treated segment and in the residual native aorta.
[d]Including: endoleak (any type), enlargement of the excluded aneurysm, and stent graft migration/separation/fracture.
[e]e.g. imaging every 6 months during the first year, thereafter every 2–3 years.
[f]Low-risk: early sac shrinkage >10 mm, relatively younger age (<70 years), proximal and distal sealing >10 mm, no endoleak.

9.3. Acute thoracic aortic syndromes

9.3.1. General concepts

Acute aortic syndromes are life-threatening emergencies, including classic AAD, IMH, PAU, aortic pseudo-aneurysm, and traumatic aortic injuries (TAI). They involve aortic wall damage and share a dynamic, overlapping pathophysiology, clinical presentation, and diagnostic and therapeutic approaches.[24,172,174,910] AAS may also be iatrogenic following open or endovascular/percutaneous procedures, or cardiac surgery.[1172]

To guide AAS management, several anatomical classifications have been developed, the Stanford and the DeBakey systems being the most widely used. The Stanford system classifies AAS according to whether the ascending aorta is involved (type A or DeBakey type I and type II) or not (type B or DeBakey type IIIa and type IIIb) regardless of the site of origin of the intimal tear.[172,174,910,1173] This classification considers not only anatomical and treatment aspects, but also prognostic implications, since patients with DeBakey type II AAS will probably be left without structural aortic wall lesions after surgery (*Figure 28*).

Furthermore, if time elapsed from symptom onset to diagnosis is considered, AAS can be divided into hyperacute (<24 h), acute (1–14 days), subacute (15–90 days), and chronic (>90 days) (*Figure 28*).[1174–1176]

A new classification considers the intimal tear's entry site and dissection extension (*Figure 29*).[136] Subscript P describes the proximal involved aorta, and subscript D indicates the distal zone. This classification guides treatment decisions for sealing the entry tear. AADs limited to the aortic arch or originating as retrograde dissections from the descending aorta that extend into the arch and stop before the ascending aorta are termed as ***non-A non-B AD***.[1177–1179]

Recently, a European update of the Stanford classification—Type Entry Malperfusion (TEM) classification—has been proposed.[1180] This combines information about the type of dissection, its extent, and the presence of complications (malperfusion), thus providing greater prognostic insights (*Figure 29*). This classification is recommended by the European Association for Cardio-Thoracic Surgery. The TEM and other classifications are described in the Supplementary data online, *Section 1.6*.

9.3.1.1. Epidemiology and risk factors

Classic AAD (comprising 80%–90% of AAS; incidence of 2.6–3.5 cases per 100 000 person-years)[24,1181] is characterized by the presence of an intimal flap separating the true from the false lumen (FL).[24,172,910]

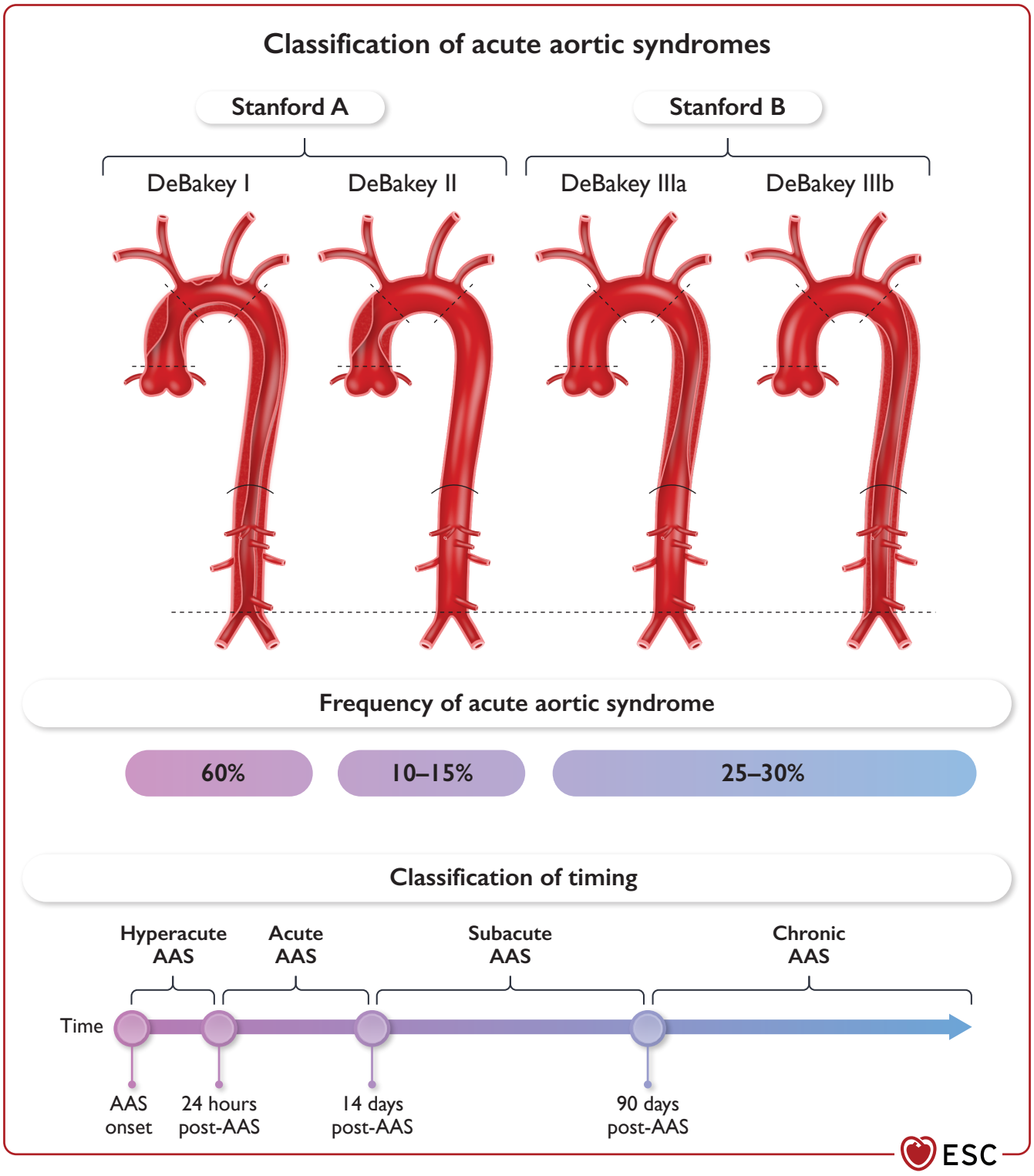

Figure 28 Anatomical and temporal classification of acute aortic syndrome. AAS, acute aortic syndrome.

Acute aortic dissection occurs mostly in males (~65%) and in the seventh decade of life (~63 years).[1175,1182] Multiple risk factors often coexist directly linked to factors like wall stress (with systemic hypertension being the most common) and/or aortic media abnormalities, including syndromic and non-syndromic genetic diseases. HTAD, BAV, prior aortic surgery, and larger aortic dimensions are more frequent among young patients (<40 years).[24,1182,1183] Systemic hypertension and cocaine abuse are more common among African-American

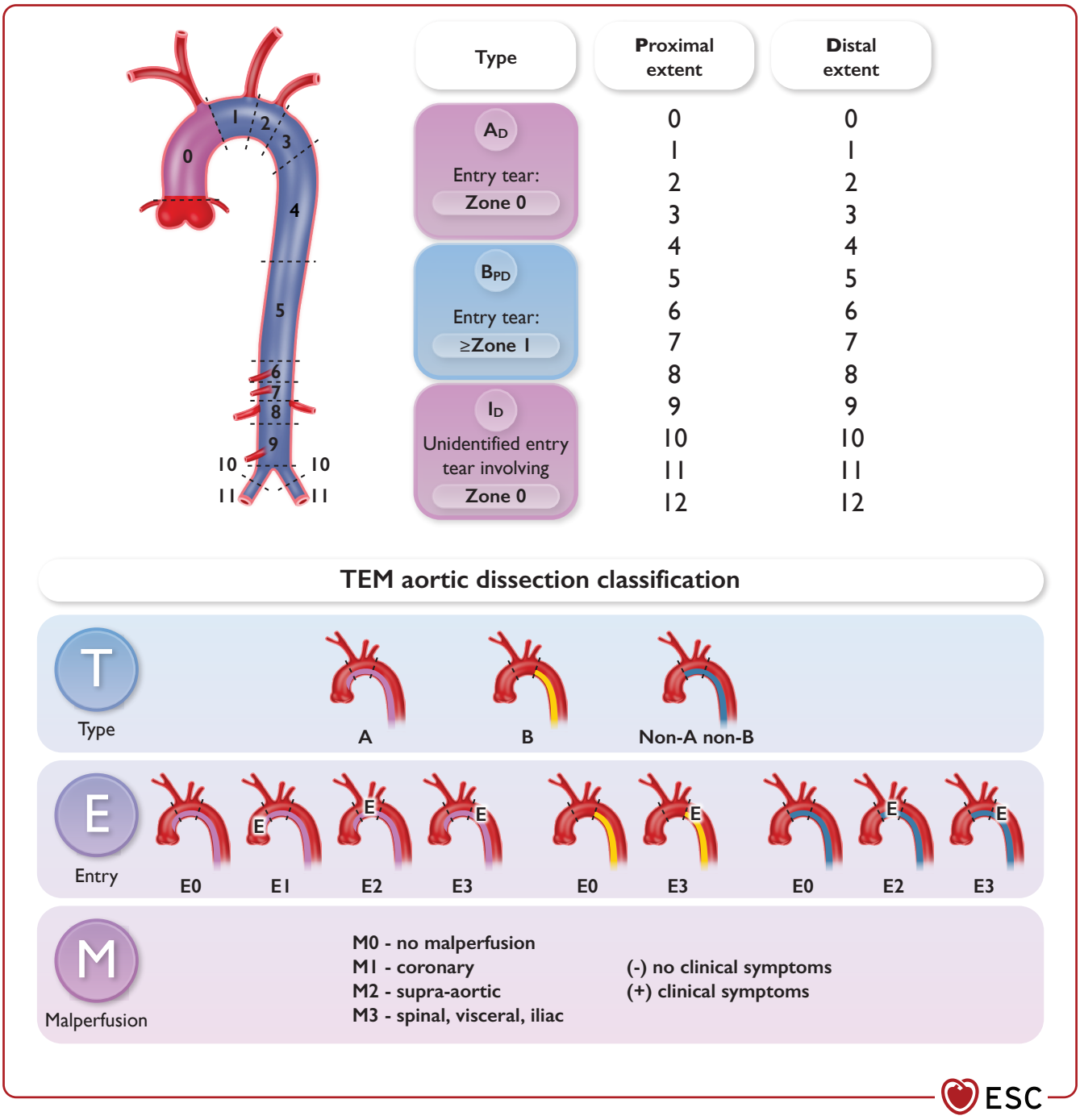

Figure 29 Aortic dissection classification system based on the 2020 Society for Vascular Surgery/Society of Thoracic Surgeons Reporting Standards and the European update of the Stanford classification—Type Entry Malperfusion classification. A, type A aortic dissection; B, type B aortic dissection; non-A, non-B, aortic dissection limited to the aortic arch or retrograde dissection extending into the arch (but not in the ascending aorta). Upper panel: Classification of AAD considering the intimal tear's entry site and dissection extension. Subscript P describes the proximal involved aorta, and subscript D indicates the distal zone. Lower panel: The TEM classification is the European update of the Stanford classification combining information about the Type of dissection (T), the Entry site (E), and the presence of Malperfusion (M). Also refer to Supplementary data online, *Section 1.6*. Society for Vascular Surgery/Society of Thoracic Surgeons (SVS/STS). Reproduced with permission from.[136,1180]

than among white patients.[1184,1185] Of note, the incidence of iatrogenic AD during cardiac catheterization is very low (around 0.01%–0.02%) and during cardiac surgery is 0.06%–0.23%, with favourable in-hospital and long-term prognosis.[1186,1187]

9.3.1.1.1. Sex differences. A specific female sex phenotype appears to be evident in acute TAAD. At admission, acute TAAD female patients are usually older but have lower body mass index (BMI), BSA, and creatinine plasma levels. They present less frequently with active smoking,

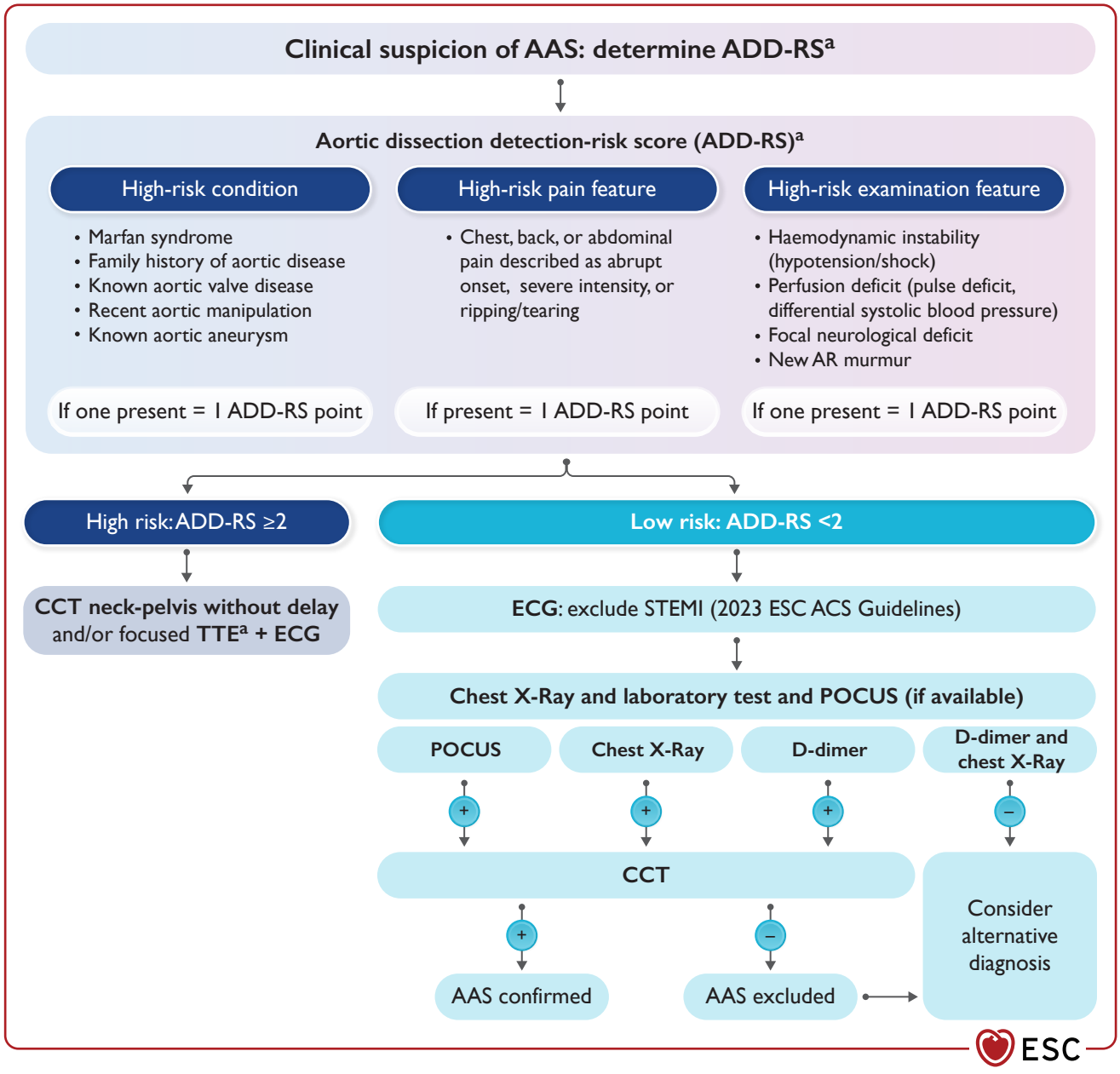

Figure 30 Multiparametric diagnostic work-up of acute aortic syndrome. AAS, acute aortic syndrome; ADD-RS, aortic dissection detection-risk score; CCT, cardiovascular computed tomography; ECG, electrocardiogram; POCUS, point-of-care ultrasound; STEMI, ST elevation myocardial infarction; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography; +, findings compatible with AAS. [a]In haemodynamically unstable patients: consider TTE and/or TOE as first-line imaging technique depending on local expertise and availability.

BAV, and previous cardiac surgery,[1188] but diabetes mellitus is more common in women than in men. In-hospital surgical mortality does not differ between sexes, although 10 year survival appears to be higher in men. Among only medically treated acute TAAD patients, prohibitive high in-hospital mortality has been equally registered for both sexes (men 58.6% vs. women 53.8%).[1188] However, further studies are needed to explore AAD sex differences to design appropriate diagnostic and therapeutic interventions and preventive strategies.[1189]

Pregnancy increases the risk of AAS, more often in the last trimester (50%) or post-partum (33%).[1190]

9.3.1.1.2. Chronobiology. Acute aortic dissection presents chronobiological patterns, with a higher incidence in morning hours (peak between 8 am and 9 am) and winter (peak in January in the Northern Hemisphere).[24,1175]

9.3.1.1.3. Outcomes. For acute TAAD, in-hospital mortality has decreased from 31% to 22% due to better surgical outcomes; for acute type B aortic dissection (acute TBAD), in-hospital mortality has remained stable over the years (14%).[1175,1182] Including deaths before admission, 30 day mortality for AAD ranges from 23% to 55.8% in Western Europe.[1181]

Non-A, non-B dissection patients tend to be younger (median age 59 years) and have a lower mortality than acute TAAD patients.[1180,1191] The 30 day mortality in patients medically treated is around 14%,[1179] and 4.4% for those successfully treated surgically.[1177]

9.3.1.2. Clinical presentation

Acute TAAD typically presents with sudden, severe chest/back pain, often described as 'sharp', alongside a history of arterial hypertension. However, around 6.4% of patients do not experience pain.[1182,1192,1193] Hypotension and shock are frequent. Unique clinical features specific to acute TAAD include pericardial effusion, aortic regurgitation, and coronary artery involvement leading to ACS (particularly the right coronary artery).[1194] Stroke may occur when supra-aortic branches are involved. Additional complications encompass paraplegia (resulting from spinal ischaemia), acute kidney injury, intestinal ischaemia, or limb ischaemia. Isolated abdominal aortic dissection occurs in about 1.3% of acute TBAD cases when the intimal flap originates below or at the renal arteries.[1195]

A complete clinical evaluation is mandatory, consisting of a central neurological evaluation, heart and lung auscultation (aortic diastolic murmur, pericardial rubbing, etc.), abdominal palpation (tenderness, etc.), and assessment of peripheral pulsations as well as mobility and sensibility in upper and lower limbs. SBP differences (pulse deficit) should be sought.

9.3.1.3. Diagnostic work-up

Early diagnosis is still a major pitfall in managing AAD patients, therefore, a diagnostic multiparametric algorithm is proposed (*Figure 30*). It combines the aortic dissection detection-risk score (ADD-RS) with D-dimer (DD) and has been validated with an excellent capacity to rule out AAS.[1196–1200]

In patients presenting with chest pain, a routine chest radiography and ECG are recommended to exclude other aetiologies; however, the absence of these findings should not delay further investigations.[163] Laboratory tests should be obtained, but awaiting results should not delay imaging if there is a high probability of AAD. The most common finding is an increase in DD level, which is the case in several other conditions such as pulmonary embolism or infections. When DD levels are below 500 ng/mL, AAD is unlikely.[172,1201]

A focused TTE at the emergency department, if available, is recommended[1202,1203] to assess pericardial effusion, wall motion abnormalities, aortic regurgitation, and aortic diameters. Sometimes a dissection flap can be visualized, especially when using contrast.[165]

When AAD is suspected, ECG-gated CCT from neck to pelvis is the preferred imaging technique, with 100% sensitivity and 98% specificity, and should be performed as soon as possible to confirm diagnosis, localize entry tear, extension (type A vs. type B), and malperfusion.[170,172,1182,1204] When ACS or pulmonary embolism are still in the differential diagnosis, a triple rule-out ECG-gated CCT scan protocol can be performed be performed to avoid motion artefacts mimicking acute TAAD.[170,1205,1206] However, this strategy is associated with higher contrast and radiation doses, might be less accurate for AAS, and does not reduce the need for additional imaging tests.[170,1207] If CCT is not available or in haemodynamically unstable patients, TOE can confirm diagnosis. TOE is especially useful pre-, intra, and postoperatively to monitor changes in the anatomical AAD configuration or surgical complications. CMR could be a valuable alternative for CCT, however, it is less available, requires a longer examination time, relies on patient collaboration, and consequently, is less frequently used in the acute setting. CCT, CMR, and TOE all provide good diagnostic accuracy[172,1204] (See Supplementary data online, *Table S4*).

Recommendation Table 44 — Recommendations for diagnostic work-up of acute aortic syndromes

Recommendations	Class[a]	Level[b]
In unstable patients who cannot be transferred to CCT, TOE is recommended for diagnosis[1204,1208,1209] and evaluation of the coeliac trunk and mesenteric artery.[1210]	I	B
In patients presenting with clinical features compatible with possible AAS, a multiparametric algorithm for ruling in or out AAS using the ADD-RS is recommended.[1196–1200]	I	B
ECG-gated CCT from neck to pelvis is recommended as the first-line imaging technique in patients with a suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).[170]	I	C
In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.[170]	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.[170]	I	C
In patients with suspected AAS, CMR should be considered as an alternative imaging technique if CCT is not available.[170]	IIa	C

AAS, acute aortic syndrome; ADD-RS, aortic dissection detection-risk score; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.
See also *Figure 30*.
[a]Class of recommendation.
[b]Level of evidence.

9.3.1.4. Therapeutic intervention in acute aortic dissection

9.3.1.4.1. Initial treatment. Acute aortic syndrome care should be centralized in experienced centres and managed by aorta teams.[1211] The cornerstone in AAS is initial reduction of the pulse pressure by lowering SBP below 120 mmHg and heart rhythm ≤60 beats per minute (b.p.m.). The aim is to decrease aortic wall stress to avoid further extension of dissection with possible rupture or malperfusion.[174,1212–1216] Intravenous beta blockade (labetalol as a first choice due to its alpha- and beta-blocking properties) is generally accepted as the best option. Also, esmolol, an ultra-short-acting beta-blocker, can be titrated quickly and easily, making it particularly useful in the acute setting. If contraindicated, i.v. non-dihydropyridine CCBs could be used for heart rate control. If the BP target is not reached after initiating beta-blockers, i.v. vasodilators such as nitrates or dihydropyridine CCBs (e.g. nicardipine) can be administered concomitantly with rate-controlling agents first to avoid reflex tachycardia. In cases of malperfusion, higher BP could be tolerated to optimize perfusion to the threatened region. Early placement of an arterial line to monitor BP invasively is mandatory and admission to an intensive care unit is advisable (including ECG and urine output monitoring).[1205,1217,1218] Antihypertensive treatment can be gradually switched to oral therapy once BP and heart rate targets are reached and the patient has normal gastrointestinal transit. Adequate pain control is necessary to help reach these haemodynamic goals. Intravenous morphine can be cautiously titrated to induce pain relief (*Figure 31*).

In-hospital mortality, reaching 60%, correlates with AAS type, location, patient comorbidities, and treatment. Risk rises with complications like pericardial tamponade, coronary involvement, or malperfusion. *Figure 32* describes the main signs and symptoms of complications and the mortality rate associated with them.[1219–1223]

Recommendation Table 45 — Recommendation for medical treatment in acute aortic syndromes

Recommendations	Class[a]	Level[b]
In patients with AAS, immediate anti-impulse treatment targeting SBP <120 mmHg and heart rate ≤60 b.p.m. is recommended. In cases of spinal ischaemia or concomitant brain injury, maintaining higher MAP is recommended.[1214–1216]	I	B
Intravenous BBs (e.g. labetalol or esmolol) are recommended as first-line agents. If necessary, i.v. vasodilators (e.g. dihydropyridine calcium blockers or nitrates) could be added.[174,1224]	I	B
Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.[1205,1217,1218,1225]	I	B
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents, is recommended after 24 h if gastrointestinal transit is preserved.[174,1216]	I	B
Adequate pain control to achieve haemodynamic targets is recommended.[174]	I	C
If the patient has a contraindication for BBs, a non-dihydropyridine calcium blocker should be considered.[174,1224]	IIa	B

AAS, acute aortic syndrome; BB, beta-blocker; BP, blood pressure; b.p.m., beats per minute; ECG, electrocardiogram; i.v., intravenous; MAP, mean arterial pressure; SBP, systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.

Interventional treatment in acute TAAD and acute TBAD is described in the next sections and summarized in *Figure 33*.

9.3.1.4.2. Type A aortic dissection interventional treatment. Immediate surgical repair is recommended for acute TAAD, however, a high mortality rate (~50% and 1%–2% per hour) within the first 48 h is described if managed medically only.[1232] Despite advances in surgical and anaesthetic techniques, there is still a high risk of perioperative mortality (17%–25%) and neurological complications (18%).[1233] In recent reports from the International Registry of Acute Aortic Dissection (IRAD), medically managed patients had a 23.7% mortality rate (0.5% per hour) compared with 4.4% (0.09% per hour) for those undergoing surgery.[1234] Analyses of pre- and post-July 2007 IRAD data showed no difference in 48 h mortality for medically treated patients, but surgical mortality decreased (from 5.5% to 3.9%).[1234] As surgical techniques have improved, data have shown improved post-operative survival rates.[1235] The use of the GERAADA (German Registry of Acute Aortic Dissection Type A) score[1236] should be considered in patients undergoing surgery to determine 30 day mortality (https://www.dgthg.de/de/GERAADA_Score).

Surgical intervention surpasses conservative therapy in long-term follow-up,[1237] even for challenging cases. Thus, all acute TAAD patients should receive surgical treatment; however, cardiogenic shock secondary to pericardial tamponade, malperfusion of coronary arteries, mesenteric circulation, lower extremities, kidneys, or brain, and/or coma are major predictors for post-operative mortality (*Figure 32*).[1234,1238] Among octogenarians, in-hospital mortality was lower after surgery than with conservative treatment (37.9% vs. 55.2%), but with a non-significant difference due to small sample size.[1239] While some have reported excellent surgical and quality of life (QoL) outcomes in elderly patients,[1239] others found

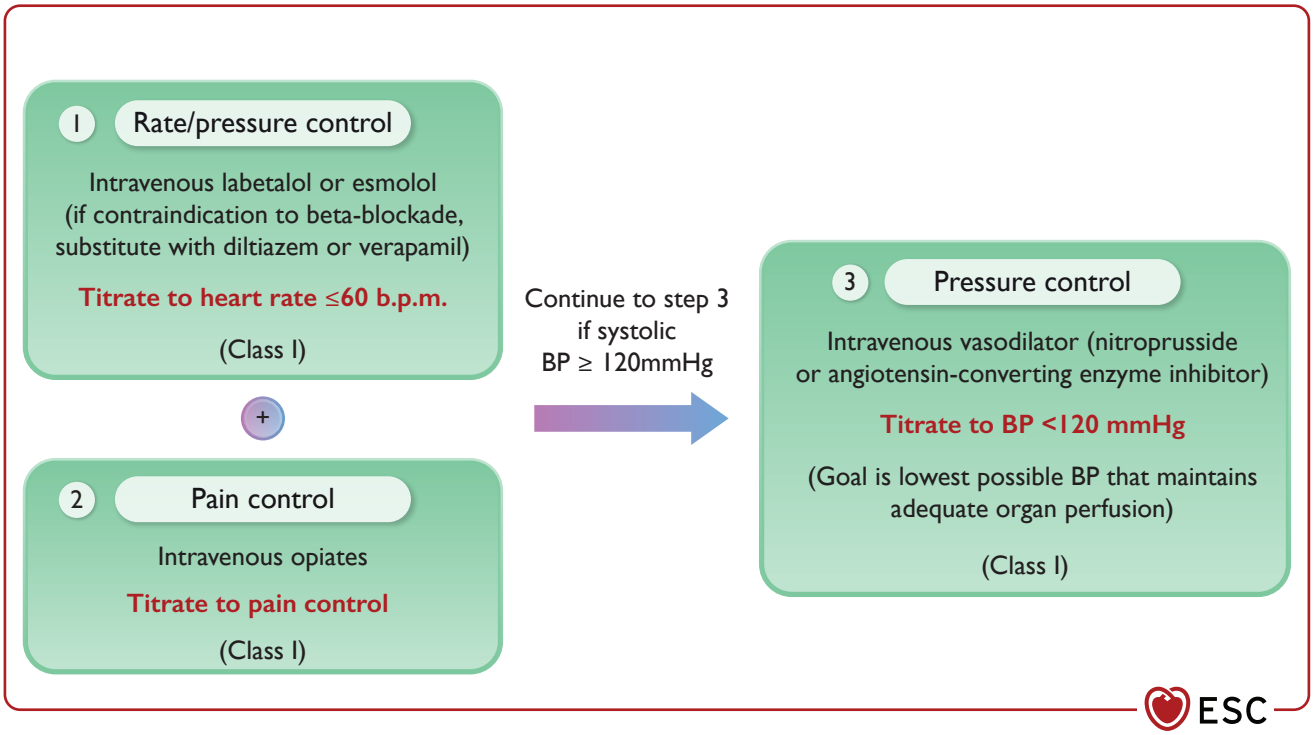

Figure 31 Medical management of acute aortic syndrome. BP, blood pressure; b.p.m: beats per minute.

a higher rate of post-operative neurological complications.[1240] Based on the current evidence, age per se should not be considered an exclusion criterion for surgery.

For optimal repair of acute TAAD regarding long-term outcomes, including risk of late death and late re-operation, the following points need to be addressed. First, in most cases of aortic regurgitation associated with acute TAAD, the aortic valve is essentially normal and can be preserved.[1241–1243] Alternatively, valve replacement can be performed in cases of pre-existent structural valve disease. The decision whether to replace the aortic root is based on the presence of tears in the sinuses, extensive dissection of sinuses/coronary ostia, or significant dilatation of the root. The risk of late dilatation of the aortic sinuses when spared should be considered.[1242,1244] Additionally, the distal extent of aortic repair is a topic of debate. Ascending aortic replacement or hemi-arch replacement alone is technically easier and effectively closes the entry site but leaves a large part of the diseased aorta untreated. In acute TAAD with visceral or renal malperfusion, the primary entry tear is often in the descending aorta. Consider extended therapies like FET repair for these patients, offering a complete repair with a low chance of late re-intervention despite increased technical complexity.[1245–1247]

For potential cardiac arrest from pericardial tamponade, consider an emergency pericardial puncture as a temporary life-saving measure before transferring to the operating room.[1248,1249]

Recommendation Table 46 — Recommendations for intervention in type A acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD, emergency surgical consultation and evaluation and immediate surgical intervention is recommended.[1182,1250]	I	B
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.[1251–1255]	I	B
In patients presenting with acute TAAD, transfer from a low- to a high-volume aortic centre with the presence of a multidisciplinary team should be considered to improve survival if transfer can be accomplished without significant delay in surgery.[1256,1257]	IIa	B
In selected patients, a valve-sparing root repair may be considered, when performed by experienced surgeons.[1251,1258,1259]	IIb	B

TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

The frozen elephant trunk technique

The FET technique addresses complex aortic and aortic arch issues in a single operation,[1260–1263] creating a secure landing zone for future interventions. Recent advances involve 'proximalization'—placing the FET in the aortic arch's zone 0 or 1, treating proximal arch aortic issues, and enhancing the landing zone for downstream procedures—which surpasses the standard elephant trunk technique.[1264,1265]

Recommendation Table 47 — Recommendations for aortic repair strategies in type A acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.[1251–1255]	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.[1266–1269]	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.[1270–1272]	I	B
In patients with acute TAAD and a secondary intimal tear in the arch or proximal DTA, an extended aortic repair with stenting of the proximal DTA (e.g. by using the frozen elephant trunk technique) may be considered to reduce late distal aortic complications (e.g. aneurysm evolution of the remaining dissected descending aorta).[1273,1274]	IIb	C

DTA, descending thoracic aorta; FL, false lumen; TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

Malperfusion in type A aortic dissection

In acute TAAD with malperfusion, operative mortality correlates with the number of affected organs. Around 30% of patients develop malperfusion syndrome due to elevated pressure in the FL caused by substantial proximal inflow and insufficient distal outflow, leading to visceral organ and limb ischaemia.[1175] The intimal flap may extend into peripheral arteries, causing a static 'stenosis-like' blockage. Malperfusion typically combines dynamic and static obstructions, necessitating surgical and hybrid interventions for affected patients (*Figure 34*).

Mesenteric malperfusion, a life-threatening complication with a mortality rate of 65%–95%, leads to diverse treatment approaches. Some centres prefer early direct reperfusion before aortic surgery,

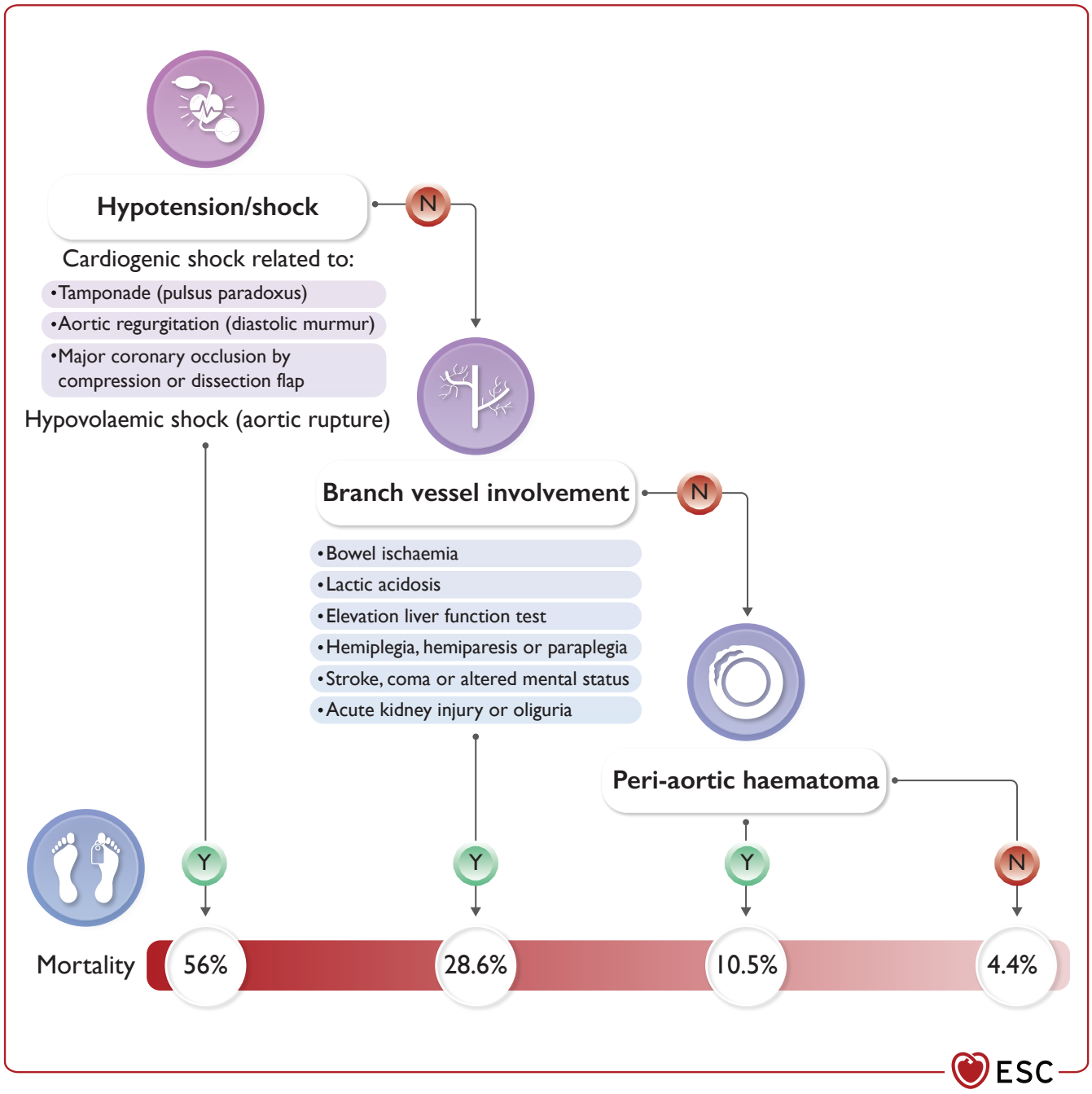

Figure 32 Complications in acute aortic syndromes, clinical evidence associated with malperfusion syndrome, and in-hospital mortality associated with these complications.

while others favour conventional central aortic repair.[1275] The IRAD registry highlights the superiority of a surgical and hybrid approach over medical or endovascular therapy alone. Central aortic repair effectively restores perfusion, showing promising results for renal malperfusion, extremity malperfusion, uncomplicated mesenteric malperfusion, or combinations.

Cerebral malperfusion, equally grave, triggers treatment debates necessitating a multidisciplinary strategy. Evidence supports surgical

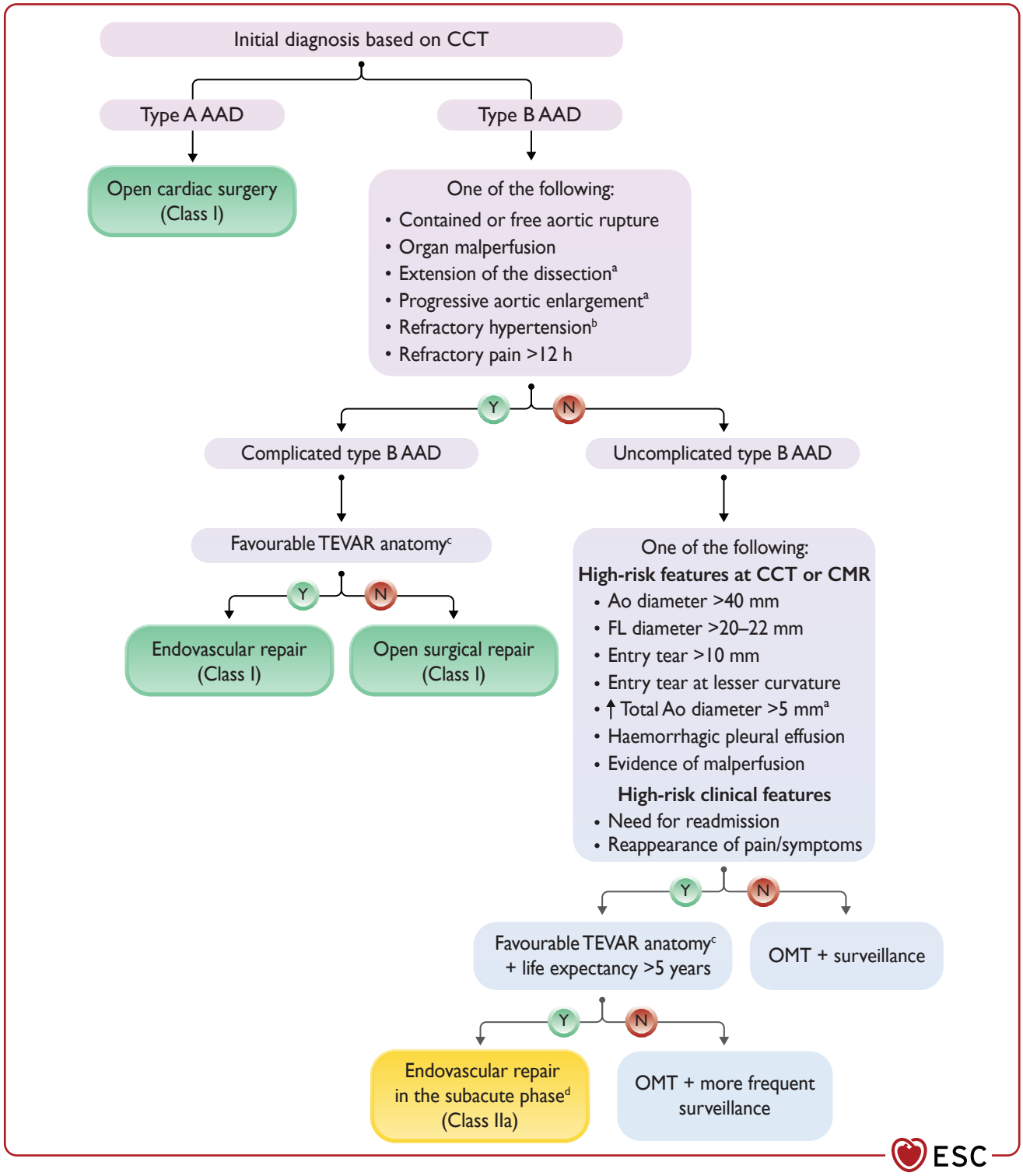

Figure 33 Interventional treatment algorithm in acute aortic dissection. AAD, acute aortic dissection; Ao, aorta; CCT, cardiovascular computed tomography; OMT, optimal medical treatment; TEVAR, thoracic endovascular aortic repair. [a]On serial imaging in the acute phase during the hospital stay. [b]Ongoing hypertension despite more than three classes of antihypertensive drugs. [c]Defined as the presence of adequate proximal and distal landing zones for the prosthesis and adequate iliac/femoral vessels for vascular access. [d]Between 14 and 90 days after dissection onset.[172,1226–1231]

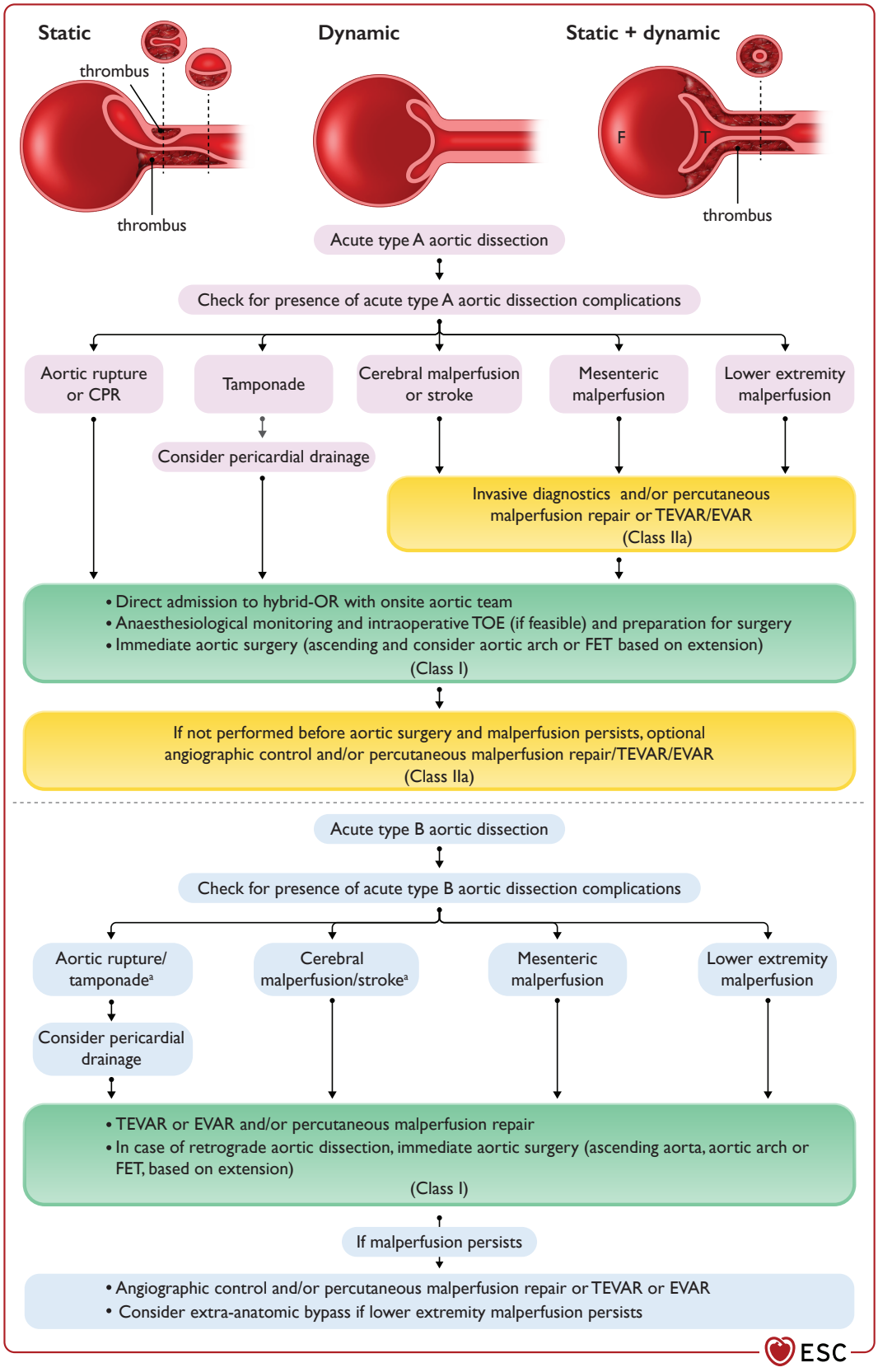

Figure 34 Mechanisms and clinical management of aortic branch obstruction in acute aortic dissection. CPR, cardiopulmonary resuscitation; F, false lumen; FET, frozen elephant trunk; OR, operating room; T, true lumen; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair. [a]Develops only in retrograde type A dissection.

intervention, reducing mortality rates to 25%–27%, compared with 76% with medical management alone.[1255,1276] Close monitoring and rapid intervention are essential to achieve optimal outcomes and minimize the risk of permanent neurological damage. A recommended algorithm for malperfusion management is displayed in *Figure 34*.

Recommendation Table 48 — Recommendations for the management of malperfusion in the setting of acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.[1275,1277]	I	B
In patients with acute TAAD presenting with cerebral malperfusion or non-haemorrhagic stroke, immediate aortic surgery should be considered to improve neurological outcome and reduce mortality.[1255,1276,1278]	IIa	B
In patients with acute TAAD presenting with clinically significant mesenteric malperfusion syndrome, immediate invasive angiographic diagnostics to evaluate percutaneous malperfusion repair before or directly after aortic surgery, in aortic centres with expertise, should be considered.[1278–1280]	IIa	C

TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

Endovascular treatment in type A aortic dissection

Endovascular therapy alone has been attempted in highly selected cases and the concept of a single endovascular valve-carrying conduit was suggested recently but has not yet been validated.[1281,1282]

Treatment in non-A non-B aortic dissection

Conservative management leads to high mortality (malperfusion, aortic rupture); thus, surgery or endovascular therapy is favoured within 14 days of symptom onset. For complicated non-A non-B aortic dissection with an arch tear, consider FET repair, though if feasible, stent-graft implantation for primary tear coverage is an alternative.[1179,1283]

9.3.1.4.3. Acute type B aortic dissection interventional treatment. Acute TBAD presents without complications (uncomplicated) in around 50% of cases.[1250] Complicated acute TBAD includes aortic rupture, malperfusion-related issues, rapid aortic expansion, paraplegia/paraparesis, aortic haematoma, refractory pain, and hypertension despite optimal therapy, which associates with an approximately 50% mortality risk with conservative treatment.[1193,1250,1284,1285]

Open surgery used to be the sole option for complicated acute TBAD but carried a mortality rate of 25%–50%. Consequently, medical management, now considered the standard for uncomplicated cases, significantly reduces mortality. Goals include lowering SBP and heart rate with BBs (see *Section 9.3.1.4.1*). However, adherence is the main limitation of chronic medical treatment, with a rate below 50%.[1286,1287] Compliance increases with previous aortic surgery, severity of hypertension, and understanding of the disease process. Thus, surveillance and disease awareness are imperative for these patients.

Endovascular therapy for complicated acute TBAD is now the first-line treatment, provided there is favourable anatomy, due to positive short- and long-term outcomes.[1288–1294] Open surgery is reserved for unsuitable cases, and fenestration could be considered as an ultima ratio. In selected instances, correcting side branch compression before proximal sealing may be considered.[136]

In recent years, the ADSORB (Acute Dissection Stentgraft OR Best Medical Treatment) and INSTEAD-XL (Investigation of Stent Grafts in Aortic Dissection with extended length of follow-up) trials[1219,1226,1295] have reported that early intervention for uncomplicated acute and subacute TBAD is beneficial compared with medical management, and there is important debate on whether to treat patients with uncomplicated acute TBAD to improve their life expectancy.[1296–1298] Intervention is considered early within 90 days after onset of symptoms and may be safer when performed in the subacute phase (>14 days after onset of symptoms), but data are scarce.[1298–1300] The Society of Thoracic Surgeons/American Association for Thoracic Surgery (STS/AATS) 2022 guidelines[1294] state that prophylactic TEVAR may be considered also in patients with suitable anatomy and high-risk features (*Figure 33*) to reduce late aortic-related adverse events. However, this matter is not entirely settled, and the Improving outcomes in vascular disease—aortic dissection (IMPROVE-AD trial) is currently underway. This trial aims to evaluate clinical outcomes in patients with subacute (from 48 h to 6 weeks) uncomplicated type B aortic dissection (uTBAD), comparing upfront TEVAR plus medical therapy against medical therapy with surveillance for deterioration.

Aortic characteristics change over time, and endovascular treatment in the chronic phase offers limited potential for aortic remodelling. Identifying specific characteristics at the time of acute TBAD diagnosis that predict a complicated course has been attempted. Independent predictors of TBAD outcomes include a primary entry tear >10 mm located at the inner aortic curvature,[1301] initial aortic diameter >40 mm,[1301,1302] initial FL diameter >20 mm,[1301] number/size of fenestrations between the true lumen and FL,[1303] stent graft-induced new entry tear,[1304,1305] and partial FL thrombosis.[1306,1307] These parameters are summarized in a new system for the categorization of AD, DISSECT (**D**uration from onset of symptoms, **I**ntimal tear location, **S**ize of the aorta based on maximum trans-aortic diameter, **S**egmental Extent, **C**linical complications related to the dissection, **T**hrombosis of the FL),[1308] which serves as a guide to support a therapeutic decision (*Figure 33*).[1308] A recent meta-analysis found TEVAR to be superior to best medical therapy in uncomplicated acute TBAD. Early outcomes were similar, but TEVAR was associated with fewer long-term events and better aortic remodelling.[1297,1298,1309] Thus, in stable TBAD with suitable anatomy and high-risk features, pre-emptive TEVAR to improve the late outcome should be considered.

Accurate endograft sizing is vital for TEVAR success, as errors may lead to complications. Disease-specific factors, such as acute thoracic aortic syndromes, pose challenges due to fluctuations in aorta diameter from haemorrhagic shock and resuscitation. Sizing decisions must account for these changes. Measuring the thoracic aorta based on admission CCT may be imprecise, even with proper centreline measurements. Real-time imaging, especially IVUS, enhances accuracy, particularly in hypovolaemic cases. However, further research is required to clarify the role of intraoperative imaging methods (e.g. IVUS, TOE, 3D CCT) in endograft sizing and long-term outcomes for optimal patient care.[194]

Recommendation Table 49 — Recommendations for the management of patients presenting with acute type B aortic dissection

Recommendations	Class[a]	Level[b]
Medical therapy including pain relief and blood pressure control is recommended in all patients with acute TBAD.[1215,1219,1310,1311]	I	B
In patients with complicated acute TBAD, emergency intervention is recommended.[1193,1250,1284,1285,1288,1289,1291–1293]	I	B
In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.[c,910,1288–1293]	I	B
In patients with acute TBAD, BBs should be considered as the first-line medical therapy.[1216,1312]	IIa	B
In patients with uncomplicated acute TBAD, TEVAR in the subacute phase (between 14 and 90 days) should be considered in selected patients with high-risk features[d] to prevent aortic complications.[1219,1226,1295,1297,1298,1308,1309]	IIa	B

BBs, beta-blockers; HTAD, heritable thoracic aortic disease; TBAD, type B aortic dissection; TEVAR, thoracic endovascular aortic repair.
See also *Figure 33*.
[a]Class of recommendation.
[b]Level of evidence.
[c]Except in patients with known or suspected HTAD.
[d]For high-risk features see *Figure 33*.

9.3.1.4.4. Chronic type B aortic dissection interventional treatment. Type B aortic dissection is considered as chronic 3 months after the onset of symptoms, but it also includes residual type B dissection after repair of TAAD. Aortic complications, especially aneurysmal degeneration, will occur in up to 50% of these patients.[1302,1313] Therefore, in chronic TBAD, indications for treatment include the onset of new aortic symptoms such as rapid expansion, malperfusion, or rupture.[1314] In asymptomatic patients, aneurysmal dilatation is the most important risk factor for rupture, reaching 20% when the diameter exceeds 55 mm.[1302,1315] Risk of rupture increases with diameter; it has been reported a risk of 15.3% and 18.8% between 50–55 mm and 54–56 mm, respectively, thus suggesting 50–55 mm as a threshold for elective surgery.[1316] However, smaller diameters should be considered in patients with HTAD. According to several studies, mortality in the chronic phase is high (40%–70%) and it is mainly related to patients' comorbidities, such as heart disease and stroke.

Open repair

Despite the lack of data comparing open repair vs. TEVAR in chronic TBAD, open surgery remains the first-line treatment in low-risk patients or those with HTAD. The STS/AATS guidelines[1294] state that open repair should be considered in chronic TBAD patients with indication for intervention, unless comorbidities are prohibitive or anatomy is not suitable for TEVAR. The surgical technique for chronic TBAD is like those for degenerative aneurysms, but repair is more complex due to the dissection flap.[1317] Surgical mortality rates between 6% and 11% and SCI rates between 3% and 11% have been reported.[1317–1321] Patients treated in low-volume centres present higher mortality rates (up to 20%), which reinforces the recommendation for centralization in experienced centres.

Endovascular repair

Thoracic endovascular aortic aneurysm repair (TEVAR) is the preferred treatment for eligible chronic TBAD patients, offering low early mortality (<5%), with stroke and SCI rates below 3%. It is also suitable for high-risk patients who are not candidates for open repair. The primary goal is to close the entry tear, induce FL thrombosis, and promote aortic remodelling to mitigate growth and rupture risk.[1322,1323] A systematic review showed 90% immediate technical success and 86% complete FL thrombosis. However, FL thrombosis usually occurs above the coeliac trunk, necessitating lifelong distal FL surveillance.[1324] Coverage of the LSA is often necessary and should be associated with revascularization. In a recent meta-analysis[1325] comparing TEVAR to open repair in chronic TBAD, TEVAR showed lower early mortality, stroke rates, SCI, and respiratory complications but a higher re-intervention rate. Long-term survival rates were similar, but open repair offered greater durability.[1326]

Adequate distal sealing poses a challenge due to the dissection extending to the iliac artery, with additional re-entries, allowing retrograde flow into the thoracic aneurysm. In chronic TBAD patients with AA enlargement, insufficient distal landing, or large re-entry tears, TEVAR alone is discouraged. Instead, a comprehensive repair involving the visceral aorta, infra-renal aorta, and iliac artery is needed. Recent studies have shown favourable results using custom or improvized fenestrated/branched endografts with careful patient selection.[1062,1327–1329] A multidisciplinary team-based approach in experienced centres is necessary for good outcomes.[1330]

Recommendation Table 50 — Recommendations for the management of patients presenting with chronic type B aortic dissection

Recommendations	Class[a]	Level[b]
Antihypertensive therapy is recommended in all patients with chronic TBAD.[1331–1333]	I	B
In chronic TBAD with acute symptoms of malperfusion, rupture, or progression of disease, emergency intervention is recommended.[1302,1313,1314]	I	C
In patients with chronic TBAD and a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.[1302,1315,1334]	I	B
In patients with chronic TBAD and a descending thoracic aortic diameter ≥55 mm, an indication for intervention should be considered in patients with low procedural risk.[1302,1316]	IIa	C
In patients with chronic post-dissection thoracoabdominal aortic aneurysms, the use of fenestrated/branched stent grafts may be considered, when treatment is indicated.[1062,1327–1329]	IIb	C

TBAD, type B aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

9.3.1.4.5. Management during pregnancy. Management of AD during pregnancy requires a multidisciplinary team and specialized centres. Initial care should consider general medical recommendations (as previously described), using drugs with the lowest teratogenic impact.

In cases of type A dissection, if the foetus is viable, caesarean delivery will be performed before aortic repair. If the foetus is not viable, surgery will be done with the foetus in place.[1335,1336] In uncomplicated type B

dissections, strict control of the pregnant patient and foetus with conservative medical management is recommended.[1224,1335] Although limited to selected cases, successful TEVAR has been described in complicated TBAD.[1227] More information is detailed in the *2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy*.[1337]

9.3.2. Intramural haematoma

Intramural haematoma, constituting 5%–25% of AAS cases, involves vasa vasorum haemorrhage within the aortic media, with or without intimal disruption (ID).[70,172,1338] Most cases (60%–70%) involve the DTA (ascending aorta ~30%, aortic arch ~10%).[70,172,1192] Although it usually occurs at an older age than AAD, risk factors and symptoms are similar;[70,172,1192,1338] however, aortic regurgitation, malperfusion syndrome, and pulse deficits are less frequent in type A IMH than in TAAD.[70,172]

9.3.2.1. Diagnostic work-up

Diagnostic IMH work-up should be similar to that proposed for AAS (*Figure 30*), but with different morphological features in the imaging techniques.

CCT and CMR (followed by TOE) are the leading techniques for diagnosis.[70,159,171–173] Unenhanced followed by contrast-enhanced CCT represents the most used tool in the acute setting (hyperintense signal of aortic wall before contrast administration).[70,171,172] The IMH diagnostic hallmark consists of crescentic or circular aortic wall thickening in the absence of an intimal flap or aortic wall enhancement following contrast administration.[70,171,172] CMR is an excellent imaging technique to detect small IMHs and for the differentiation of IMH (hyperenhanced images in T1-weighted images) from atherosclerotic thickening of the aorta, thrombus, or thrombosed dissection.[172] TTE yields low sensitivity (<40% for IMH cut-off limit of 5 mm).[171]

9.3.2.2. Clinical outcomes

Intramural haematoma may evolve into AAD (12% of patients), saccular (8%) or fusiform aneurysm (22%), and/or ID (54%).[1192,1339–1342] Partial or total regression is reported in 34% of patients.[70,1192,1343] Outcomes are comparable to those in AAD. In-hospital mortality for type A IMH is 26.6% (surgical 24.1% and medical 40.0%). In this regard, higher mortality for IMH involving the aortic valvular complex has been observed.[1175] In-hospital mortality for type B IMH is 4.4% but worsens once surgery is indicated (surgical 20.0% vs. medical 3.8%).[1175,1344]

9.3.2.3. Geographical variations

Reports from South Korea and Japan reveal notable disparities with Western nations in IMH incidence (28.9% vs. 5.7% of overall AAD as reported by IRAD), treatment strategies, and outcomes. In Eastern regions, the majority (80.8%) of type A IMH patients received medical treatment, resulting in significantly improved clinical outcomes (in-hospital mortality 6.6% [5.9% for medical and 9.4% for surgical]).[1345] These results may be partially explained by the detection of early-stage IMH (mild, uncomplicated cases) at primary centres.[1345–1347]

Table 16 High-risk features of intramural haematoma type A and B

Ascending aorta involvement
Difficult BP control
Persistent/recurrent pain despite aggressive BP control
Maximum aortic diameter: • Type A: >45–50 mm • Type B: >47–50 mm
Progression to aortic dissection
Focal intimal disruption with ulcer-like projection
Haematoma thickness >10 mm (type A) or >13 mm (type B)
Enlarging haematoma thickness
Enlarging aortic diameter
Pericardial effusion at admission (type A)
Recurrent pleural effusion
Detection of organ malperfusion

BP, blood pressure.
Adapted with permission from.[172]

9.3.2.4. Management

Current IMH therapeutic interventions are similar to AAD, with the first step consisting mainly of pain and BP control regardless of the anatomopathological features (*Figure 31*).

9.3.2.4.1. Type A intramural haematoma. As in AAD, type A IMH involves the ascending aorta. Surgery (emergency or urgent depending on clinical status) is recommended. In selected patients with increased operative risk (i.e. multiple comorbidities) and uncomplicated type A IMH without high-risk imaging features (*Table 16*) a 'wait-and-see strategy' in a reference/experienced centre may be reasonable.[70,172,1348,1349]

9.3.2.4.2. Type B intramural haematoma. In type B IMH, the disease is in the descending aorta, distal to the left subclavian artery. For uncomplicated type B IMH, initial management involves medical treatment and thorough clinical and imaging monitoring.[70,172] If uncomplicated type B IMH presents high-risk imaging characteristics (see *Table 16*), the multidisciplinary team should consider endovascular repair as an option. In contrast, complicated type B IMH warrants consideration of TEVAR.[1350,1351] However, in unfavourable anatomy, open surgery remains an alternative.

ID has been described in 54% of type B IMH cases.[1192,1339–1342] Approximately 28% of them are tiny intimal disruptions (≤3 mm) that are not related to AAEs. However, 14% of them evolve into focal intimal disruptions (FID) (>3 mm), with prognostic implications; thus, all patients with ID require close follow-up with imaging techniques. In the acute phase, FID has a poor prognosis owing to the high risk of aortic rupture and should be treated early and invasively, especially large FID (≥10 mm length and ≥5 mm depth).[1342,1352] However, in the chronic phase, most FIDs evolve with slow aortic dilatation and without complications, and they can be managed with medical treatment and close imaging surveillance.[1352]

Recommendation Table 51 — Recommendations for the management of intramural haematoma

Recommendations	Class[a]	Level[b]
In patients with IMH, medical therapy including pain relief and blood pressure control is recommended.[24,172]	I	C
In type A IMH, urgent surgery is recommended.[172,1175,1192]	I	C
In type B IMH, initial medical therapy under careful surveillance is recommended.[1175,1192,1347,1350,1353]	I	C
In uncomplicated[c] type B IMH, repetitive imaging (CCT or CMR) is indicated.[1175,1192,1347,1350,1353]	I	C
In complicated[c] type B IMH, TEVAR is recommended.[1175,1192,1347,1350,1353]	I	C
In uncomplicated[c] type B IMH but with high-risk imaging features[d], TEVAR should be considered.[1347,1350]	IIa	C
In complicated[c] type B IMH, surgery may be considered in patients with anatomy unfavourable for TEVAR.[1175,1192,1347,1350,1353]	IIb	C
In selected patients with increased operative risk and uncomplicated[c] type A IMH without high-risk imaging features[d], a 'wait and see' strategy may be considered.[1348,1354–1356]	IIb	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; IMH, intramural haematoma; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]Uncomplicated/complicated IMH refers to the absence or presence of recurrent pain, expansion of the IMH, periaortic haematoma, and intimal disruption.
[d]High-risk features of intramural hematoma type A and B are described in *Table 16*.

9.3.3. Penetrating atherosclerotic ulcer

Penetrating atherosclerotic ulcer (2%–7% of all AAS cases) is characterized by localized ulceration of an aortic atherosclerotic plaque penetrating through the internal elastic lamina into the media, frequently associated with IMH and diffuse atherosclerosis.[70,172,174,910,1338,1343]

Often, multiple PAUs are present, ranging from 5 to 25 mm in diameter and 4 to 30 mm in depth.[70,172,174,1338] They occur mostly in the middle and lower DTA, with the aortic arch and AA less involved. The ascending aorta is rarely affected,[70,172,910,1192] but when this occurs, especially complicated with IMH, the risk of rupture is 33%–75% and progression to dissection is associated with a high mortality rate.

Most patients are older males, smokers, aged >65, with multiple comorbidities like systemic hypertension, CAD, COPD, renal insufficiency, and concurrent abdominal aneurysm.[24,172,910,1357]

Symptoms are like those in AAD and may manifest in older age after a long asymptomatic phase (often PAU is diagnosed as an incidental finding during an imaging examination).[24,172,910,1357] It should be highlighted that symptom onset may indicate PAU expansion (tunica adventitia involvement); thus, urgent imaging (CCT or CMR) and appropriate therapeutic intervention are needed to prevent aortic rupture.[70,171,172,174]

9.3.3.1. Diagnosis

Diagnostic work-up is described in *Figure 30*. CCT represents the technique of choice for diagnosis. TOE and CMR represent possible valid alternatives considering availability and local expertise.[70,159,171–173] Of note, ^{18}FDG-PET-CT is a promising technique since it can detect increased glucose uptake in PAUs as a marker of increased metabolic activity and inflammation, which has been associated with major adverse events.[1358,1359] This information may be used to guide treatment decisions, such as the selection of patients who may benefit from endovascular or surgical intervention.[1360]

9.3.3.2. Treatment

Medical treatment as described for AD is recommended (*Figure 31*). Management of incidental cases is not clearly defined.[174] Small series suggest that isolated, asymptomatic, small PAUs may be safely managed conservatively with regular surveillance.[1361,1362]

Surgery is recommended in type A PAU with the option of a 'wait-and-see strategy' in highly selected high-risk patients with no high-risk features (*Figure 35*). However, in uncomplicated type B PAU, medical treatment along with careful clinical and imaging surveillance is recommended.[174,1350] When intervention is needed, endovascular treatment (early and 3 year aortic mortality 7.2% and 10.4%, respectively)[1350] should be preferred to open surgery (early and 3 year aortic mortality of 15.9% and 25.0%, respectively).[174,1350] In cases of uncomplicated PAU with high-risk imaging features[1363–1365] (*Figure 35*), endovascular treatment should also be considered. The natural history of PAU of the abdominal aorta (AA) with associated IMH is less known. In a review of PAU of the AA, endovascular stenting was the preferred treatment of choice (62%), followed by open surgical repair (35%) and conservative therapy (3%).[1366]

Recommendation Table 52 — Recommendations for the management of penetrating atherosclerotic ulcer

Recommendations	Class[a]	Level[b]
In all patients with PAU, medical therapy including pain relief and blood pressure control is recommended.[24,172]	I	C
In cases of type A PAU, surgery is recommended.[172]	I	C
In cases of type B PAU, initial medical therapy under careful surveillance is recommended.[1347,1350]	I	C
In uncomplicated type B PAU, repetitive imaging (CMR, CCT, or TOE) is recommended.[1347,1350]	I	C
In complicated type B PAU, endovascular treatment (TEVAR) is recommended.[1347,1350,1357]	I	C
In uncomplicated type B PAU with high-risk imaging features,[c] endovascular treatment should be considered.[1347,1350]	IIa	C
In selected patients with increased operative risk and uncomplicated type A PAU without high-risk imaging features,[c] a 'wait-and-see' strategy may be considered.[1367]	IIb	C
In complicated type B PAU, surgery may be considered based on anatomy and medical comorbidities.[1347,1350]	IIb	C
In isolated, asymptomatic, small PAUs with no high-risk features,[c] conservative management with regular surveillance and medical treatment may be considered.[24,1361]	IIb	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; PAU, penetrating atherosclerotic ulcer; TOE, transoesophageal echocardiography; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 35* for high-risk imaging features of PAU.

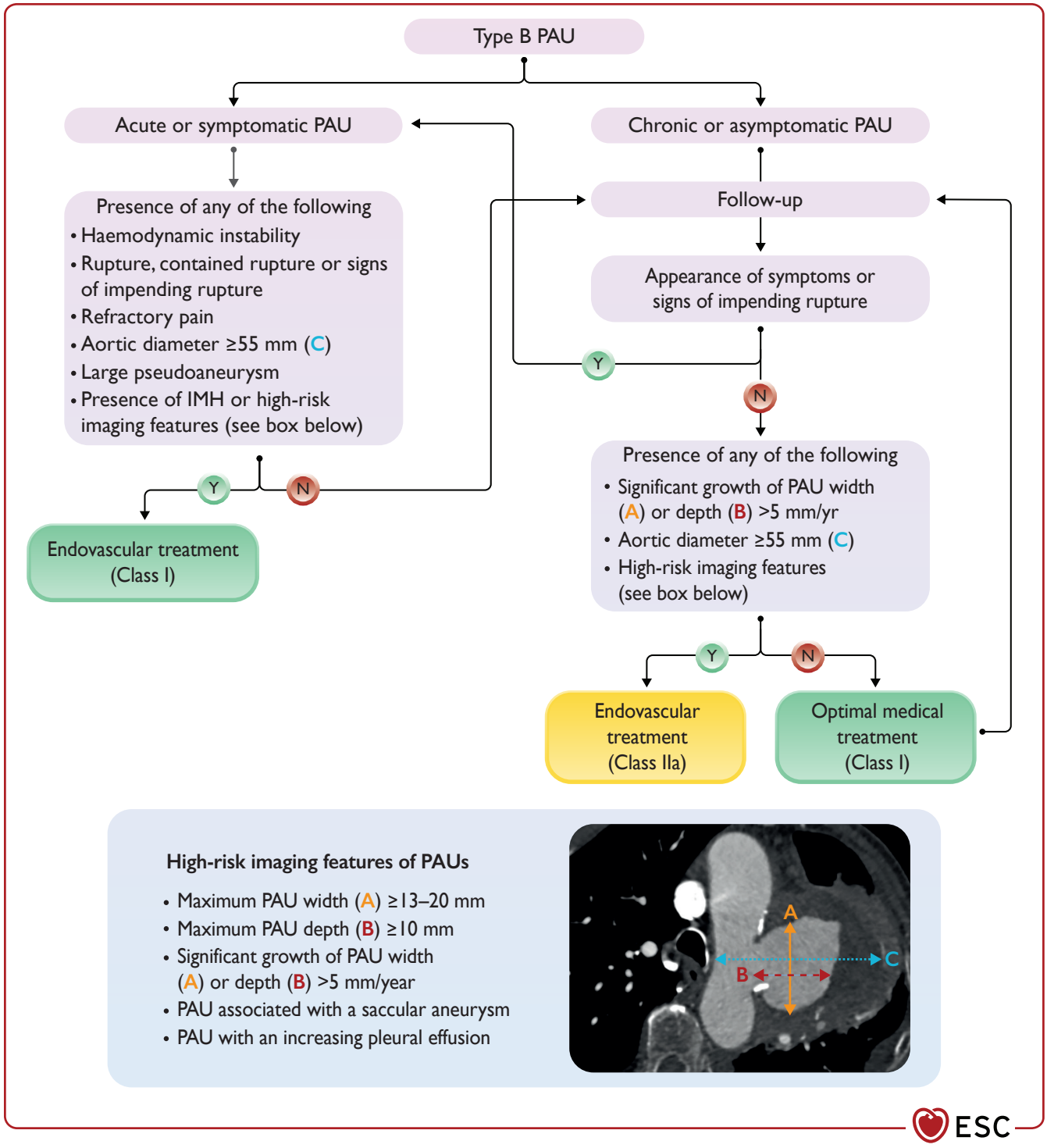

Figure 35 High-risk features in penetrating atherosclerotic ulcer and management of patients with type B penetrating atherosclerotic ulcer. IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer; TEVAR, thoracic endovascular aortic repair. (*A*) Maximum PAU width. (*B*) Maximum PAU depth; (*C*) Maximal aortic diameter at the site of the PAU.[910]

9.3.4. Aortic pseudo-aneurysm

Aortic pseudo-aneurysms, or false aneurysms, result from aortic wall disruption, typically caused by factors like trauma,[1368] surgery, or infections. They are often symptomless, detected incidentally during post-aortic procedure imaging. Symptoms may include chest pain, compression, and if untreated, they can lead to fatal rupture or other severe complications.[1369,1370]

Pseudo-aneurysm repair seems always indicated regardless of size or position to prevent progression and rupture. Nevertheless, in some circumstances and under close follow-up, patients could be monitored by CCT, CMR, or TOE and intervention could be postponed unless size expansion, symptoms, or compression of surrounding structures occur.[1371] Pseudo-aneurysms could be treated by open surgery or endovascular treatment (occluders, stent grafts, or coils). There is no randomized study comparing open surgery vs. TEVAR; however, treatment of choice is commonly based on anatomical features, clinical presentation, and the patient's comorbidities and decided by a multidisciplinary team in specialized centres.[1045,1371]

9.3.5. Traumatic aortic injury

Traumatic aortic injury (TAI), commonly from high-speed motor accidents or falls, involves partial or complete aorta transection. It results from rapid deceleration causing torsion and shearing forces, often affecting relatively immobile aorta segments like the aortic isthmus (90%), aortic root (5%), or diaphragmatic hiatus (5%).[24,70,172]

Traumatic aortic injury is classified based on the degree of lesion in the aortic wall (*Figure 36*): grade I (intimal tear), grade II (IMH), grade III (pseudo-aneurysm), and grade IV (aortic rupture). In the Crash Injury Study, 130/613 deaths (21%) were associated with TAI (mortality associated with aortic rupture 91%; at-scene survival 9%).[1372]

9.3.5.1. Diagnosis and therapeutic interventions

Due to non-specific symptoms and signs (often obscured by concomitant multiple organ injury) a timely diagnosis relies on a high level of clinical suspicion.[70,172] CCT (accuracy close to 100%) represents the technique of choice, acting as a 'one-stop shop' to rapidly assess the entire skeletal system and internal organs.[70,171,172] TOE may be an alternative, although limited by availability, local expertise, and potentially a patient's multiple traumas.[24,70,172] Therapeutic interventions are dependent on the extent of aorta lesion and patient clinical status as assessed by a multidisciplinary team. Generally, aggressive fluid administration should be avoided because it may exacerbate bleeding, coagulopathy, and hypertension. To reduce risk of rupture, mean BP should not exceed 80 mmHg.[172] Minimal aortic injury (grades 1 and 2) may be managed medically along with strict clinical and imaging surveillance; moderate aortic injury (grade 3) with semi-elective repair (within 24–72 h) to allow patient stabilization (though in some patients urgent repair is needed);[24,1373] and severe aortic injury (grade 4) with immediate repair.[1374] If there is progression of the IMH (grade 2), semi-elective repair (within 24–72 h) may be considered. TEVAR is preferred (if feasible) to open surgery (in-hospital mortality 7.9% vs. 20% and 1 year mortality 8.7% vs. 17%). In semi-elective repair, if the LSA needs to be covered, prior LSA revascularization before TEVAR is suggested to reduce the risk of paraplegia [172,1373,1374]

9.3.5.2. Long-term surveillance in traumatic aortic injury

In addition to clinical assessment, CCT is the imaging choice for follow-up.[70,171,172] Cumulative exposure to radiation and iodinated contrast medium remains the major limitation in young patients, especially in women. A combination of a chest X-ray and CMR (if no graft artefacts) would be a valid alternative.[24,171,172]

Recommendation Table 53 — Recommendations for traumatic aortic injury

Recommendations	Class[a]	Level[b]
In cases of severe aortic injury (grade 4), immediate repair is recommended.[24,1373,1374]	I	A
In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.[24,1373,1374]	I	A
In all TAI patients, medical therapy including pain relief, and blood pressure and heart rate control, is recommended.[24,172]	I	C
In cases of TAI suspicion, CCT is recommended.[159,172]	I	C
In cases of moderate aortic injury (grade 3), repair is recommended.[24,1373]	I	C
If CCT is not available, TOE should be considered.[159,172]	IIa	C
In minimal aortic injury (grades 1 or 2), initial medical therapy under careful clinical and imaging surveillance should be considered.[24,1374]	IIa	C
In cases of progression of the IMH (grade 2), semi-elective repair (within 24–72 h) should be considered.[24,1374]	IIa	C

CCT, cardiovascular computed tomography; IMH, intramural haematoma; TAI, traumatic aortic injury; TOE, transoesophageal echocardiography; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.

9.3.6. Iatrogenic aortic injuries

Iatrogenic aortic lesions are those associated with invasive procedures (cardiac surgery, most commonly dissection type A, or coronary angiography, with a similar proportion of type A and B dissections) (see *Section 9.3.2.1*). Incidence is low and ADs are the most common lesions. Main risk factors are advanced age, presence of CVRFs, atherosclerosis, aortic aneurysms, or PAD (*Figure 37*). Patients with iatrogenic AAS are often painless with correspondingly less chest or back pain.[1375]

While historically associated with high mortality,[1375] recent registries like the German GERAADA indicate a mortality rate similar to that for spontaneous dissections.[1186]

Clinical management is based on the underlying lesion (AAD, IMH) and location; however, conservative management has been described with good results in type A iatrogenic dissection if the coronary flow is preserved and the dissection is small.[1376] Iatrogenic lesion classification is depicted in *Figure 37*.[1377] Although scarce, data support a conservative approach based on evolution in type 1 and 2 lesions (Dunning classification), and surgery in type 3.[1377] In cases of coronary involvement, stent implantation sealing the flap may be proposed.[1376,1377]

9.3.7. Long-term follow-up of acute aortic syndrome

Imaging modalities and time intervals for surveillance vary according to lesion location (ascending/descending aorta), type of treatment (medical, endovascular, surgical), and underlying disease (HTAD).[70,1062,1153] Compared with the chronic disease setting, follow-up of AAS patients is characterized by a higher risk of complications and need for re-operation.[1378] Patients receiving TEVAR for AAS involving the descending aorta are more prone

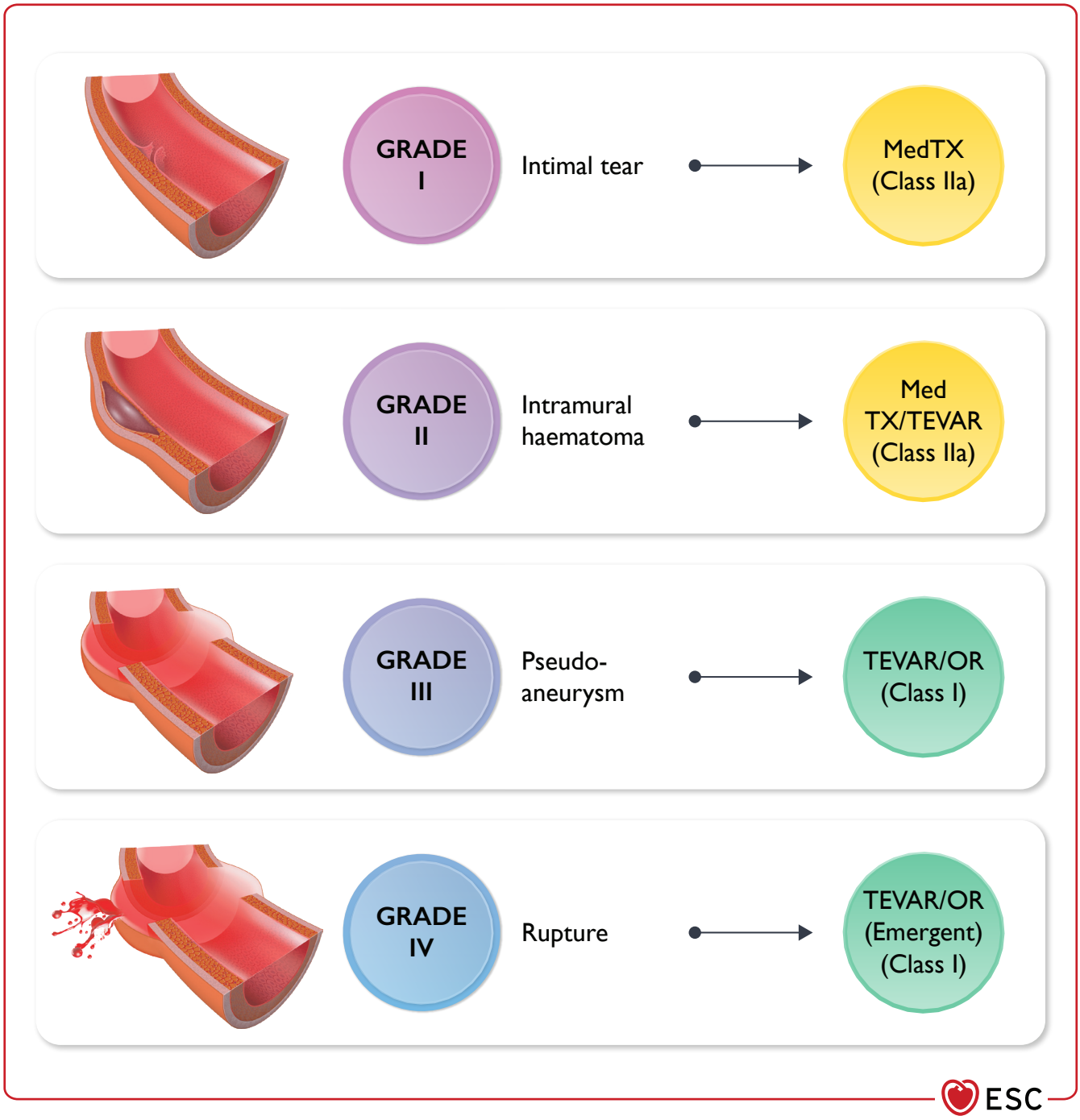

Figure 36 Classification and treatment of traumatic aortic injuries. Med, medical; OR, open surgery repair; TEVAR, thoracic endovascular aortic repair; Tx, treatment.

(27%–49%) to requiring a second intervention than patients undergoing surgical repair.[1379,1380] However, need for re-intervention at follow-up (after initial treatment of AAD) seems to have a significant impact on survival for TAAD[1381] but not for TBAD.[1380]

9.3.7.1. Follow-up after invasive treatment

Following surgery for AAS, imaging surveillance will focus on persistence/obliteration of the FL, anastomotic dehiscence, progressive dilatation of residual native aorta (with or without residual dissection), or graft infection. CCT is the most used modality, but in patients requiring frequent examinations CMR can be considered to reduce radiation.

Compared with outcomes of open surgery for aortic aneurysms, time to re-intervention in patients developing complications is significantly shorter,[1159] also due to the faster average growth of the dissected aorta (about 1 mm per year).[70] Considering the reported incidence rates (around 10%) of complications requiring re-operation, it is reasonable to follow patients every 6 months in the first year (including an early—within 1 month—echocardiography to follow native or prosthetic aortic valve function), then yearly up to the third post-operative

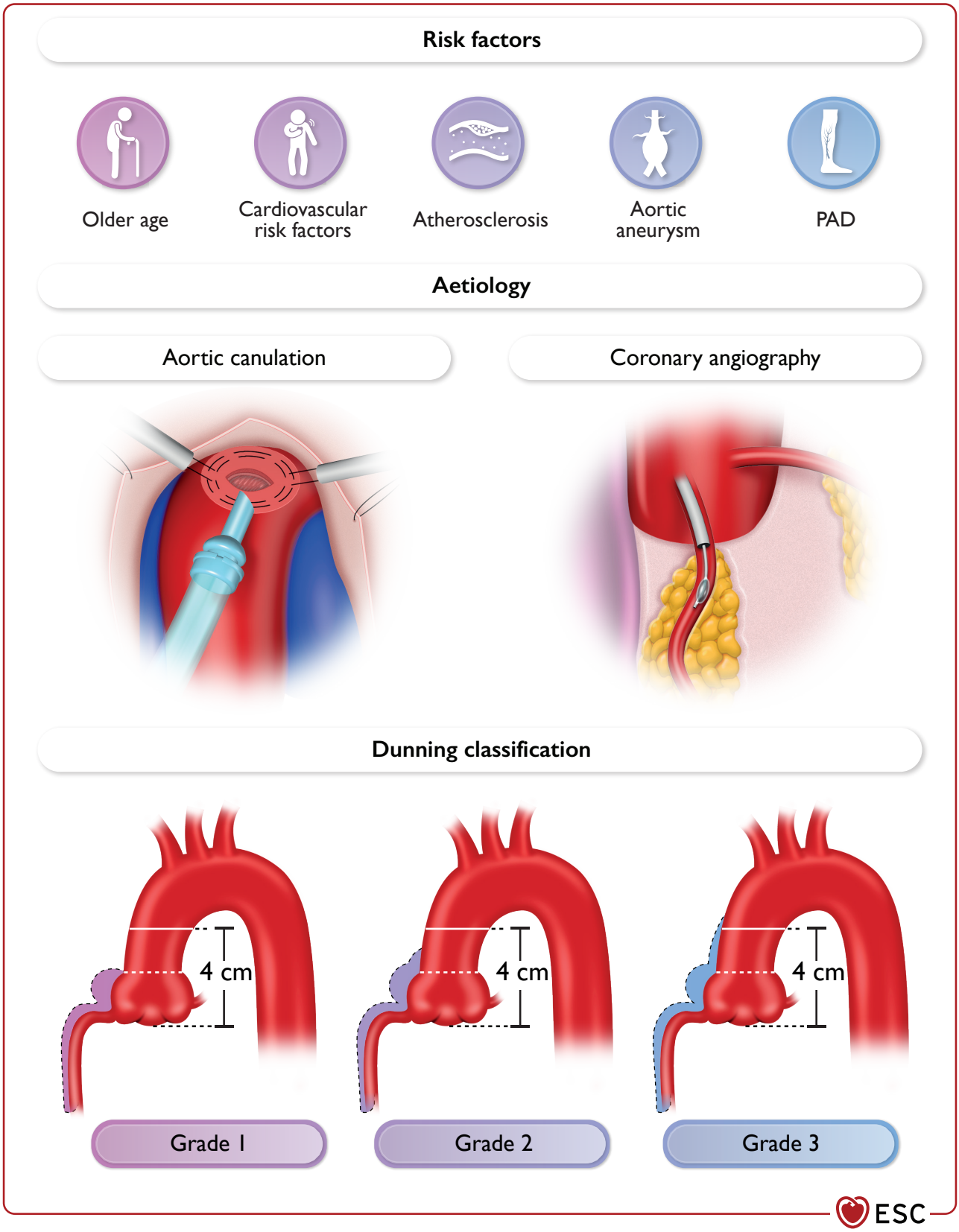

Figure 37 Aetiology, risk factors, and classification of iatrogenic aortic injuries. PAD, peripheral arterial disease. Dunning classification of iatrogenic aortic dissection:[1377]: type 1, dissection limited to the sinuses of Valsalva; type 2, dissection of the ascending aorta outside the sinuses but < 40 mm from the aortic annulus. type 3, dissection > 40 mm from the annulus.

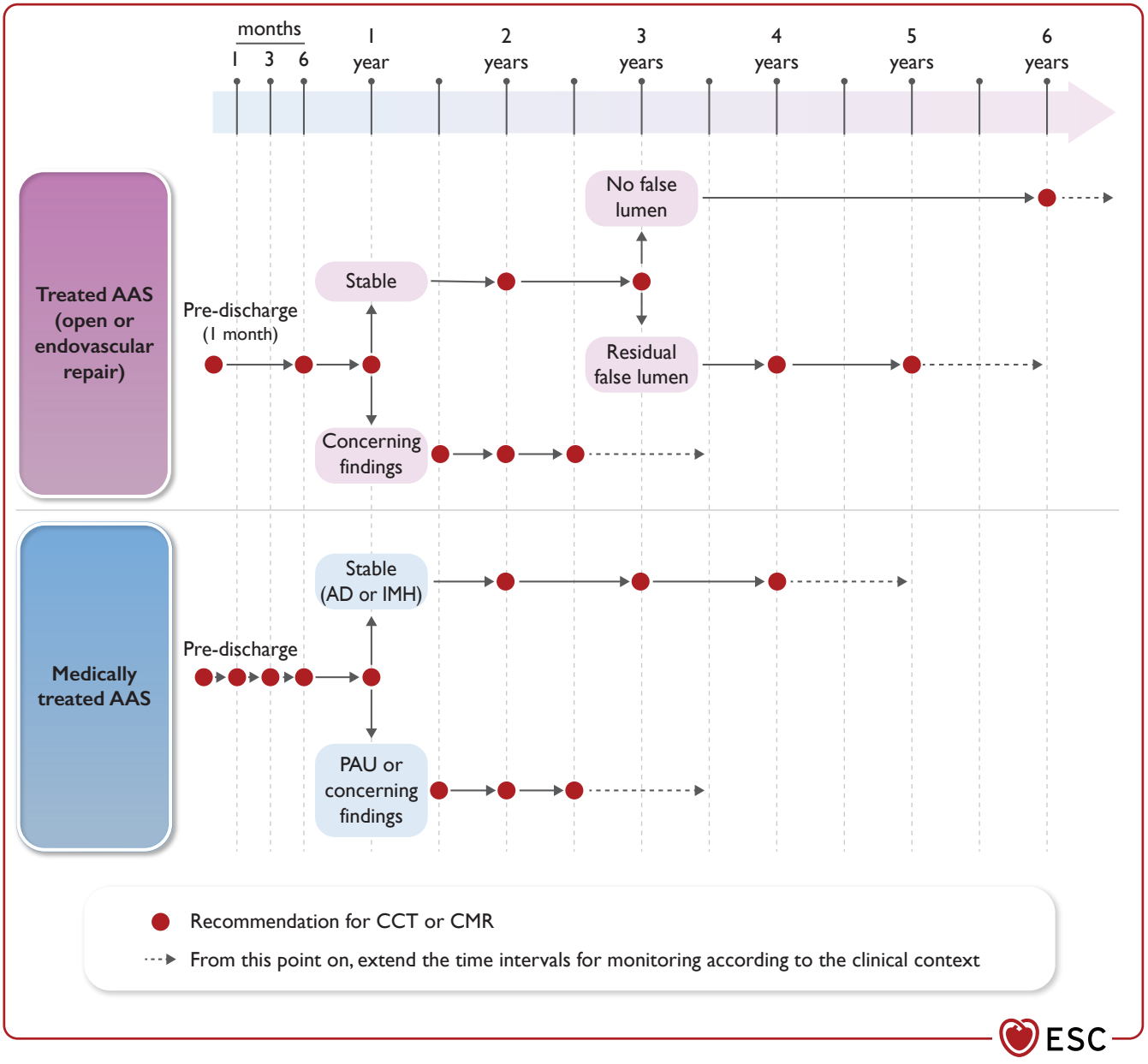

Figure 38 Algorithm for follow-up after acute aortic syndrome. AAS, acute aortic syndrome; AD, aortic dissection; CMR, cardiovascular magnetic resonance; CCT, cardiovascular computed tomography IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer.

year and then every 2–3 years if there are no complications (*Figure 38*).[1153,1159]

TEVAR implies a higher risk for late re-interventions,[1159,1378] and a sequence of imaging intervals at 1, 6, 12, 24, 36, 48, and 60 months is recommended if no abnormality is detected (shorter intervals should be considered in high-risk patients). Thereafter, controls can be performed every 2–3 years. Compared with the time points after surgery, an adjunctive early control at 1 month is necessary to exclude asymptomatic retrograde type A dissection induced by TEVAR (70% of cases occurring within 30 post-operative days).[1382]

Besides imaging surveillance, clinical follow-up is aimed at achieving strict BP control, limiting the burden of CVRFs, and providing patients with counselling for lifestyle modifications and prescriptions for sport activity.[24] There is evidence that statin treatment may improve survival in AAS patients under medical treatment, whereas BBs may improve survival in surgically treated patients.[1333]

9.3.7.2. Follow-up under medical treatment (chronic type B aortic dissection, intramural haematoma, penetrating atherosclerotic ulcer)

Around 70% of TBAD patients survive the hyperacute phase. If there is no malperfusion, uncontrolled hypertension, or impending rupture, initiate anti-impulse therapy alongside surveillance.

Chronic aortic dilatation, reaching 55 mm, is the leading cause (about 40%) of intervention, while acute complications necessitating immediate treatment are rare.[1301,1383] Imaging controls should be performed at least at 1, 6, and 12 months after discharge and yearly thereafter; however, one additional earlier scan, e.g. within 3 months, may reveal important changes occurring in the subacute phase, when the dissected aorta remains successfully amenable to early TEVAR.[1383] During surveillance, late complications may be predicted by imaging features, including the number and location of the entry tear(s), and dimensions of the FL, total (true + false) lumen, or entry tear.[1383] This might help in risk stratification to modulate the stringency of surveillance in the individual patient (*Figure 33*).[1213]

Type B IMH and PAU are usually conservatively treated with antihypertensive therapy and watchful monitoring. Most of the medically treated IMHs have a favourable course, whereas PAUs are less predictable in terms of risk of acute TBAD or rupture.[1350] Therefore, for IMH the same surveillance criteria as for medically treated uncomplicated TBAD can be employed; for PAU more frequent controls are advisable, i.e. one every 6 months instead of every year. Selectively, in asymptomatic patients with 2 year growth-rate stabilization and no high-risk features, intervals between controls can be longer (every 1–2 years) (*Figures 35* and *38*).[70,1384]

Recommendation Table 54 — Recommendations for follow-up after treatment of acute aortic syndrome

Recommendations	Class[a]	Level[b]
After TEVAR for AAS, follow-up imaging is recommended at 1, 6, and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities[c] are documented.[1159,1378,1382]	I	B
In medically treated type B AAS or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.[1301,1383]	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.[70,1350,1384]	I	C
After open surgery for AAS, follow-up imaging by CCT and TTE within 6 months, then CCT at 12 months and then yearly if findings are stable,[d] should be considered.[1153,1159,1383]	IIa	B
If no complications[c] occur within the first 5 years, CCT every 2 years thereafter should be considered.[1159,1378]	IIa	B
If no residual patent FL is documented for 3 post-operative years, subsequent surveillance by CCT every 2–3 years should be considered.[1153,1159,1383]	IIa	C
If abnormalities[c] are documented at any time of follow-up after TEVAR for AAS, then CCT should be considered every 3–6 months.[1159,1378,1382]	IIa	C
When frequent controls are required in AAS patients treated either by open or endovascular repair, CMR should be considered instead of CCT after the first-year follow-up.[70,1153]	IIa	C
In the follow-up of medically treated PAU, after 2 years of imaging stability, larger intervals should be considered in low-risk patients[e].[70,1350,1384]	IIa	C

AAS, acute aortic syndrome; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FL, false lumen; IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer; TEVAR, thoracic endovascular aortic repair; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Including: pseudo-aneurysm, graft infection, endoleak (any type), enlargement of the excluded aneurysm, and stent graft migration/separation/fracture.
[d]Both in terms of extent of residual FL and of aortic diameters at any level.
[e]Low-risk: based on width and depth of PAU (See *Figure 35* for high-risk features).

10. Genetic and congenital diseases of the aorta

10.1. Genetic and chromosomal diseases

This section discusses genetic and congenital aortic diseases. Aortic root and ascending aortic disease is commonly linked to congenital or hereditary factors, while descending aortic problems, especially in the AA, often result from atherosclerosis.[1385] Unless noted otherwise, recommendations provided herein are intended for adults.

Genetic diseases affecting the thoracic aorta are grouped under the broader term of HTAD. HTAD comprises a clinically and genetically heterogeneous group of disorders sharing the common denominator of aneurysm or dissection of the thoracic aorta. Familial forms (thoracic aortic disease [TAD] affecting ≥2 individuals in one family) or confirmed genetic entities (familial or sporadic) as well as syndromes conferring a risk for TAD fall under the definition of HTAD.[70] Due to the rarity of these conditions, robust evidence for many scenarios, such as intervention thresholds, surgical methods, open surgery vs. endovascular approaches, and pregnancy planning, is lacking. Thus, a multidisciplinary and individualized approach is advisable.[70,1386,1387]

Recommendation Table 55 — Recommendations for the management of patients with heritable thoracic aortic disease

Recommendations	Class[a]	Level[b]
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.[1386]	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.[888]	I	C

HTAD, heritable thoracic aortic disease.
[a]Class of recommendation.
[b]Level of evidence.

Clinically, HTADs can manifest as either syndromic or non-syndromic entities. The genes identified to date may underly both entities and predominantly show autosomal dominant inheritance patterns. While TAD is the primary feature in HTAD, extra-aortic features (skeletal/ocular) may be key to diagnosing certain syndromic cases. In some cases, the presence of extra-aortic manifestations may aid in risk stratification and hence in defining optimal management.[1388–1390] The main clinical and genetic data on syndromic and non-syndromic HTADs are summarized in the Supplementary data online, *Table S5*.

Numerous underlying gene defects have been discovered in both syndromic and non-syndromic cases, leading to the constitution of three major molecular groups: genes encoding components of: (i) the extracellular matrix; (ii) the transforming growth factor-beta (TGF-ß) signalling pathway; and (iii) the smooth muscle cell contractile apparatus. Clinical and CV outcomes vary between these groups and will

help pave the way to precision medicine in HTAD.[1391] Extensive clinical and imaging studies in HTAD revealed arterial vasculature involvement beyond the thoracic aorta. Patients may develop aneurysms and/or dissections beyond the aorta in diseases such as MFS, Loeys–Dietz or vascular Ehlers–Danlos syndrome (vEDS),[1390,1392,1393] or can be prone to occlusive vascular disease in the setting of alpha-actin gene (*ACTA2*) variants.[1394] Large clinical variability is observed within families carrying an identical variant and instances of incomplete penetrance (a 'skipped generation') are observed. All HTAD entities display cystic medial degeneration, hindering precise diagnosis using pathology.

Both genetic testing and imaging (mainly by TTE, but also consider CMR or CCT if the aortic root/ascending aorta are not properly visualized) in patients and family members are important in the diagnosis of HTAD. In those patients in whom no genetic cause is identified, but in whom there is a high suspicion of an underlying genetic defect, genetic re-evaluation needs to be considered after 3–5 years. Genetic testing should always be accompanied with appropriate counselling. Furthermore, appropriate assessment of HRQoL and psychological support should be offered to patients and families.[1395] Indications for genetic testing and aortic screening in HTAD are illustrated in the algorithm in *Figure 39*.

Although isolated AAA is less frequently associated with a genetic basis, patients with high-risk features (syndromic features, early onset of disease, absence of CVRFs, and/or family history of TAD or AAA) should be evaluated in centres with experience in HTAD to evaluate the need for genetic testing and specific surveillance, including active clinical screening in family members.

Recommendation Table 56 — Recommendations for genetic testing and aortic screening in aortic disease

Recommendations	Class[a]	Level[b]
Genetic testing		
In patients with aortic root/ascending aneurysms or thoracic aortic dissection, gathering family history information for at least three generations about TAD, unexplained sudden deaths, and peripheral and intracranial aneurysms is recommended.[880,1396–1402]	I	B
In patients with aortic root/ascending aortic aneurysms or thoracic aortic dissection and risk factors for HTAD,[c] genetic counselling at an expert centre and subsequent testing, if indicated, is recommended.[1399,1403–1408]	I	B
In patients with HTAD who have a pathogenic/likely pathogenic variant, genetic testing of at-risk biological relatives (i.e. cascade testing) is recommended, irrespective of age.[70,1407,1409]	I	C
In patients with HTAD, guidance of clinical management by the underlying gene/variant, when known, should be considered.[70,1391,1410–1416]	IIa	B
Aortic imaging screening		
In patients with TAD with risk factors for HTAD,[c] with a negative family history of TAD and in whom no (likely) pathogenic variant is identified, TTE[d] screening aortic imaging of FDRs[e] is recommended.[1396,1402]	I	B
Imaging screening of family members of patients with TAD with risk factors for HTAD[c] in whom no (likely) pathogenic variant is identified should be considered starting at age 25, or 10 years below the youngest case, whichever is younger. If the initial screening is normal, continued screening every 5 years until the age of 60 should be considered.[25]	IIa	C

Continued

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; TAD, thoracic aortic disease; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 39*.
[d]CMR/CCT may be indicated if the aortic root/ascending aorta cannot be visualized adequately.
[e]Parents, siblings, children.

10.1.1. Turner syndrome

10.1.1.1. Diagnosis, clinical presentation, and natural history

Turner syndrome (TS), resulting from partial or complete monosomy of the X-chromosome, affects 1 in 2500 live-born females.

About 50% of patients experience CV issues like ascending aortic dilatation, BAV, aortic coarctation, elongated aortic arch, and partial abnormal pulmonary venous return.[1417–1419] All women present with generalized arteriopathy and TS itself is an independent risk factor for thoracic aortic dilatation. AD risk (type A in 85% and type B in 15%) is elevated in this population,[1420–1422] although recent studies indicate that this risk may be lower with proper treatment guidelines.[1423–1426] Risk factors include aortic dilatation, BAV, coarctation, and arterial hypertension. Defining aortic dilatation in TS requires adjustment for anthropometric parameters and aortic growth data for dissection risk estimation.[1427] Z-scores used in the general population are equivalent to Turner-specific z-scores.[1428]

Imaging surveillance

In newly diagnosed TS, TTE and CMR are recommended at baseline for the evaluation of congenital heart defects and aortic anatomy/diameters. For women aged 15 years and older with TS, adjusting for their smaller body size is essential when assessing aortic dimensions. Utilize metrics like the ascending aortic size index (ASI), aortic height index (AHI), or aortic z-scores to gauge aortic dilation and dissection risk. Further follow-up is dictated by baseline aortic diameters, age, and risk factors (*Figure 40*).

Recommendation Table 57 — Recommendations for imaging in women with Turner syndrome

Recommendations	Class[a]	Level[b]
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.[153,1417,1421,1423,1428,1429]	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.[c,1420,1421]	I	C

AHI, aortic height index; ASI, aortic size index; BSA, body surface area; TS, Turner syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Concomitant lesions: hypertension, aortic coarctation, bicuspid aortic valve (*Figure 40*).

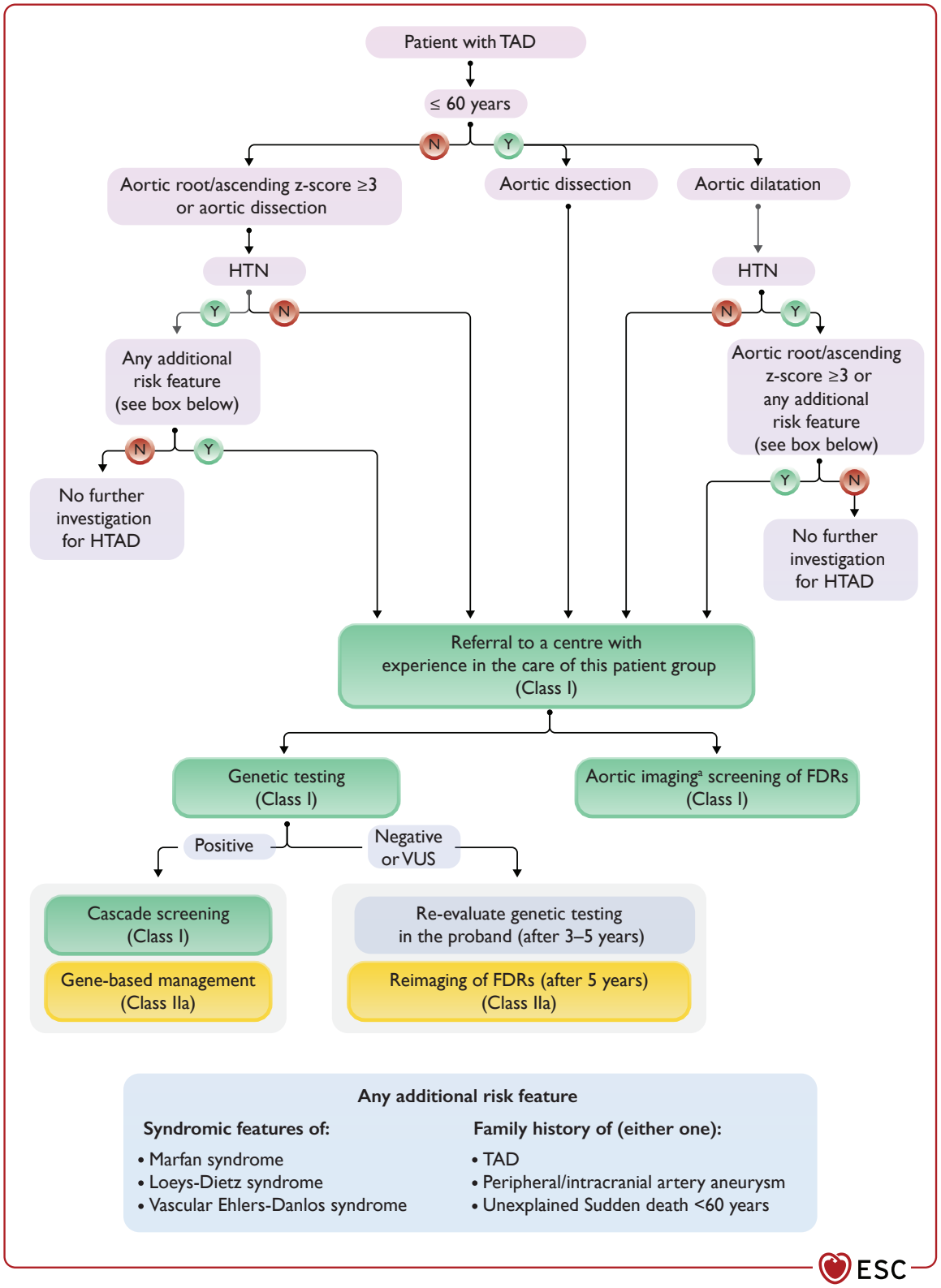

Figure 39 Algorithm for genetic and imaging screening in patients with thoracic aortic disease. CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; HTN, arterial hypertension; TAD, thoracic aortic disease; TTE, transthoracic echocardiography; VUS, variant of uncertain significance. [a]mainly by TTE, but also consider CMR or CCT if the aortic root/ascending aorta are not properly visualized.

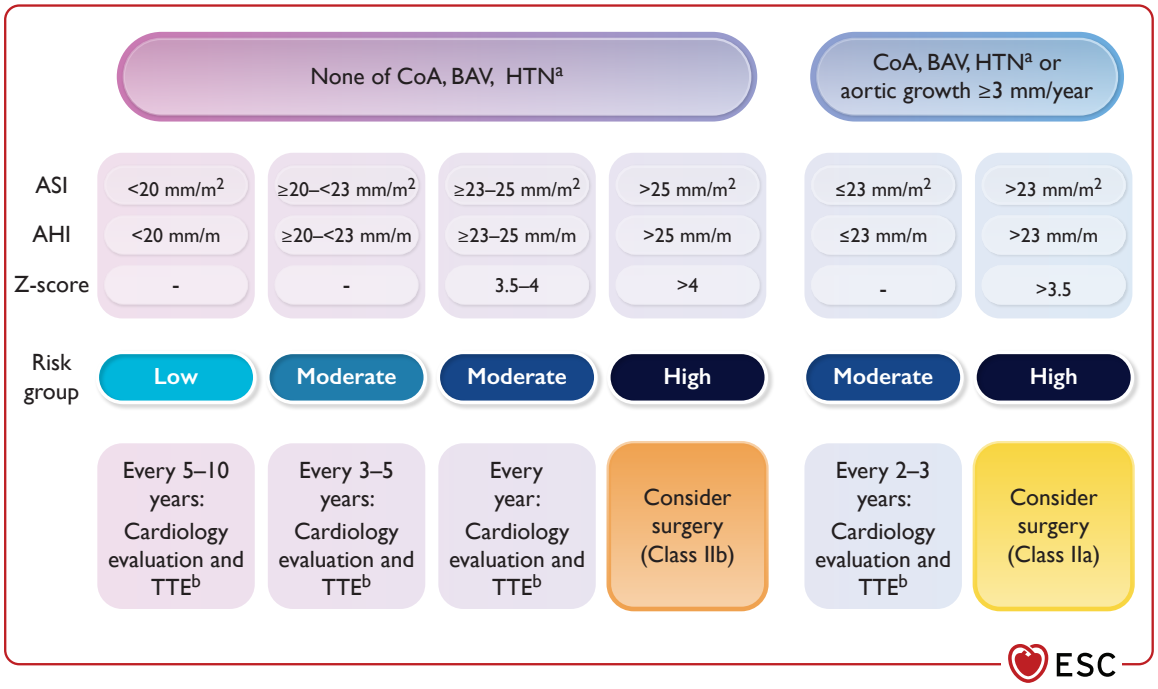

Figure 40 Algorithm for surveillance in women (≥15 years) with Turner syndrome. AHI, aortic height index (ratio of aortic diameter [mm] to height [m]); ASI, aortic size index (ratio of aortic diameter [mm] to BSA [m^2]); BAV, bicuspid aortic valve; BSA, body surface area; CCT, Cardiovascular Computed Tomography; CMR, cardiovascular magnetic resonance; CoA, coarctation of the aorta; HTN, arterial hypertension; TTE, transthoracic echocardiography. [a]HTN: arterial hypertension, not under control despite more than three classes of antihypertensive drugs. [b]CMR (preferably) or CCT if inadequate visualization of the ascending aorta.

10.1.1.2. Medical treatment

In the absence of clinical trials, a pragmatic approach in a shared-decision model is adopted regarding TS medical treatment. Adoption of the strategy for inhibition of aortic growth with BBs and/or ARBs as in MFS may be considered. Hypertension should be treated according to general guidelines.[300]

Hormonal treatment with growth hormone (in childhood), sex (oestrogen and/or progesterone), and thyroid hormones needs to be discussed in a multidisciplinary team with the paediatrician and endocrinologist.[1430–1434]

10.1.1.3. Surgery of aortic aneurysms

Aortic aneurysm surgery in TS should be informed, individualized, and consider factors beyond aortic diameter (indexed). These include BAV, coarctation, uncontrolled hypertension (despite more than three classes of antihypertensive drugs), rapid aortic growth (≥3 mm per year) and planned pregnancy.

Recommendation Table 58 — Recommendations for aortic surgery in women with Turner syndrome

Recommendations	Class[a]	Level[b]
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered in women with TS who are ≥15 years of age, have an ascending ASI >23 mm/m^2, an AHI >23 mm/m, a z-score >3.5, and have associated risk factors for aortic dissection[c] or are planning pregnancy.[70,1417,1421]	IIa	C
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with TS who are ≥15 years of age, have an ascending ASI >25 mm/m^2, an AHI >25 mm/m, a z-score >4, and who do not have associated risk factors for aortic dissection[c].[70,1417,1421]	IIb	C

AHI, aortic height index (ratio of aortic diameter [mm] to height [m]); ASI, aortic size index (ratio of aortic diameter [mm] to BSA [m^2]); TS, Turner syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Bicuspid aortic valve, elongation of the transverse aorta, coarctation of the aorta, and/or uncontrolled hypertension (despite more than three classes of antihypertensive drugs). See *Figure 40*.

10.1.1.4. Pregnancy and physical exercise

Turner syndrome often involves fertility challenges, but assisted reproductive therapy has increased pregnancy rates. However, pregnancy in TS can elevate the risk of AD, particularly with additional risk factors (*Figure 40*). Recent studies suggest improved pregnancy outcomes due to better guideline adherence.[1435,1436] Prophylactic aortic root surgery in women with TS contemplating pregnancy is recommended when the ASI reaches 25 mm/m^2.[1337] These decisions should be made by an expert team in a shared-decision process.

Physical exercise has a beneficial impact on CVD risk and HRQoL in TS.[1437] Structural congenital heart defects and aortic diameters (ASI, AHI and z-score) (*Figure 40*) need to be considered in the recommendations on the level of sports practice.[1418]

10.1.2. Vascular Ehlers–Danlos syndrome

10.1.2.1. Diagnosis, clinical presentation, and natural history

Vascular Ehlers–Danlos syndrome is a rare (prevalence of 1/50 000 to 1/200 000) autosomal dominant disease caused by pathogenic variants in the *COL3A1* gene, which encodes the pro-alpha1 chains of type III procollagen. The most common *COL3A1* variants provoke a disruption in the assembly of type III collagen fibrils, causing an important loss of mechanical strength of arteries and other hollow organs, especially the bowel and uterus.[1438] Identification of a causal *COL3A1* variant is a requirement for the diagnosis of vEDS.[1439]

vEDS is the most severe form of Ehlers–Danlos syndrome because of its clinical life-threatening vascular complications, making early identification and a thorough family inquiry particularly crucial.

Clinical complications may start during adolescence and repeat at unpredictable time intervals. The most common complications involve medium-sized arteries: dissections, aneurysms, arterial ruptures, and arteriovenous fistulas. AD (both type A and B) occurs in up to 10% of patients.[1440]

Prognosis depends on the type of *COL3A1* variant, with null variants (no gene product or absence of function) showing a better outcome.[1441] The rate of recurrence of organic complications in patients with vEDS is 1.6 events per 5 year period. Life expectancy is reduced to an average of 51 years.[1442]

10.1.2.2. Surveillance and imaging

Management of vEDS is complex and requires a multidisciplinary approach. Recommendations include: lifestyle modification to minimize injury and risk of vessel/organ rupture, identification of a care team, individualized emergency care plans, maintaining BP in the normal range, aggressive hypertension treatment, and annual surveillance of the vascular tree by DUS, CCT (low radiation alternatives), or CMR (if feasible).[1439] A recent survey among European expert centres indicated that arterial monitoring is standard clinical practice and that frequency of follow-up should be adapted individually.[1443] The prognosis improves when patients are properly managed.[1441]

10.1.2.3. Medical treatment

Medical management is based on optimal BP control. Celiprolol, a BB with vasodilatory properties, has been shown to reduce vascular morbidity in two retrospective studies[1441,1444] and one randomized, open-label trial.[1445] There is no consensus about the age at which to start treatment, but starting after 10 years of age is considered reasonable by many experts.

Recommendation Table 59 — Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome (see also Evidence Table 13)

Recommendations	Class[a]	Level[b]
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.[1439,1443]	I	C
Treatment with celiprolol should be considered in patients with vEDS.[1441,1444,1445]	IIa	B

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; vEDS, vascular Ehlers–Danlos syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.2.4. Surgical treatment

Acute, unexplained pain requires urgent imaging to exclude arterial rupture. Acute arterial complications usually require hospitalization and a conservative approach in most cases. Interventional vascular or intestinal procedures are limited to vital risk. Procedures requiring organ inflation should be avoided or performed with extreme caution. There are no clear recommendations regarding aortic/arterial diameters at which to intervene in patients with vEDS. Thus, decisions need to be made on a case-by-case basis.

10.1.2.5. Pregnancy

Pregnancy in vEDS incurs a risk of (fatal) arterial and uterine complications. Pregnancy does not appear to affect overall mortality compared with nulliparous vEDS women.[1446] However, patients need to be engaged in a shared-decision process, informed by vascular status and underlying variant type.

10.1.3. Marfan syndrome

10.1.3.1. Diagnosis, clinical presentation, and natural history

Marfan syndrome, the most common syndromic HTAD condition (prevalence of 1/5000–1/10 000), arises from pathogenic fibrillin-1 gene (*FBN1*) variants. Beyond the CV system, multiple organ systems are often affected, including the eyes and skeleton. Diagnosis relies on recognizing clinical features in line with the revised Ghent nosology, which includes genetic testing.[1447]

Aortic aneurysm and dissection involving the aortic root are a hallmark of the disease. Less commonly, the descending thoracic and abdominal aorta may be involved. With increasing survival and age in MFS, the prevalence of TBAD seems to be increasing, exceeding type A dissection rates in recent reports.[1448,1449] TBAD will often occur at diameters below surgical thresholds. Previous aortic root replacement, mitral valve surgery, and a longer life span are associated with TBAD. Additional CV features include mitral valve prolapse, extra-aortic arterial involvement, myocardial dysfunction, and arrhythmias.[1393,1450–1452] Thanks to improved diagnosis in earlier stages, proper management including surveillance, medical treatment, and timely prophylactic aortic surgery, life expectancy in MFS patients is now approaching that of the general population.[1416,1453]

The major determinant of TAAD is the aortic root diameter, with increased risk of rupture when it exceeds 50 mm.[1454] Other risk factors include family history of AAS at low diameter, aortic root growth rate (annualized growth rate ≥3 mm or more in adults), pregnancy, and hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment). Increasing evidence for variant-based differences in aortic risk is emerging and may be considered.[1413,1416]

10.1.3.2. Imaging surveillance

Transthoracic echocardiography is the appropriate imaging modality for initial evaluation and follow-up of the aortic root in most patients and allows evaluation of the distal segments of the aorta in many. Also, TTE is useful for assessing mitral and aortic valve regurgitation, mitral valve prolapse with/out annular disjunction, and LV dysfunction. In some cases (especially when pectus abnormalities are present) TTE windows may be suboptimal, and CMR (preferably)/CCT may be preferred. Periodical evaluation of the global aorta and peripheral arteries with CMR/CCT and DUS (every 3–5 years based on the patient's evolution) is indicated since they also present a higher incidence of

peripheral aneurysms,[1455] which are associated with more aggressive forms of the disease.[1393] CMR is preferred over CCT to avoid radiation exposure; however, its use should be adapted to local availability/expertise. Additionally, CMR allows evaluation of biomechanical and haemodynamic parameters that can be useful in risk stratification.[181,1456,1457] Given its superior spatial resolution, CCT may be recommended for pre-operative planning and in cases of measurement inconsistency. Imaging of intracerebral vessels is indicated in cases of symptoms and/or clinical manifestations of aneurysms/rupture. Recommendations for imaging surveillance are illustrated in *Figure 41* and should be adjusted to the individual patient, taking the history and presence of abnormalities during preceding studies into account.

Recommendation Table 60 — Recommendations for vascular imaging in Marfan syndrome

Recommendations	Class[a]	Level[b]
In patients with MFS, TTE is recommended:[70,171,1458,1459] • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors[c] • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors[c] • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors[c]	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aorta imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.[70,1455,1459]	I	C
In patients with MFS who have undergone aortic root replacement, surveillance imaging of the thoracic aorta by CMR (or CCT) is recommended at least every 3 years.[70,1458]	I	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; MFS, Marfan syndrome; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Risk factors: aortic root diameter >40 to ≤45 mm and family history of aortic dissection at small aortic dimensions (i.e. <50 mm); resistant hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment); and rapid growth of the aorta (annualized growth rate ≥3 mm or more in adults).

10.1.3.3. Medical treatment

Medical treatment is described in Recommendation Table 61. Some caution may be warranted with the use of CCBs: these have shown an increased aortic risk in a mouse model and in retrospective case control studies,[1460] and alternatives are preferred for hypertension treatment.

Recommendation Table 61 — Recommendations for medical treatment in Marfan syndrome (see also Evidence Table 14)

Recommendations	Class[a]	Level[b]
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.[1461,1462]	I	A
In patients with MFS, the use of both a BB and an ARB, in maximally tolerated doses (unless contraindicated), should be considered to reduce the rate of aortic dilatation.[1463,1464]	IIa	A

ARB, angiotensin receptor blocker; BB, beta-blocker; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.3.4. Aortic surgery

Open surgery is preferred over endovascular procedures in patients with MFS. Endovascular procedures may be considered in selected cases in emergency settings and/or in centres with a high level of expertise.[1465] The thresholds for aortic root surgery need to take additional risk factors, as well as the expertise of the team, into account.[1466]

Recommendation Table 62 — Recommendations for aortic surgery in Marfan syndrome

Recommendations	Class[a]	Level[b]
Surgery is indicated in patients with MFS who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.[70,172,1466–1468]	I	B
Surgery to replace the aortic root and ascending aorta, using the valve-sparing surgery technique, is recommended in patients with MFS or related HTAD with aortic root dilatation when anatomical features of the valve allow its preservation and the surgeon has specific expertise.[70,1466,1469]	I	B
Surgery should be considered in patients with MFS who have an aortic root aneurysm with a maximal aortic sinus diameter ≥45 mm and additional risk factors.[c,1467,1469]	IIa	C
In patients with MFS and an aneurysm of the ascending aorta, aortic arch, descending thoracic aorta, or abdominal aorta of ≥50 mm, surgical replacement of the aneurysmal segment by a surgeon with specific expertise should be considered.[1467,1469]	IIa	C

HTAD, heritable thoracic aortic disease; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Family history of aortic dissection at small aortic dimensions (i.e. <50 mm); resistant hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment); and rapid growth of the aorta (annualized growth rate ≥3 mm or more in adults).

10.1.3.5. Pregnancy and physical exercise

In pregnant MFS women, the risk of AD increases up to eight times relative to the general population.[1470] The risk for TAAD is determined by the aortic diameter, but type B dissections tend to occur even more commonly and may occur without prior dilatation.[1470,1471] Patients should be aware of the persisting risk of TBAD after aortic root replacement.[1471] Women unaware of the diagnosis are at the highest risk of dissection.[1470–1472]

The Registry Of Pregnancy And Cardiac disease (ROPAC) indicates that women managed according to guidelines are at low risk of pregnancy-related complications and major effects of BBs on foetal growth were not shown, although this needs to be carefully monitored.[70,1337,1435,1471,1472]

Recommendation Table 63 — Recommendations for pregnancy in women with Marfan syndrome

Recommendations	Class[a]	Level[b]
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team.[1473]	I	C
It is recommended that couples in which a partner has or is at risk for HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.[1337,1474,1475]	I	C
Intake of BBs during pregnancy is recommended.[1476]	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.[1435,1472]	I	C
Prophylactic aortic root surgery may be considered in women desiring pregnancy with aortic diameters of 40–45 mm.[1472,1475,1477]	IIb	C
ARBs are not recommended during pregnancy.[1478–1480]	III	B

ARBs, angiotensin receptor blockers; BBs, beta-blockers; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CV, cardiovascular; HTAD, heritable thoracic aortic disease; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

Exercise is potentially associated with an increased risk of aortic dilatation and AAD. It is recommended to individualize physical activity in MFS based on aortic diameter, family history of dissection or sudden death, and pre-existing fitness status.[71] Although competitive sports are contraindicated, moderate aerobic exercise is recommended with a level of intensity based on aortic diameters.[71]

Two studies[1481,1482] showed that mild-moderate dynamic exercise improved aortic wall structure and function and reduced aortic growth rate in MFS mouse models. Recent data in MFS children and young adults indicate that adhering to daily physical exercise (10 000 steps a day) had a beneficial effect on aortic root growth.[1483] Although a limited number of clinical studies have evaluated physical activity rehabilitation programmes, two studies[1484,1485] evidenced that physical activity, up to a moderate specific intensity, may be recommended. Thus, although physical activity poses a dilemma, individualized adapted programmes are most likely successful in encouraging exercise in MFS.

Recommendation Table 64 — Recommendations for physical exercise in patients with Marfan syndrome

Recommendations	Class[a]	Level[b]
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C
For patients who present with aortic dissection and/or have undergone aortic surgery, post-operative cardiac rehabilitation aiming at improving both physical and mental health should be considered.[73,1483,1484,1486]	IIa	B

MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.4. Other syndromic and non-syndromic heritable thoracic aortic diseases and/or arterial disorders

Main clinical and genetic data of known syndromic and non-syndromic HTAD entities are summarized in the Supplementary data online, *Table S5*. The two most prevalent diseases for each entity include Loeys–Dietz syndrome and *ACTA2*-related HTAD, respectively. Given the rarity of these entities, specific recommendations regarding surveillance and treatment are lacking and largely adopted from the recommendations for MFS. Some disease-specific recommendations are mentioned below.

10.1.4.1. Loeys–Dietz syndrome

10.1.4.1.1. Diagnosis, clinical presentation, and natural evolution.

The spectrum of clinical presentations in Loeys–Dietz syndrome is very wide. Some patients fulfil criteria for MFS,[1447] while some features such as bifid uvula and hypertelorism are very specific to the disease. Clinical manifestations are listed in the Supplementary data online, *Table S5*. There is a tendency for AD and rupture at lower vessel dimensions than is typically seen in other similar conditions.[1390,1487] Pathogenic variants in six genes (*TGFBR1* and *TGFBR2*, *TGFB2* and *TGFB3*, *SMAD2* and *SMAD3*), all encoding components of the TGF-ß signalling pathway, cause Loeys–Dietz syndrome. Differences in clinical manifestations and aortic outcome according to the underlying gene and the extent of extra-aortic features have been reported and need to be considered in surveillance and defining thresholds for surgery.[1388,1390,1391]

Surveillance in Loeys–Dietz syndrome is described in Recommendation Table 65 and *Figure 41*. Although the indication for surgery must be considered according to the underlying genetic defect and the presence of risk factors (Recommendation Table 66 and *Figure 42*), a 45 mm aortic diameter threshold should be considered (≥40 mm in cases of associated high-risk features).

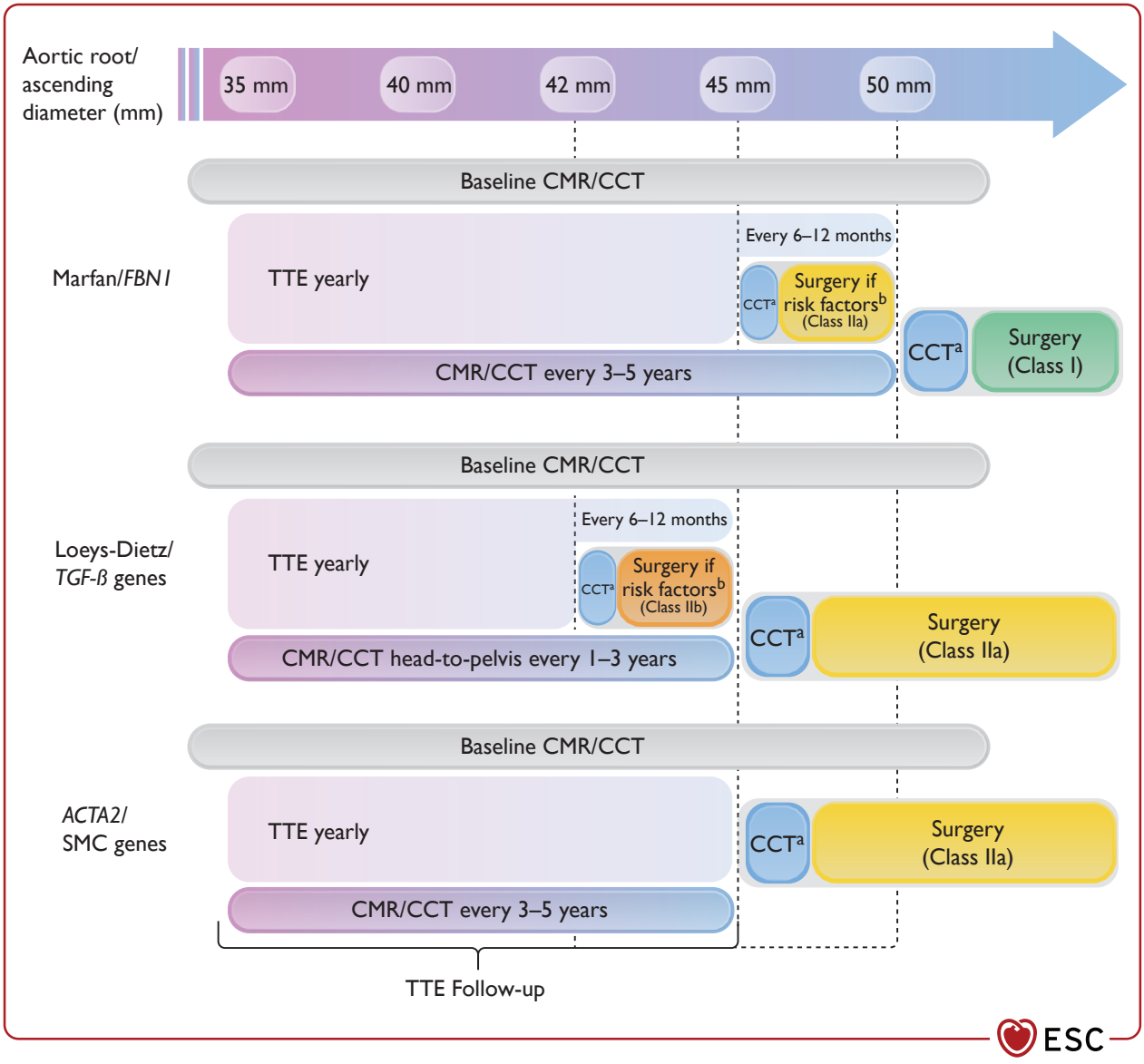

Figure 41 Algorithm for imaging surveillance in patients with syndromic and non-syndromic heritable thoracic aortic disease. CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; HTAD, heritable thoracic aortic disease; SMC, smoth muscle cell; TTE, transthoracic echocardiography. [a]Pre-surgical CCT. [b]See respective tables of recommendations for aortic surgery in Marfan (Table 62) and Loeys-Dietz syndrome (Table 66).

Recommendation Table 65 — Recommendations for imaging follow-up in Loeys–Dietz syndrome

Recommendations	Class[a]	Level[b]
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth,[c] is recommended.[70,1390,1488]	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.[70,1488]	I	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]More frequent imaging if aortic root/ascending diameter >42 mm and aortic growth rate ≥3 mm per year.

Recommendation Table 66 — Recommendations for aortic root surgery in Loeys–Dietz syndrome

Recommendations	Class[a]	Level[b]
Aortic root replacement should be considered for patients with Loeys–Dietz syndrome if the aortic root diameter exceeds 45 mm.[1388,1390,1489–1492]	IIa	C
It may be considered to adjust the threshold for surgery according to the underlying gene, taking associated risk features[c] into account.[1391]	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]High-risk features include certain specific pathogenic variants; women with *TGFBR2* variants and small body size; severe extra-aortic features; family history of aortic dissection (especially at young age or relatively small aortic diameter); and aortic growth rate ≥3 mm per year.

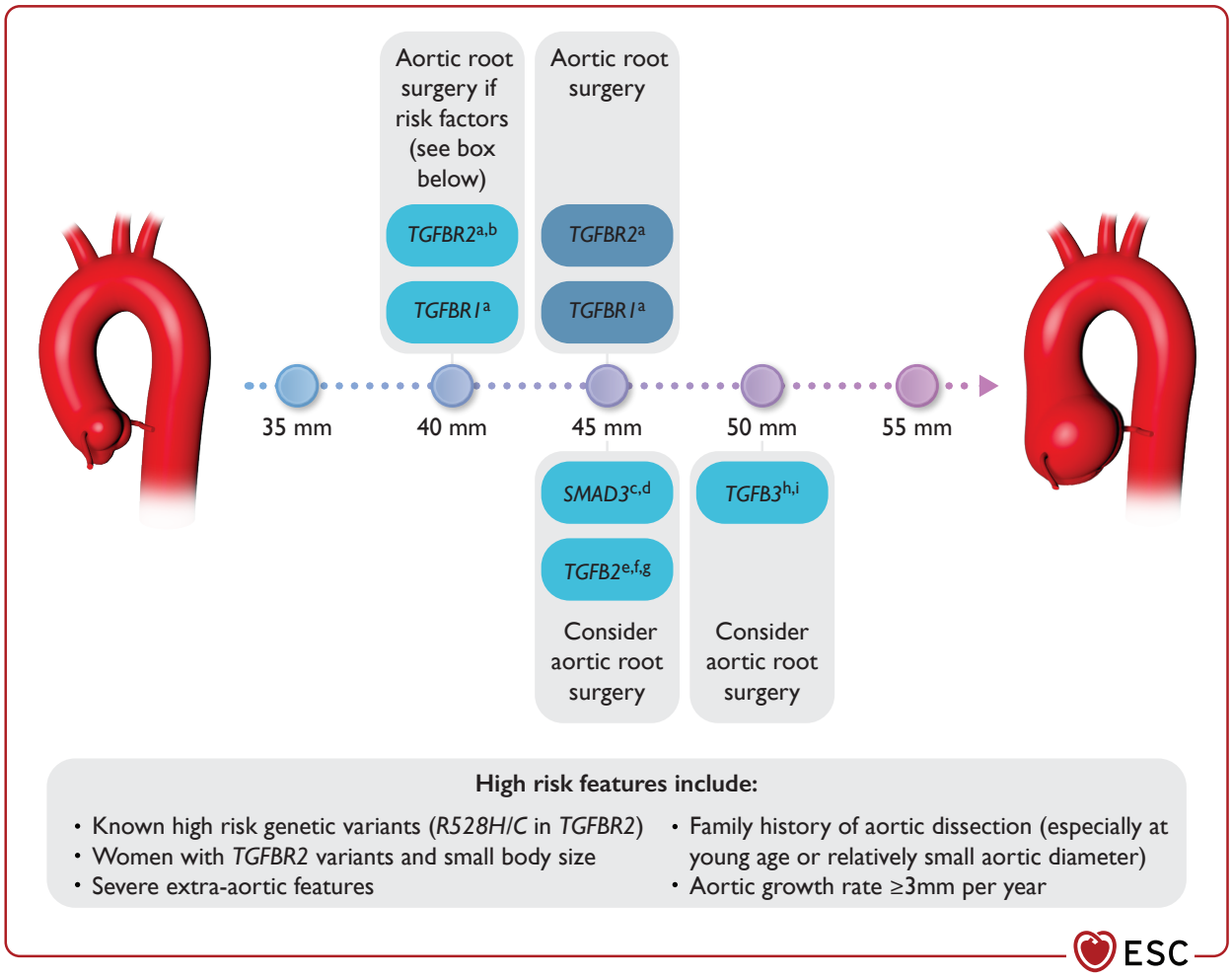

Figure 42 Suggested thresholds for prophylactic aortic root/ascending replacement in Loeys–Dietz syndrome. From a[1388], b[1391], c[1492], d[1491], e[1490], f[1489], g[1493], h[1494], i[1495].

10.1.4.2. ACTA2-related heritable thoracic aortic disease

Pathogenic variants in the *ACTA2* gene, encoding for smooth muscle-specific alpha-actin (a critical component of the vascular smooth muscle cell contractile apparatus), lead to aortic aneurysms and dissections in non-syndromic patients.[1496] Patients primarily present with type A or B aortic dissection, and with aneurysms that involve the root and/or ascending aorta. A subset of pathogenic variants predisposes to occlusive vascular diseases.[1497] Surveillance is summarized in Recommendation Table 67 and *Figure 41*. TAAD may occur at aortic diameters <45 mm, and consideration of surgery at diameters <45 mm should be informed by the presence of additional clinical and genetic risk factors.[1410] Genetic and imaging cascade screening of first-degree family members is an essential element of care, as treatable disease may otherwise be missed in family members—with fatal consequences.

Recommendation Table 67 — Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease (see also Evidence Table 11)

Recommendations	Class[a]	Level[b]
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate aortic root/ascending aorta enlargement is recommended.[1498]	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.[1498]	I	C
Prophylactic aortic root surgery should be considered with an aortic diameter ≥45 mm, or lower in cases with other risk factors.[c,1499]	IIa	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Risk factors for aortic dissection: family history of dissection with no or minimal dilatation or young age; rapid growth ≥3 mm per year.

10.2. Aortic disease associated with bicuspid aortic valves

Bicuspid aortic valves, the most common congenital heart defect (0.5%–2% of live births), besides being a risk factor for aortic valve disease, is associated with a peculiar form of aortopathy, characterized by morphological and clinical heterogeneity (bicuspid valvulo-aortopathy). Its inheritance is high, with autosomal dominant transmission of BAV in a minority of cases, but no single-gene model clearly explaining BAV inheritance.[1500–1502] Several genes, generally implicated in embryogenesis and cell differentiation, have been associated with BAV/BAV-related aortopathy, but each of them explained <5% of cases.[1503–1507] Therefore,

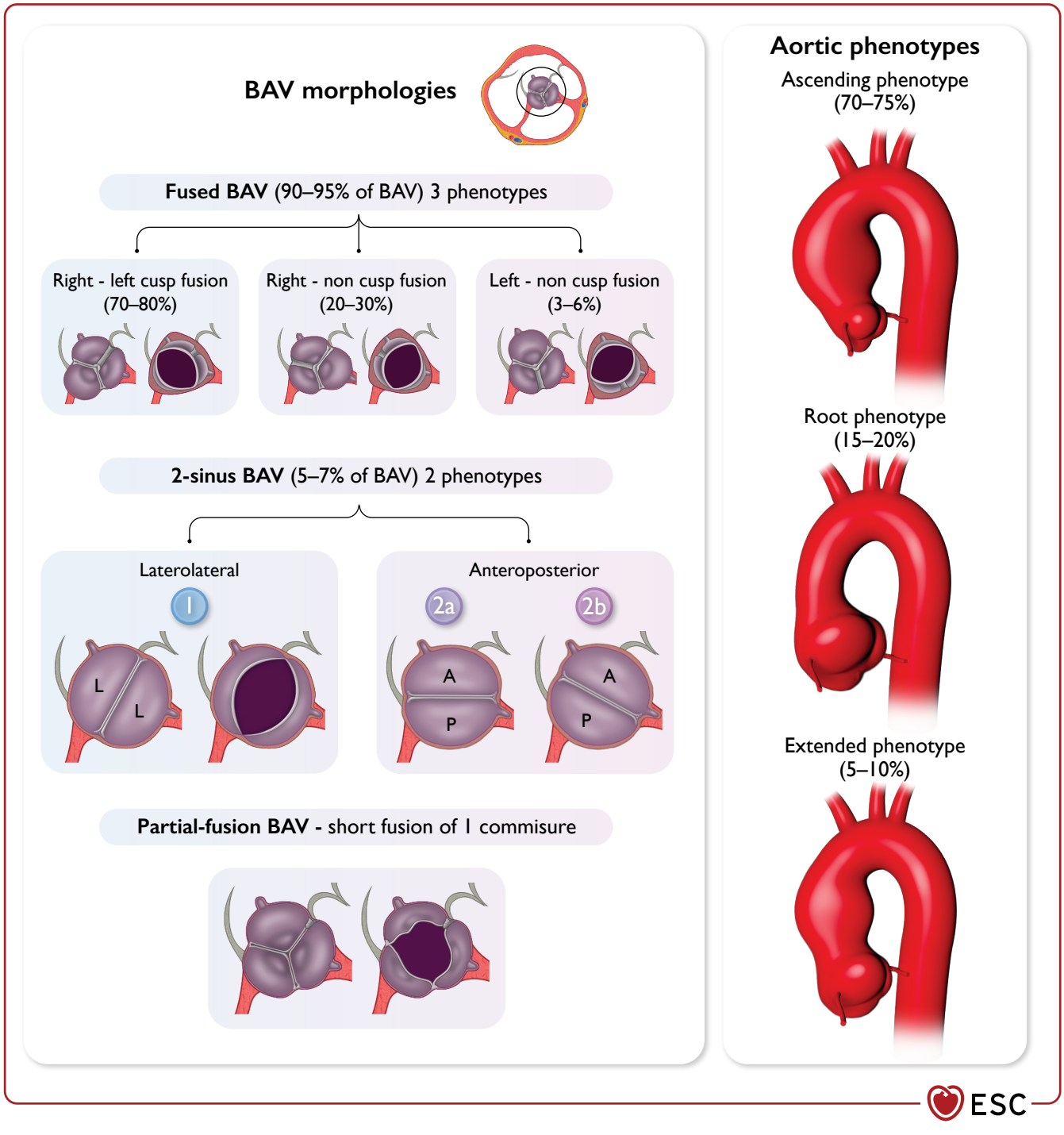

Figure 43 Bicuspid aortic valve, valvulo-aortopathy nomenclature. Modified from Michelena *et al.*[1510] A, anterior; BAV, bicuspid aortic valve; L, lateral; P, posterior. Although preferential associations exist, each of the three valve types—'fused BAV', '2-sinus BAV', and 'partial-fusion BAV'—can be variably associated with dilatation predominantly located at the sinuses of Valsalva ('root phenotype', 15%–20%) or at the tubular (supra-coronary) tract ('ascending phenotype', 70%–75%). A minor proportion of patients present with equal dilatation of the sinusal and tubular segments or ascending dilatation extending into the proximal arch ('extended phenotype', 5%–10%).

genetic testing is not indicated for isolated BAV disease, but reserved for patients with syndromic features, family history of aortic disease, or aneurysms/dissections of medium-sized arteries other than the thoracic aorta, and may be considered in patients with the root phenotype.[1389,1508,1509]

We recommend adopting a new international consensus nomenclature and classification, established by a panel of experts, to replace the previous various concurrent nomenclatures used[1510] (*Figure 43*). Aneurysm prevalence reaches 40% in clinical series and 0.85 per 100 patient-years in population studies. AAEs are rare, but 8- to 10-fold more frequent than in the general population.[1001,1511] The longest available follow-up of BAV subjects was recently reported,[1512] showing a total lifetime morbidity burden as high as 86%, a predominant part of which was driven by valve-related complications (aortic stenosis, endocarditis, HF).

When a BAV is first detected, a complete study of the thoracic aorta is necessary; vice versa, in every patient with ascending aortic dilatation, valve morphology should be ascertained.[70,969] When TTE detects BAV-associated aortic dilatation, CCT or CMR is recommended to confirm measurements, exclude coarctation, and record baseline diameters at different levels for subsequent periodic assessments.[137,1001] Surveillance by TTE becomes necessary when the maximum diameter exceeds 40 mm. In mixed tricuspid aortic valve (TAV) and BAV series, AAEs occurred in 2/10 000 patient-years with a diameter >40 mm (vs. 0.1–0.3/10 000 patient-years in the general population)[894] (*Figure 43*). Considering average aortic diameter growth of 0.2–0.6 mm per year,[893,1513] once fast progression is excluded, follow-up can be scheduled every 2–3 years (according to risk profile). In 5%–15% of cases, BAV patients have at least one FDR with either BAV or ascending aortic dilatation; root phenotype and aortic regurgitation in the proband predict ascending dilatation in FDRs.[1514] FDR screening is considered cost-effective, but the age at which relatives should undergo TTE remains to be determined.[1515,1516]

A diameter exceeding 55 mm at any level mandates surgery.[70,969,1001] However, the historically known relation between diameter and acute complications has been recently reappraised. Both in large mixed[153] and purely BAV series,[981] an ascending diameter of about 52 mm already marked an AAE risk increase from ~1% to 4%–5%. Additionally, early post-operative mortality for elective surgery of the proximal aorta ranges today between 0.25% and 2%.[980,981] Therefore, aortic surgery in low surgical risk (<3%) patients with an ascending diameter >52 mm implies a lower risk than observed in the natural history of the disease. For aortic root dilatation in BAV patients, the 'hinge point' was at 50 mm;[981] this phenotype is associated with faster growth rate,[893] higher risk of events following isolated aortic valve replacement,[1517] worse survival if not operated,[1518] and higher risk of acute TAAD.[976,1519]

Surgery should be considered when the diameter is ≥50 mm in selected ascending phenotype patients (*Figures 23*, *24* and *43*).[70,1001] Among those factors, family history of AAEs, poorly controlled hypertension, aortic coarctation, and rapid (≥3 mm per year) diameter growth should be noted. Surgery at >50 mm may also be considered in a shared decision with the patient, taking lifestyle and psychological factors into consideration,[70,1001] since 50 mm should correspond to an approximately 10-fold increase in the risk of AAEs.[894] In a study of patients with aortic diameter ≥40 mm, those with diameters of 50 mm faced a 1% risk of AAEs within 5 years, compared with 0.1% for those with 40 mm diameters, explaining the 10-fold difference; however, this study did not exclusively involve BAV patients.[894] Another recent study[1520] specifically focused on BAV patients found a 0.4% incidence of AAEs per patient-year for diameters above 50 mm, in contrast to the general BAV population's 0.03% incidence.[1521] Previous guidelines also suggested aortic repair for a cross-sectional area-to-height ratio (CSA/h) >10 cm^2/m;[70] nevertheless, more recently, it has been suggested that the CSA/h threshold for the ascending tract in BAV should be 13 cm^2/m.[981] For the average height of male and female Europeans (1.8 m and 1.67 m, respectively), a CSA/h of 10 cm^2/m would correspond to a diameter of 48 mm or 46 mm, respectively, whereas 13 cm^2/m means 54 mm or 53 mm. It is reasonable to refer to the 13 cm^2/m CSA/h cut-off for ascending aortic repair, especially in individuals ≤1.69 m in height (since 13 cm^2/m corresponds to ≤52 mm diameter). Recently, besides dilatation, aortic elongation is also considered a risk factor,[974] and a curvilinear length >11.5 cm at the vessel's centreline increases the yearly risk of AAEs.[155] Age is another factor to consider: at 50 years, a 40 mm ascending aorta corresponds to the upper normal limit for patients with large body size,[149] and therefore the same diameter at a higher age could imply a lower risk of AAEs.

Recommendation Table 68 — Recommendations for bicuspid aortic valve-associated aortopathy management

Recommendations	Class[a]	Level[b]
When a BAV is first diagnosed, initial TTE to assess diameters of the aorta at several levels is recommended.[1001,1510,1522]	I	B
Surgery for bicuspid aortopathy is recommended when the maximum aortic diameter is ≥55 mm.[70,172,899,969,1001]	I	B
Surgery for bicuspid aortopathy of the root phenotype[c] is recommended when the maximum aortic diameter is ≥50 mm.[70,893,981,986,1001,1519,1523]	I	B
CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.[1001,1510]	I	C
Screening by TTE in FDRs of BAV patients with root phenotype[c] aortopathy and/or isolated aortic regurgitation is recommended.[1001,1510,1514]	I	C
Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.[70,1001]	I	C
Screening by TTE in FDRs of all BAV patients should be considered.[70,1001,1500,1510,1515]	IIa	B
In patients with low surgical risk, surgery for bicuspid aortopathy of ascending phenotype[d] should be considered when the maximum aortic diameter is >52 mm.[153,172,981]	IIa	B

Continued

In patients with low surgical risk and ascending phenotype bicuspid aortopathy, surgery should be considered at a maximum diameter ≥50 mm if any of the following is the case:[70,153,155,981,1001] • Age <50 years • Shorter stature[e] • Ascending aortic length ≥11 cm[f] • Aortic diameter growth rate ≥3 mm per year[g] • Family history of acute aortic syndrome • Aortic coarctation • Resistant hypertension[h] • Concomitant non-aortic-valve cardiac surgery • Desire for pregnancy	IIa	C
Surgery for bicuspid aortopathy in patients undergoing aortic valve surgery should be considered at a root or ascending diameter ≥45 mm.[70,172,969]	IIa	C

BAV, bicuspid aortic valve; BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CSA/h, cross-sectional area-to-height ratio; FDRs, first-degree relatives; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Root phenotype = aortic dilatation with sinus diameter > tubular diameter.
[d]Ascending phenotype = aortic dilatation with tubular diameter > sinus diameter.
[e]Patient height between 1.50 and 1.69 m (yielding a CSA/h ratio >13 cm^2/m).
[f]Curvilinear distance at aortic centreline between the ventriculo-aortic junction and the origin of the innominate artery.
[g]In order to ascertain real rapid growth, side-by-side re-evaluation of images obtained with the same modality and technique should be performed.
[h]Hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment, including diuretics.

10.3. Coarctation of the aorta and aortic arch variants

10.3.1. Coarctation of the aorta

This topic is extensively discussed in the *ESC 2020 Guidelines for the management of adult congenital heart disease*.[1468] Coarctation of the aorta (CoA) manifests as a discrete stenosis or a hypoplastic segment typically located at the insertion of the ductus arteriosus. More distal locations are known as mid-aortic syndrome and require dedicated management.[1524] Associated lesions include BAV (up to 50%–85%), intracerebral aneurysms (10%), and ascending aortic aneurysms.[1525,1526] CoA may be associated with syndromes such as TS. Research indicates that up to 12.6% of females diagnosed with CoA also have TS, and coarctation is observed in 7%–18% of patients with TS.[1417,1468,1527]

10.3.1.1. Diagnostic work-up

Mild cases of CoA may only become evident in adulthood. Symptoms reflect pre-stenotic hypertension (e.g. headache, nosebleeds) and post-stenotic hypoperfusion (e.g. abdominal angina and claudication). The natural course is largely driven by hypertension-related complications, including HF, intracranial haemorrhage, premature coronary/cerebral artery disease, and aortic rupture/dissection.[1528] Presently, there is no evidence supporting screening for intracerebral aneurysms in asymptomatic patients.

A systolic non-invasive gradient between upper and lower extremities, an abnormal ABI, or an invasive peak-to-peak gradient ≥20 mmHg indicates significant CoA. In the presence of collaterals or decreased LV function, gradients or ABI may underestimate severity. A diastolic tail in the DTA or abdominal diastolic antegrade flow by TTE is suggestive of significant narrowing. Criteria to consider significant CoA are listed in *Figure 44*. TTE is also useful to detect LV hypertrophy, which is a marker of disease. CMR and CCT are the preferred imaging techniques, depicting the narrowing as well as the surrounding anatomy, necessary for interventional decision-making.

10.3.1.2. Treatment and follow-up

In native CoA and re-coarctation (*Figure 44*) covered stenting is the first-choice treatment. Interposition of a tube graft is the preferred surgical therapy if stenting is less suitable.[1529] Hypertension remains an important complication, even after successful treatment, and is more common when the initial repair is performed in adulthood.[1528] Right arm 24 h ambulatory BP measurement or exercise tests better detect hypertension.[1530,1531]

All CoA patients require lifelong follow-up.[1532] Imaging of the aorta with CMR/CCT every 3–5 years, adjusted to previous imaging findings and type of intervention, is required to document post-repair or post-interventional complications (such as re-coarctation). Patch repairs are at particular risk of repair-site para-anastomotic aneurysms or pseudo-aneurysms, the latter possibly occurring following interposition grafts as well.[1533]

Recommendation Table 69 — Recommendations for evaluation and medical treatment of patients with coarctation of the aorta

Recommendations	Class[a]	Level[b]
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).[1534,1535]	I	B
Coarctation or re-coarctation repair (either surgical or endovascular) is indicated in patients with hypertension with an increased non-invasive gradient between the upper and lower limbs (decreased ABI) confirmed with invasive measurement (peak-to-peak >20 mmHg), with a preference for stenting when technically feasible.[1536]	I	C
In patients with coarctation, BP measurements at both arms and one lower extremity are recommended.	I	C
It is recommended to treat hypertension in patients with coarctation according to ESC hypertension guidelines.[300]	I	C
Endovascular treatment should be considered in patients with hypertension with >50% narrowing relative to the aortic diameter at the diaphragm, even if the invasive peak-to-peak gradient is <20 mmHg, when technically feasible.[1537]	IIa	C
Endovascular treatment should be considered in normotensive patients with an increased non-invasive gradient confirmed with invasive peak-to-peak gradient >20 mmHg, when technically feasible.[1468]	IIa	C

ABI, ankle–brachial index; BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ESC, European Society of Cardiology.
[a]Class of recommendation.
[b]Level of evidence.

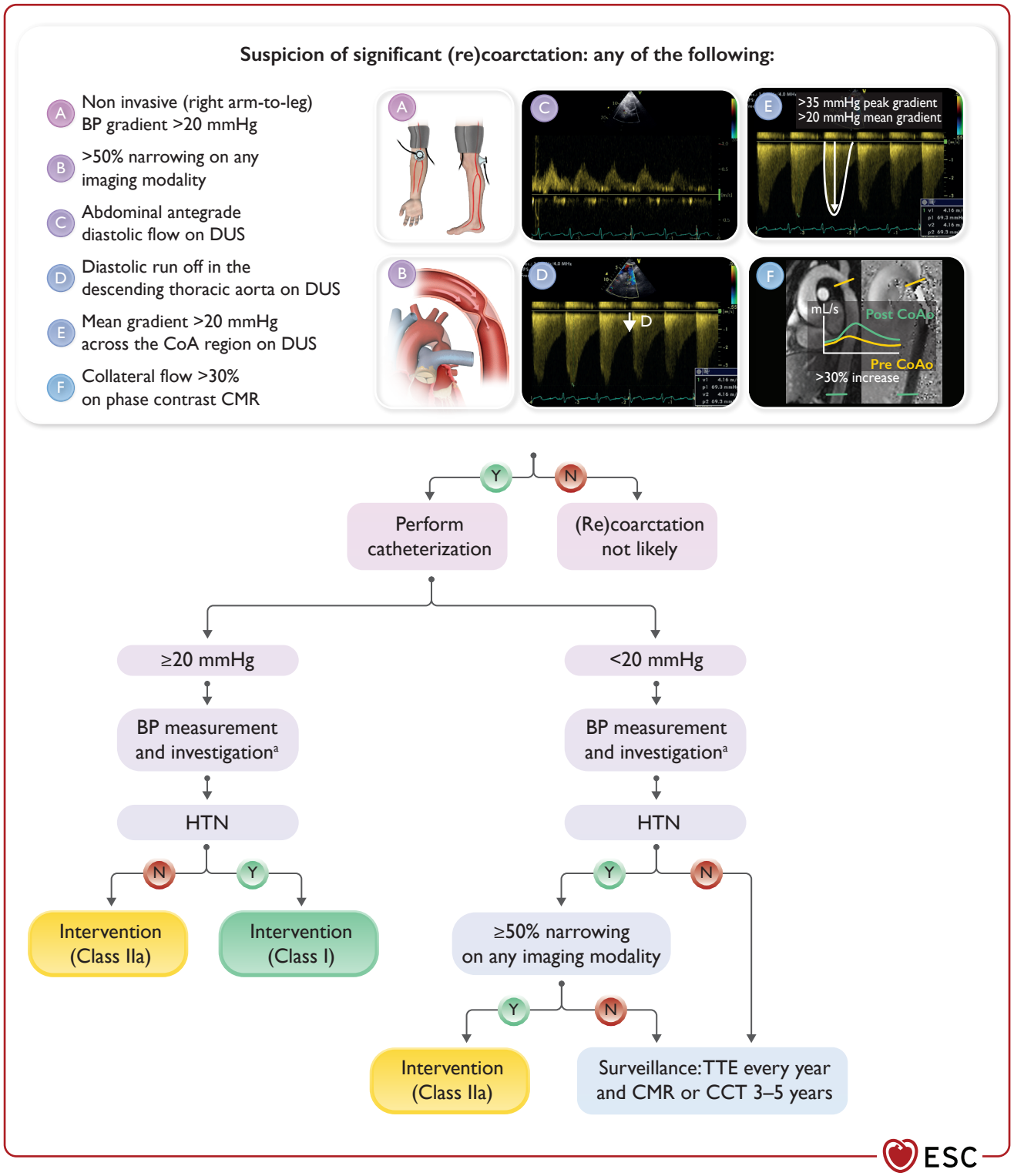

Figure 44 Criteria for significant coarctation/re-coarctation of the aorta and management algorithm. BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CoA, coarctation of the aorta; DUS, duplex ultrasound; HTN, hypertension; TTE, transthoracic echocardiography. [a]Diagnosis of hypertension may require confirmation with ambulatory BP measurement and should also be considered in cases of exercise-induced hypertension and/or left ventricular hypertrophy on TTE.

10.3.2. Aortic arch anatomic variants

A type I arch, where the three great vessels directly arise from the aorta, is the most common form, occurring in about 70% of the population. The type II (bovine) arch is the most frequent variant: type II-A (9% of the population) has the left common carotid artery arising from the innominate artery, and type II-B (13% of the population) has both the innominate and left common carotid arteries originating from a common point on the aortic arch.[1538,1539] Limited data suggest that a bovine arch is associated with a higher risk of aortic dilation and aortic events/complications.[1540,1541] These variations are important to report as they can impact specific medical procedures and diagnostic interpretations.

10.3.3. Aberrant subclavian artery and Kommerell's diverticulum

The most common variant is the aberrant right subclavian artery, where the right subclavian artery arises as the last branch of the aortic arch, usually after the left subclavian artery, and often passes behind the oesophagus through the mediastinum, potentially causing dysphagia lusoria, respiratory symptoms, or recurrent laryngeal nerve palsy. The less common variant, the aberrant left subclavian artery, is typically associated with congenital heart defects, such as a right aortic arch. However, in adulthood, both variations are often incidental findings.[1542]

Kommerell's diverticulum is a remnant of the fourth dorsal aortic arch due to incomplete regression, found in 20%–60% of those with an aberrant subclavian artery.[1543] Surgical intervention is advised for a diverticulum orifice >30 mm or combined diverticulum and adjacent descending aorta diameter >50 mm, or both.[1544] Successful repair has been described using open, endovascular, or hybrid approaches depending on anatomy, comorbidities, and expertise.[1543]

11. Polyvascular peripheral arterial disease and peripheral arterial disease in patients with cardiac diseases

11.1. Polyvascular disease

Polyvascular disease is defined as the simultaneous presence of clinically relevant obstructive atherosclerotic lesions in at least two major arterial territories.

11.1.1. Epidemiology and prognosis

Approximately 1 in 4–6 patients with atherosclerosis have PVD (*Figure 45*).[620,1545] According to the REACH registry, patients with PAD were most likely both to have PVD at baseline and to develop PVD over the observational period.[1546,1547]

PVD independently increases major CV event risk, roughly doubling it compared with single arterial bed symptoms.[1547–1549] Event rates rise with the number of affected arterial beds.[1546,1550]

11.1.2. Screening for atherosclerosis in other arterial territories

Screening for PVD in atherosclerotic patients relies on medical history, clinical exam, and ABI measurement. If suspected, start with non-invasive DUS, followed by CTA/MRA if needed.[1557] Assessing concurrent atherosclerosis in other vascular regions is detailed in *Table 17*.

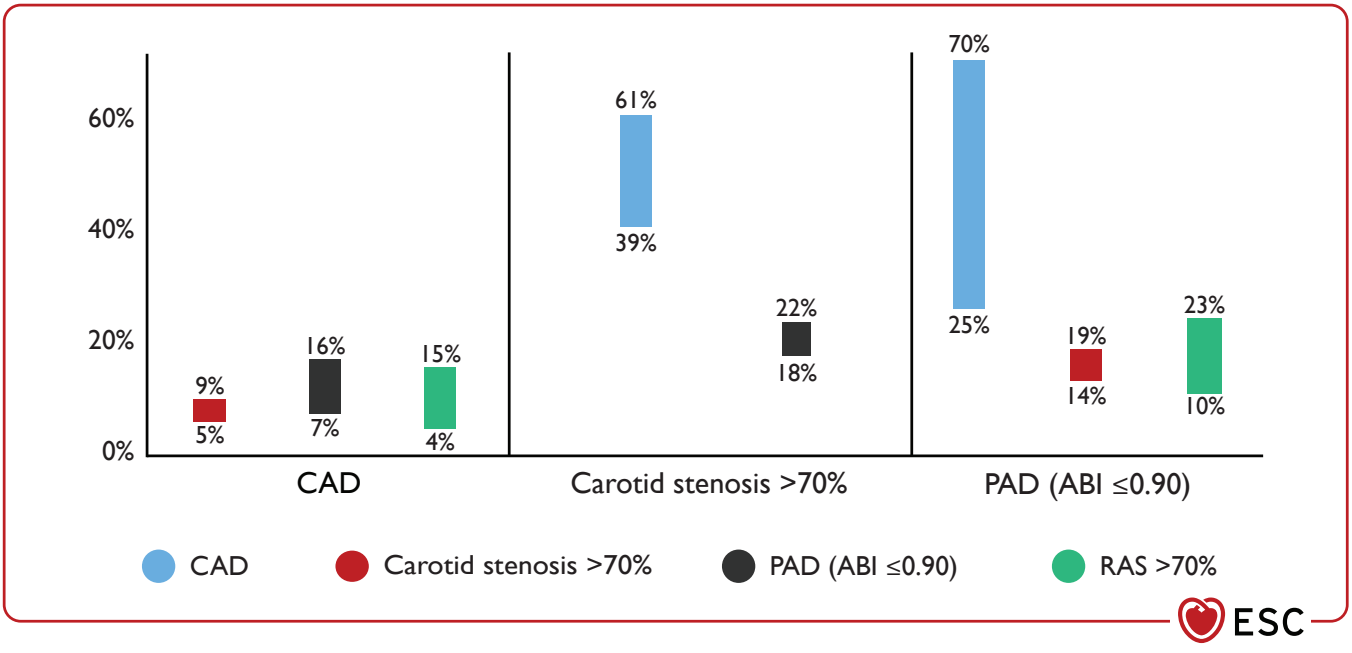

Figure 45 Reported rate ranges of other localizations of atherosclerosis in patients with a specific arterial disease. The graph reports the rates of concomitant arterial diseases in patients presenting an arterial disease in one territory (e.g. in patients with CAD, 5%–9% of cases have concomitant carotid stenosis >70%). Adapted from 2017 ESC Guidelines on PAD.[77,493,784,1549,1551–1556] ABI, ankle–brachial index; CAD, coronary artery disease; PAD, peripheral arterial disease; RAS, renal artery stenosis.

Table 17 Need for assessment of associated atherosclerotic disease in additional vascular territories in symptomatic patients with coronary artery disease, peripheral arterial disease, or carotid stenosis

	Leading disease		
Assessment in other vascular territories	**CAD**	**PAD**	**Carotid stenosis**
CAD		May be helpful to optimize medical treatment[431] and to be considered in patients scheduled for open vascular surgery with poor functional capacity or significant risk factors or symptoms. [1080]	Consider in patients scheduled for carotid endarterectomy and suspected CAD.[1558]
PAD	Potential benefits in identifying high-risk patients and guiding treatment decisions.[429,1559–1561]		
Carotid stenosis	Useful in patients undergoing elective CABG.[1555,1562]		

CABG, coronary artery bypass grafting; CAD, coronary artery disease; PAD, peripheral arterial disease.

11.1.2.1. Screening for coronary artery disease in patients with symptomatic peripheral arterial disease

The morbidity and mortality of patients with PAD is high due to CV complications. Given high CAD event rates in patients with PAD, CAD screening may be helpful to optimize medical treatment and is not intended to increase the rate of coronary interventions.[431] Evaluation can be performed by stress testing or CCT; however, there is no evidence that systematic screening for CAD in stable PAD improves outcomes. Coronary angiography is less suitable due to invasiveness. In patients requiring lower-limb revascularization, CAD management should be based on the *2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery*.[1080]

11.1.2.2. Screening for peripheral arterial disease in patients with coronary artery disease

In high-risk CAD patients with three-vessel disease or recent ACS, systematic screening for multisite atherosclerotic disease through ABI and DUS of carotids, lower-extremity, and renal arteries did not improve outcomes.[1563] However, a subgroup analysis of the COMPASS trial suggests potential benefits when adding vascular-dose rivaroxaban to aspirin in stable patients with CAD and PAD, raising the question of whether identifying PAD in stable CAD patients could be advantageous.[429,1559] In patients undergoing CABG, the presence of concomitant PAD is associated with a three-fold risk of subsequent CV events after CABG.[1560,1561] The GSV should be spared whenever possible, since the success of peripheral arterial revascularization in complex lesions is strongly associated with the availability of sufficient autologous venous segments.[567,1564]

11.1.2.3. Screening for coronary artery disease in patients with carotid stenosis

Due to the high prevalence of CAD among patients scheduled for elective CEA,[1565,1566] pre-operative CAD screening, including coronary angiography, may be considered in suspected patients.[1558] CAD requires prioritization of revascularization according to the patient's clinical status and the severity of carotid disease and CAD. Coronary revascularization should generally be performed first; the exception is recently symptomatic patients with unstable neurological symptoms in whom carotid revascularization should be prioritized.[680]

11.1.2.4. Screening for carotid stenosis in patients with coronary artery disease

Carotid artery stenosis screening may be useful in patients undergoing elective CABG. Ischaemic stroke after CABG is multifactorial,[1567] but also depends on the degree of carotid disease.[1556] Two studies suggest that limiting DUS to patients with at least one risk factor (age >65 years, history of cerebrovascular disease, presence of a carotid bruit, multivessel CAD or PAD) identifies most patients with significant (≥70%) CS.[1555,1562] Nevertheless, addition of CEA to CABG is unlikely to provide significant stroke reduction. In a study in patients with CAD with >80% CS undergoing staged or synchronous carotid procedures (two-thirds were neurologically asymptomatic and 73% had unilateral asymptomatic carotid stenosis), in-hospital stroke rates and 30 day mortality were similar in patients treated with CABG + CEA and in those treated with isolated CABG.[1568] Another study suggests that selective use of DUS should be considered before CABG in patients with a history of neurological events or PAD.[1569]

11.1.3. Management of patients with polyvascular disease

Polyvascular disease requires proactive management of all modifiable risk factors through lifestyle changes and drug therapy. Scientific evidence suggests the benefit of intensified antithrombotic therapy, with no increase in risk of bleeding.[1570] ILT offers comparable benefits for PVD patients and those with single arterial territory disease. However, the benefits of ILT in patients with PVD are not dependent on baseline LDL-C.[1571]

Revascularization should be reserved for symptomatic arterial territories, using the least invasive strategy in a multidisciplinary vascular team approach.

11.2. Peripheral arterial disease and heart failure

Left ventricular (LV) dysfunction is observed in 20%–30% of PAD patients,[1572,1573] mostly associated with CAD.[1574] High aortic stiffness

can increase LV afterload and impair coronary blood flow, resulting in hypertension, LV hypertrophy, LV diastolic dysfunction, and HF.[1575,1576] Skeletal muscle involvement and deconditioning due to PAD may aggravate HF severity.[1577,1578]

Peripheral arterial disease and HF are independently associated with poor outcomes and those with concomitant HF have a 30% higher risk of MACE and 40% higher risk of all-cause mortality.[1574] Evaluation of LV function in patients with PAD may be useful for better CV risk stratification and comprehensive management of their CV disease.[1579] This is of particular importance when an intermediate- or high-risk vascular intervention is planned. Expectedly, the presence of PAD in patients with HF is also associated with poor outcomes.[1580–1584] These patients represent a high-risk group in which intense risk-factor modification strategies and optimization of HF therapy are warranted.

11.3. Peripheral arterial disease and AF

The prevalence of AF among patients with PAD is around 12%.[1585–1590] A meta-analysis revealed that in patients with AF and PAD, risk of all-cause mortality, CV mortality, and MACE is 40%, over 60%, and over 70% higher, respectively compared with patients with AF without PAD.[1591] PAD is included in the CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74 and sex category [female]) risk score, which underlies the prognostic importance of PAD in patients with AF.[1592]

11.4. Peripheral arterial disease and aortic stenosis

Peripheral arterial disease frequently accompanies symptomatic aortic stenosis, especially among patients not eligible for surgical aortic valve replacement (20%–30%).[198,1593–1595] In these patients, pre-procedural CCT/CTA or CMR[1596] of the aorta and major peripheral arteries is mandatory to evaluate the access site for transcatheter aortic valve implantation (TAVI) and plan a closure strategy for the access site. Patients with PAD have increased risk of all-cause mortality and vascular complications after TAVI,[198] thus, screening for PAD in these patients may be helpful.

Recommendation Table 70 — Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases (see also Evidence Table 15)

Recommendations	Class[a]	Level[b]
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[242,1571]	I	A
In patients with PAD and newly diagnosed AF with a CHA_2DS_2-VASc score ≥2, full oral anticoagulation is recommended.[1597]	I	C
Screening for ilio-femoral PAD is recommended in patients undergoing TAVI.[198,1598]	I	B
Carotid DUS should be considered for stable patients scheduled for CABG with TIA/stroke within the past 6 months without carotid revascularization.[1556,1569]	IIa	B
In patients with stable PVD who are symptomatic in at least one territory and without high bleeding risk,[c] treatment with a combination of rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.[429,1559]	IIa	A
Carotid DUS may be considered for stable patients scheduled for CABG without TIA/stroke within the past 6 months.[1555,1562]	IIb	C

AF, atrial fibrillation; b.i.d., twice daily; CABG, coronary artery bypass grafting; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female); DUS, duplex ultrasound; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; o.d., once daily; PAD, peripheral arterial disease; PVD, polyvascular disease; TAVI, transcatheter aortic valve implantation; TIA, transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

[c]Prior history of intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m^2.

12. Key messages

Peripheral arterial and aortic diseases are highly prevalent, often asymptomatic, and linked to increased morbidity and mortality. Early diagnosis is crucial for better outcomes and management requires a multidisciplinary team. CVRF control is crucial to prevent progression and complications. Despite the benefit of medical therapy, lifestyle changes, healthy diet, abstinence from smoking, exercise/rehabilitation, and education are essential for effective management. Patient empowerment is essential to improve adherence and close/regular monitoring is essential to improve prognosis. Use of web- or app-based calculators for estimation of CV risk in the secondary prevention of ASCVD may aid patient motivation for lifestyle changes and adherence to medication.

Peripheral arteries

Atherosclerotic lower-extremity PAD is a chronic disease needing lifelong follow-up.

Assessment of walking impairment, functional status, and amputation risk is crucial in PAD management.

Ankle–brachial index should be the initial diagnostic test for screening and diagnosing PAD, and serves as a surrogate marker for CV and all-cause mortality. DUS is the first-line imaging method to confirm PAD lesions.

Supervised exercise training or, if not available, HBET, improves walking and functional performances, and reduces CV risk. Exercise training remains underused and increased awareness is warranted.

In asymptomatic PAD patient revascularization is not recommended. In symptomatic PAD patient need for interventional treatment, following a period of optimal medical treatment and exercise, should be discussed in a multidisciplinary setting.

Chronic limb-threatening ischaemia increases the risk of CV events, needs early diagnosis, rapid referral to a multidisciplinary vascular team, and revascularization for limb salvage.

Acute limb ischaemia warrants rapid clinical assessment by a vascular team and urgent revascularization.

Duplex ultrasound is the first-line diagnostic modality for carotid stenosis. Routine revascularization is not recommended if asymptomatic. In symptomatic patients multidisciplinary assessment is recommended.

Atherosclerotic UEAD is most frequently located in the subclavian artery and may be suspected because of an absolute inter-arm SBP difference >10–15 mmHg. DUS is first-line imaging and routine revascularization is not recommended.

The key to early diagnosis of acute and chronic mesenteric ischaemia is a high level of clinical suspicion—laboratory tests are unreliable for the diagnosis. Acute SMA occlusion requires immediate revascularization.

Aorta

Aortic aneurysms are managed based on size, location, and growth rate. Small aneurysms are monitored regularly (Guidelines provide disease-specific follow-up algorithms), while larger ones may require surgical/endovascular repair to prevent rupture.

In aortic root aneurysms, aortic replacement may be considered at >52 mm in low-risk patients and at experienced centres.

Aortic diameter is the primary risk factor for aortic events. However, evidence supports diameter indexation (especially in extreme BSA populations) and the use of aortic length (>11 cm), the AHI (>32.1 mm/m), growth rate (≥3 mm per year for ascending aorta and arch or >5 mm per 6 months in the thoracoabdominall aorta), and age/sex for risk assessment.

Multidisciplinary collaboration, hybrid operating rooms, and advanced stent technology have increased the adoption of hybrid approaches and endovascular therapies for different thoracoabdominal aortic diseases.

Acute aortic syndrome management involves medical treatment in critical care units and selective surgical intervention based on location and complications. The main problem in these conditions continues to be a delay in diagnosing patients or transferring them to an aortic centre. Improved diagnostic algorithms and reduced surgical complications have lowered mortality rates. Surgical/endovascular treatment in the subacute phase is advised for high-risk patients with type B aortic syndrome.

Suspected genetic aortic conditions require evaluation at experienced centres to assess both the patient and their FDRs for genetic studies. Genetic aortic conditions should be considered based on family history, syndromic features, age <60 years, and no CVRFs (Guidelines offer a screening algorithm for thoracic aorta disease). A comprehensive evaluation of the entire aorta and other vascular territories is recommended in HTAD. Recent advances in genetics are enabling personalized and patient-centred assessment. This includes using different aortic diameter thresholds to indicate surgery and implementing diverse surveillance algorithms.

13. Gaps in evidence

There are several areas where robust evidence is still lacking and which deserve to be addressed in future clinical research.

(1) Epidemiology and risk factors in PAAD:
   (a) Improve PAAD risk definition.
   (b) Provide contemporary data on PAAD prevalence in Europe.
   (c) Inflammation biomarkers, metabolomics, and proteomics may have prognostic value in PAAD.
(2) Evaluation of peripheral arteries and aorta:
   (a) Follow-up algorithms can assist PAAD patient management but have limitations and evidence on cost-effectiveness is needed.
   (b) The best methodology for aortic measurements remains to be elucidated.
(3) Screening for carotid, peripheral arterial, and aortic diseases:
   (a) Screening in specific populations: research is needed to understand the nuances of screening in particular populations and whether modifications to current guidelines are necessary.
   (b) Patient outcomes and benefits of screening: impact of screening on patient outcome should be assessed.
(4) OMT and PAAD:
   (a) Research needed on QoL and workability.
   (b) Research needed for optimal preventive strategies.
   (c) Exercise therapy and rehabilitation for PAAD should be more accessible and employed.
   (d) Anti-inflammatory therapy should be investigated.
   (e) Antithrombotic therapies in specific risk groups of PAAD and patients undergoing revascularization should be addressed.
(5) Aortic aneurysms:
   (a) Discovering novel individualized risk stratification parameters beyond well-established markers.
   (b) Assessing the safety of fluoroquinolone use in patients with aortic aneurysm.
(6) Acute aortic syndromes:
   (a) Assess the management of pregnancy-related AAS.
   (b) Identify diagnostic biomarkers other than D-dimer.
   (c) Management in uncomplicated TBAD and IMH should be assessed.
(7) Genetic aortic diseases:
   (a) Need to refine risk estimation in AD, particularly in HTAD, especially the risk of type B aortic dissection.
   (b) There is insufficient evidence to support the efficacy of any medication in reducing the risk of AD.
(8) Sex differences in PAAD:
   (a) Investigate sex and age differences.
   (b) Assess the optimal parameter or indexed parameter to guide intervention decisions in women with aortic and PAD diseases.

14. Sex differences

Sex differences have been evaluated and discussed in the specific sections.

15. 'What to do' and 'What not to do' messages from the guidelines

Table 18 'What to do' and 'What not to do'. 'What to do and What not to do' lists all Class I and Class III recommendations from the text.

Table 18 'What to do' and 'What not to do'

Recommendations	Class[a]	Level[b]
Recommendations for clinical and laboratory, and for functional and quality of life, assessment in patients with peripheral arterial and aortic disease		
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of arterial circulation.	I	B
To assess PAAD, it is recommended to perform thorough clinical, vascular, and CVRF laboratory evaluation.	I	C
Recommendations for diagnostic tests in patients with peripheral arterial disease		
Measurement of the ABI is recommended as the first-line non-invasive test for screening and diagnosis of PAD, using an ABI ≤0.90 as a diagnostic criterion.	I	B
In the case of non-compressible ankle arteries or ABI >1.40, additional methods such as TP, TBI or Doppler waveform analysis are recommended.	I	B
Recommendations for imaging of the aorta		
It is recommended that aortic diameters are measured at prespecified anatomical landmarks, and the largest diameter of the section be perpendicular to the longitudinal axis.	I	C
It is recommended in cases of serial imaging of the aorta over time to use the same imaging modality with the same measurement method.	I	C
It is recommended to consider renal function, pregnancy, age, and history of allergy to contrast media to select the optimal imaging modality with minimal radiation exposure and lowest iatrogenic risk, except for emergency cases.	I	C
Recommendations for thoracic aortic measurements		
TTE is recommended as the first-line imaging technique in evaluating thoracic aortic diseases.	I	B
It is recommended to report aortic diameters using the leading-to-leading edge convention in end-diastole by echocardiography.	I	C
It is recommended to report aortic diameters using the inner-to-inner edge convention in end-diastole by CCT or CMR.	I	C
It is recommended to report aortic diameters from images obtained with the double-oblique technique (not axial images) by CCT or CMR.	I	C
ECG-triggered CCT is recommended for comprehensive diagnosis, follow-up, and pre-invasive treatment assessment of the entire aorta, particularly the root and ascending aorta.	I	C
CMR is recommended for diagnosis and follow-up of thoracic aortic diseases, especially when chronic follow-up is required.	I	C
Recommendations for abdominal aortic aneurysm screening		
Screening is recommended in men aged ≥65 years and with a history of smoking to reduce the risk of death from ruptured AAA.	I	A
Screening is recommended in FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.	I	C
Recommendations for lifestyle, physical activity, and patient education		
In patients with PAAD, cessation and abstinence from smoking of any kind is recommended to reduce the risk of AD, MI, death, and limb ischaemia.	I	A
A healthy diet rich in legumes, dietary fibre, nuts, fruits, and vegetables, with a high flavonoid intake (Mediterranean diet), is recommended for CV disease prevention in patients with PAAD.	I	A
Low- to moderate-intensity (or high if tolerated) aerobic activities are recommended in patients with PAD to increase overall and pain-free walking distance.	I	A
In patients with PAAD, behavioural counselling to promote healthy diet, smoking cessation, and physical activity is recommended to improve the CV risk profile.	I	B
It is recommended to promote patient and caregivers' education and empowerment through tailored guidance on lifestyle adjustments and the importance of regular physical activity.	I	C
Recommendations for antihypertensive therapy in patients with peripheral and aortic disease		
In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.	I	A
In unilateral RAS patients, it is recommended that antihypertensive medication include ACEIs/ARBs.	I	B
Recommendations for lipid-lowering therapy for patients with peripheral arterial and aortic diseases		
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
Statins are recommended in all patients with PAD.	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.	I	B

Continued

If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.	I	A
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.	I	B
Fibrates are not recommended for cholesterol lowering.	III	B
Recommendations for the medical management of patients with peripheral arterial and aortic diseases and diabetes		
It is recommended to apply tight glycaemic control (HbA1c <53 mmol/mol [7%]) to reduce microvascular complications in patients with PAAD.	I	A
SGLT2i with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.	I	A
GLP-1RAs with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.	I	A
It is recommended to avoid hypoglycaemia in patients with PAAD.	I	B
It is recommended to individualize HbA1c targets according to comorbidities, diabetes duration, and life expectancy.	I	C
It is recommended to prioritize the use of glucose-lowering agents with proven CV benefits, followed by agents with proven CV safety, over agents without proven CV benefit or safety.	I	C
Recommendations for diagnostic tests in patients with peripheral arterial disease and diabetes, renal failure and wounds		
Measuring TP or TBI is recommended in patients with diabetes or renal failure if resting ABI is normal.	I	C
Recommendations for imaging in patients with peripheral arterial disease		
DUS is recommended as first-line imaging method to confirm PAD lesions.	I	C
In symptomatic patients with aorto-iliac or multisegmental/complex disease, CTA and/or MRA are recommended as adjuvant imaging techniques for preparation of revascularization procedures.	I	C
Analysis of anatomical imaging tests in conjunction with symptoms and haemodynamic tests prior to an invasive procedure is recommended.	I	C
Recommendations for exercise therapy in patients with peripheral arterial disease		
In patients with symptomatic PAD, SET is recommended.	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.	I	A
Recommendations for antithrombotic therapy in patients with peripheral arterial disease		
Use of antiplatelet therapy with aspirin alone (range 75–160 mg o.d.) or clopidogrel alone (75 mg o.d.) is recommended for the reduction of MACE in patients with symptomatic PAD.	I	A
Long-term DAPT in patients with PAD is not recommended.	III	A
Oral anticoagulant monotherapy for PAD (unless for another indication) is not recommended.	III	A
The routine use of ticagrelor in patients with PAD is not recommended.	III	A
It is not recommended to systematically treat patients with asymptomatic PAD without any sign of clinically relevant ASCVD with antiplatelet drugs.	III	B
Recommendations on interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)		
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.	I	C
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.	III	B
In patients with asymptomatic PAD, revascularization is not recommended.	III	C
Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease		
It is recommended to regularly, at least once a year, follow-up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.	I	C
Recommendations for the management of chronic limb-threatening ischaemia		
For limb salvage in patients with CLTI, revascularization is recommended.	I	B
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.	I	C
Recommendations for medical treatment in patients with chronic limb-threatening ischaemia		
It is recommended that patients with CLTI are managed by a vascular team.	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is recommended to allow wound healing.	I	C

Continued

It is recommended to treat infection with antibiotics.	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.	III	C
Recommendations for interventional treatment of chronic limb-threatening ischaemia		
In CLTI patients, it is recommended to perform revascularization as soon as possible.	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
An individual risk assessment (weighing the patient's individual procedural risk of endovascular vs. surgical revascularization) by a multidisciplinary vascular team is recommended.	I	C
Recommendations for follow-up in patients with chronic limb-threatening ischaemia		
In patients with CLTI, following revascularization it is recommended to follow-up patients on a regular basis.	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.	I	C
Recommendations for the management of patients presenting with acute limb ischaemia		
In patients with ALI, it is recommended that an urgent evaluation is performed by a vascular clinician with sufficient experience to assess limb viability and implement appropriate therapy.	I	C
In cases of neurological deficit, urgent revascularization is recommended; diagnostic imaging is recommended to guide treatment, provided it does not delay treatment, or if the need for primary amputation is obvious.	I	C
In the absence of severe neurological deficit, revascularization is recommended within hours of initial imaging in a case-by-case decision.	I	C
Treatment with analgesics is recommended as soon as possible for pain control.	I	C
It is recommended to monitor for compartment syndrome after revascularization and treat (fasciotomy).	I	C
It is recommended to assess clinical and haemodynamic success following revascularization.	I	C
In patients with ALI, it is recommended to obtain a comprehensive medical history and determine the cause of thrombosis and/or embolization.	I	C
Recommendations for carotid artery stenosis assessment		
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.	I	B
It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.	I	C
It is not recommended to use the ECST method for ICA stenosis assessment.	III	C
Recommendations for antithrombotic treatment in patients with carotid stenosis		
In patients with symptomatic CS, not undergoing carotid endarterectomy or stenting, DAPT with low-dose aspirin and clopidogrel (75 mg) is recommended for the first 21 days or longer, followed by clopidogrel 75 mg or long-term aspirin to reduce the risk of stroke.	I	A
Recommendations for interventional treatment in patients with asymptomatic carotid artery stenosis		
In asymptomatic patients with ICA stenosis, in the absence of high-risk features and with a life expectancy <5 years, routine revascularization is not recommended.	III	A
Recommendations for evaluation and medical treatment in patients with symptomatic carotid artery stenosis		
DAPT is recommended in the early phase of minor strokes in patients with ICA stenosis, if not revascularized, for at least 21 days, considering the bleeding risk.	I	A
It is recommended that symptomatic ICA stenosis patients are assessed by a vascular team including a neurologist.	I	C
Recommendations for interventions in patients with symptomatic carotid artery stenosis		
It is recommended to perform CEA of symptomatic 70%–99% ICA stenosis provided a documented 30 day risk of procedural death/stroke is <6%.	I	A
If indicated, it is recommended to perform CEA within 14 days in symptomatic ICA stenosis patients.	I	B
OMT is recommended for all symptomatic ICA stenosis patients.	I	A
Revascularization is not recommended in patients with ICA lesions <50%.	III	A
Recommendations for follow-up in patients with carotid artery stenosis		
Once-yearly follow-up is recommended to check for CVRFs and treatment compliance.	I	A
After ICA stent implantation, DAPT with aspirin and clopidogrel is recommended for at least 1 month.	I	A
After ICA revascularization, long-term aspirin or clopidogrel is recommended.	I	B
During follow-up, it is recommended to assess neurological symptoms, CVRFs, and treatment adherence at least yearly in patients with CS.	I	C
After ICA revascularization, surveillance with DUS is recommended within the first month.	I	C

Continued

Recommendations for the management of subclavian artery stenosis		
Bilateral arm BP measurement is recommended for all patients with PAAD.	I	B
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.	III	C
Recommendations for diagnostic strategies for renal artery disease		
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.	I	B
In cases of DUS-based suspicion of RAS or in inconclusive DUS, MRA or CTA are recommended.	I	B
In patients with atherosclerotic RAS, it is recommended to assess clinical high-risk features and kidney viability when evaluating renal artery revascularization.	I	B
Recommendations for treatment strategies for renal artery disease		
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.	III	A
Recommendations in patients with visceral artery stenosis		
In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.	I	B
In patients with suspected acute or chronic mesenteric ischaemia, CTA is recommended.	I	C
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C
Recommendations for primary and secondary prevention in aortic atheromatous plaques		
Anticoagulation or DAPT are not recommended in aortic plaques since they present no benefit and increase bleeding risk.	III	C
In patients with an embolic event and evidence of an aortic arch atheroma, intensive lipid management to an LDL-C target <1.4 mmol/L (<55 mg/dL) is recommended to prevent recurrences.	I	A
In patients with an embolic event and evidence of an aortic arch atheroma, SAPT is recommended to prevent recurrences.	I	C
Recommendations for initial evaluation of thoracic aorta aneurysm and abdominal aortic aneurysm		
When an aortic aneurysm is identified at any location, assessment of the entire aorta is recommended at baseline and during follow-up.	I	C
When a TAA is identified, assessment of the aortic valve (especially for BAV) is recommended.	I	C
Recommendation for the surveillance of patients with thoracic aortic aneurysms (non-heritable thoracic aortic disease)		
In thoracic aortic dilatation, TTE is recommended at diagnosis to assess aortic valve anatomy and function, aortic root, and ascending aorta diameters. Additionally, a global aortic evaluation using all echocardiographic views is recommended.	I	C
CMR or CCT is recommended for surveillance of patients with aneurysm at the distal ascending aorta, aortic arch, DTA, or TAAA.	I	C
In thoracic aortic dilatation, CCT or CMR is recommended to confirm TTE measurements, rule out aortic asymmetry, and determine baseline diameters for follow-up.	I	C
TTE is not recommended for the surveillance of aneurysms in the distal ascending aorta, aortic arch, or DTA.	III	C
Recommendations for surveillance of patients with abdominal aortic aneurysm		
DUS surveillance is recommended every 6 months in men with AAA of 50–55 mm and in women with AAA of 45–50 mm.	I	B
DUS is recommended for AAA surveillance.	I	C
CCT or CMR is recommended if DUS does not allow adequate measurement of AAA diameter.	I	B
Recommendations for medical treatment in patients with thoracic aorta or abdominal aortic aneurysms		
In patients with aortic aneurysm (TAA and/or AAA), optimal implementation of CV risk management and medical treatment (see detailed recommendations in dedicated Tables of Recommendations) are recommended to reduce MACE.	I	C
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve		
Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.	I	B
Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.	I	B
VKAs are recommended lifelong for all patients with a Bentall procedure with an MHV prosthesis.	I	B
Recommendations for surgery in aortic arch aneurysms		
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.	I	C

Continued

Recommendations for the management of patients presenting with descending thoracic aortic and thoracoabdominal aortic aneurysms		
In patients with unruptured DTA aneurysm (without HTAD), elective repair is recommended if diameter ≥55 mm.	I	B
In patients without HTAD with unruptured DTA aneurysm, when elective repair is indicated and anatomy is suitable, TEVAR is recommended over open repair.	I	B
In patients with DTA aneurysm who undergo TEVAR with planned LSA coverage, it is recommended to revascularize the LSA before TEVAR to reduce the risk of SCI and stroke.	I	B
In patients with unruptured degenerative TAAA, elective repair is recommended when the diameter is ≥60 mm.	I	B
Recommendations for the management of patients presenting with abdominal aortic aneurysm		
Elective repair is recommended if AAA diameter is ≥55 mm in men or ≥50 mm in women.	I	A
In ruptured AAA with suitable anatomy, endovascular repair is recommended over open repair to reduce peri-operative morbidity and mortality.	I	B
In patients with AAA and limited life expectancy (<2 years), elective AAA repair is not recommended.	III	B
Prior to AAA repair, routine evaluation with coronary angiography and systematic revascularization in patients with chronic coronary syndromes is not recommended.	III	C
Recommendations for the management of patients presenting with endoleaks		
It is recommended to perform 30 day imaging after TEVAR/EVAR, by CCT + DUS/CEUS, to assess the success of intervention.	I	B
It is recommended to re-intervene to achieve a seal in patients with type I endoleak after TEVAR/EVAR.	I	B
It is recommended to re-intervene, principally by endovascular means, to achieve a seal in patients with type III endoleak after TEVAR/EVAR.	I	B
Recommendations for follow-up after treatment of aortic aneurysms		
After open repair of TAA, early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.	I	B
After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and then every 5 years thereafter if findings are stable.	I	A
After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.	I	A
Recommendations for diagnostic work-up of acute aortic syndrome		
In unstable patients who cannot be transferred to CCT, TOE is recommended for diagnosis and evaluation of the coeliac trunk and mesenteric artery.	I	B
In patients presenting with clinical features compatible with possible AAS, a multiparametric algorithm for ruling in or out AAS using the ADD-RS is recommended.	I	B
ECG-gated CCT from neck to pelvis is recommended as the first-line imaging technique in patients with a suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).	I	C
In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendation for medical treatment in acute aortic syndromes		
In patients with AAS, immediate anti-impulse treatment targeting SBP <120 mmHg and heart rate ≤60 b.p.m. is recommended. In cases of spinal ischaemia or concomitant brain injury, maintaining higher MAP is recommended.	I	B
Intravenous BBs (e.g. labetalol) are recommended as first-line agents. If necessary, i.v. vasodilators (e.g. dihydropyridine calcium blockers or nitrates) could be added.	I	B
Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.	I	B
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents, is recommended after 24 h if gastrointestinal transit is preserved.	I	B
Adequate pain control to achieve haemodynamic targets is recommended.	I	C

Continued

Recommendations for intervention in type A acute aortic dissection		
In patients with acute TAAD, emergency surgical consultation and evaluation and immediate surgical intervention is recommended.	I	B
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.	I	B
Recommendations for aortic repair strategies in type A acute aortic dissection		
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.	I	B
Recommendations for the management of malperfusion in the setting of acute aortic dissection		
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.	I	B
Recommendations for the management of patients presenting with acute type B aortic dissection		
Medical therapy including pain relief and blood pressure control is recommended in all patients with acute TBAD.	I	B
In patients with complicated acute TBAD, emergency intervention is recommended.	I	B
In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.	I	B
Recommendations for the management of patients presenting with chronic type B aortic dissection		
Antihypertensive therapy is recommended in all patients with chronic TBAD.	I	B
In chronic TBAD with acute symptoms of malperfusion, rupture, or progression of disease, emergency intervention is recommended.	I	C
In patients with chronic TBAD and a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.	I	B
Recommendations for the management of intramural haematoma		
In patients with IMH, medical therapy including pain relief and blood pressure control is recommended.	I	C
In type A IMH, urgent surgery is recommended.	I	C
In type B IMH, initial medical therapy under careful surveillance is recommended.	I	C
In uncomplicated type B IMH, repetitive imaging (CCT or CMR) is indicated.	I	C
In complicated type B IMH, TEVAR is recommended.	I	C
Recommendations for the management of penetrating atherosclerotic ulcer		
In all patients with PAU, medical therapy including pain relief and blood pressure control is recommended.	I	C
In cases of type A PAU, surgery is recommended.	I	C
In cases of type B PAU, initial medical therapy under careful surveillance is recommended.	I	C
In uncomplicated type B PAU, repetitive imaging (CMR, CCT, or TOE) is recommended.	I	C
In complicated type B PAU, endovascular treatment (TEVAR) is recommended.	I	C
Recommendations for traumatic aortic injury		
In cases of severe aortic injury (grade 4), immediate repair is recommended.	I	A
In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.	I	A
In all TAI patients, medical therapy including pain relief, and blood pressure and heart rate control, is recommended.	I	C
In cases of TAI suspicion, CCT is recommended.	I	C
In cases of moderate aortic injury (grade 3), repair is recommended.	I	C
Recommendations for follow-up after treatment of acute aortic syndrome		
After TEVAR for AAS, follow-up imaging is recommended at 1, 6, and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
In medically treated type B AAD or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.	I	C

Continued

Recommendations for the management of patients with heritable thoracic aortic disease		
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.	I	C
Recommendations for genetic testing and aortic screening in aortic disease		
In patients with aortic root/ascending aneurysms or thoracic aortic dissection, gathering family history information for at least three generations about TAD, unexplained sudden deaths, and peripheral and intracranial aneurysms is recommended.	I	B
In patients with aortic root/ascending aortic aneurysms or thoracic aortic dissection and risk factors for HTAD, genetic counselling at an expert centre and subsequent testing, if indicated, is recommended.	I	B
In patients with HTAD who have a pathogenic/likely pathogenic variant, genetic testing of at-risk biological relatives (i.e. cascade testing) is recommended, irrespective of age.	I	C
In patients with TAD with risk factors for HTAD, with a negative family history of TAD and in whom no (likely) pathogenic variant is identified, TTE screening aortic imaging of FDRs is recommended.	I	B
Recommendations for imaging in women with Turner syndrome		
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.	I	C
Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome		
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.	I	C
Recommendations for vascular imaging in Marfan syndrome		
In patients with MFS, TTE is recommended: • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aorta imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.	I	C
In patients with MFS who have undergone aortic root replacement, surveillance imaging of the thoracic aorta by CMR (or CCT) is recommended at least every 3 years.	I	C
Recommendations for medical treatment in Marfan syndrome		
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.	I	A
Recommendations for aortic surgery in Marfan syndrome		
Surgery is indicated in patients with MFS who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.	I	B
Surgery to replace the aortic root and ascending aorta, using the valve-sparing surgery technique, is recommended in patients with MFS or related HTAD with aortic root dilatation when anatomical features of the valve allow its preservation and the surgeon has specific expertise.	I	B
Recommendations for pregnancy in women with Marfan syndrome		
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team	I	C
It is recommended that couples in which a partner has or is at risk of HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.	I	C
Intake of BBs during pregnancy is recommended.	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.	I	C
ARBs are not recommended during pregnancy.	III	B
Recommendations for physical exercise in patients with Marfan syndrome		
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C

Continued

Recommendations for imaging follow-up in Loeys–Dietz syndrome		
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth, is recommended.	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.	I	C
Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease		
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate aortic root/ascending aorta enlargement is recommended.	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.	I	C
Recommendations for bicuspid aortic valve-associated aortopathy management		
When a BAV is first diagnosed, initial TTE to assess diameters of the aorta at several levels is recommended.	I	B
Surgery for bicuspid aortopathy is recommended when the maximum aortic diameter is ≥55 mm.	I	B
Surgery for bicuspid aortopathy of the root phenotype is recommended when the maximum aortic diameter is ≥50 mm.	I	B
CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.	I	C
Screening by TTE in FDRs of BAV patients with root phenotype aortopathy and/or isolated aortic regurgitation is recommended.	I	C
Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.	I	C
Recommendations for evaluation and medical treatment of patients with coarctation of the aorta		
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).	I	B
Coarctation or re-coarctation repair (either surgical or endovascular) is indicated in patients with hypertension with an increased non-invasive gradient between the upper and lower limbs (decreased ABI) confirmed with invasive measurement (peak-to-peak >20 mmHg), with a preference for stenting when technically feasible.	I	C
In patients with coarctation, BP measurements at both arms and one lower extremity are recommended.	I	C
It is recommended to treat hypertension in patients with coarctation according to ESC hypertension guidelines.	I	C
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases		
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
In patients with PAD and newly diagnosed AF with a CHA_2DS_2-VASc score ≥2, full oral anticoagulation is recommended.	I	C
Screening for ilio-femoral PAD is recommended in patients undergoing TAVI.	I	B

AAA, abdominal aortic aneurysm; AAS, acute aortic syndrome; ABI, ankle–brachial index; ACEI, angiotensin-converting enzyme inhibitor; AD, aortic dissection; ADD-RS, aortic dissection detection-risk score; AF, atrial fibrillation; AHI, aortic height index; ALI, acute limb ischaemia; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; ASI, aortic size index; BAV, bicuspid aortic valve; BB, beta-blocker; BP, blood pressure; b.p.m., beats per minute; CCT, cardiovascular computed tomography; CEA, carotid endarterectomy; CEUS, contrast-enhanced ultrasound; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female); CLTI, chronic limb-threatening ischaemia; CMR, cardiovascular magnetic resonance; CS, carotid artery stenosis; CTA, computed tomography angiography; CV, cardiovascular; CVRF, cardiovascular risk factor; DAPT, dual antiplatelet therapy; DTA, descending thoracic aorta; DUS, duplex ultrasound; ECG, electrocardiogram; ECST, European Carotid Surgery Trial; ESC, European Society of Cardiology; FDR, first-degree relative; FL, false lumen; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; i.v., intravenous; LDL-C, low-density lipoprotein cholesterol; LSA, left subclavian artery; MACE, major adverse cardiac event; MAP, mean arterial pressure; MFS, Marfan syndrome; MHV, mechanical heart valve; MI, myocardial infarction; MRA, magnetic resonance angiography; NASCET, North American Symptomatic Carotid Endarterectomy Trial; o.d., once daily; OMT, optimal medical treatment; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; PCSK9, proprotein convertase subtilisin/kexin type 9; PVD, polyvascular disease; RAS, renal artery stenosis; QoL, quality of life; SAPT, single antiplatelet therapy; SBP, systolic blood pressure; SCI, spinal cord ischaemia; SET, supervised exercise training; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SMA, superior mesenteric artery; T2DM, type 2 diabetes mellitus; TAA, thoracic aortic aneurysm; TAAA, thoracoabdominal aortic aneurysm; TAAD, type A aortic dissection; TAD, thoracic aortic disease; TAI, traumatic aortic injury; TAVI, transcatheter aortic valve implantation; TBAD, type B aortic dissection; TBI, toe–brachial index; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TP, toe pressure; TS, Turner syndrome; TTE, transthoracic echocardiography; vEDS, vascular Ehlers–Danlos syndrome; VKA, vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

16. Evidence tables

Evidence tables are available on the *European Heart Journal* website.

17. Data availability statement

No new data were generated or analysed in support of this research.

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19. Appendix

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20. References

1. van Kuijk JP, Flu WJ, Welten GM, Hoeks SE, Chonchol M, Vidakovic R, *et al.* Long-term prognosis of patients with peripheral arterial disease with or without polyvascular atherosclerotic disease. *Eur Heart J* 2010;**31**:992–9. https://doi.org/10.1093/eurheartj/ehp553
2. Dolmaci OB, El Mathari S, Driessen AHG, Klautz RJM, Poelmann RE, Lindeman JHN, *et al.* Are thoracic aortic aneurysm patients at increased risk for cardiovascular diseases? *J Clin Med* 2023;**12**:272. https://doi.org/10.3390/jcm12010272
3. Tully L, Gianos E, Vani A, Guo Y, Balakrishnan R, Schwartzbard A, *et al.* Suboptimal risk factor control in patients undergoing elective coronary or peripheral percutaneous intervention. *Am Heart J* 2014;**168**:310–6.e3. https://doi.org/10.1016/j.ahj.2014.05.011
4. Saratzis A, Jaspers NEM, Gwilym B, Thomas O, Tsui A, Lefroy R, *et al.* Observational study of the medical management of patients with peripheral artery disease. *Br J Surg* 2019;**106**:1168–77. https://doi.org/10.1002/bjs.11214
5. McDermott MM, Mandapat AL, Moates A, Albay M, Chiou E, Celic L, *et al.* Knowledge and attitudes regarding cardiovascular disease risk and prevention in patients with coronary or peripheral arterial disease. *Arch Intern Med* 2003;**163**:2157–62. https://doi.org/10.1001/archinte.163.18.2157
6. Grayson PC, Ponte C, Suppiah R, Robson JC, Gribbons KB, Judge A, *et al.* 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. *Ann Rheum Dis* 2022;**81**:1654–60. https://doi.org/10.1136/ard-2022-223482
7. Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, *et al.* 2018 update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis* 2020;**79**:19–30. https://doi.org/10.1136/annrheumdis-2019-215672
8. Ponte C, Grayson PC, Robson JC, Suppiah R, Gribbons KB, Judge A, *et al.* 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis. *Ann Rheum Dis* 2022;**81**:1647–53. https://doi.org/10.1136/ard-2022-223480
9. Stone JR, Bruneval P, Angelini A, Bartoloni G, Basso C, Batoroeva L, *et al.* Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology: I. Inflammatory diseases. *Cardiovasc Pathol* 2015;**24**:267–78. https://doi.org/10.1016/j.carpath.2015.05.001
10. Diseases GBD, Injuries C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease study 2019. *Lancet* 2020;**396**:1204–22. https://doi.org/10.1016/S0140-6736(20)30925-9
11. Lin J, Chen Y, Jiang N, Li Z, Xu S. Burden of peripheral artery disease and its attributable risk factors in 204 countries and territories from 1990 to 2019. *Front Cardiovasc Med* 2022;**9**:868370. https://doi.org/10.3389/fcvm.2022.868370
12. GBD 2019 Peripheral Artery Disease Collaborators. Global burden of peripheral artery disease and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease study 2019. *Lancet Glob Health* 2023;**11**:e1553–65. https://doi.org/10.1016/S2214-109X(23)00355-8
13. Liu W, Yang C, Chen, Lei F, Qin J-J, Liu H, *et al.* Global death burden and attributable risk factors of peripheral artery disease by age, sex, SDI regions, and countries from 1990 to 2030: results from the Global Burden of Disease study 2019. *Atherosclerosis* 2022;**347**:17–27. https://doi.org/10.1016/j.atherosclerosis.2022.03.002
14. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al.* Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol* 2020;**76**:2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010
15. Pu L, Wang L, Zhang R, Zhao T, Jiang Y, Han L. Projected global trends in ischemic stroke incidence, deaths and disability-adjusted life years from 2020 to 2030. *Stroke* 2023;**54**:1330–9. https://doi.org/10.1161/STROKEAHA.122.040073
16. Summers KL, Kerut EK, Sheahan CM, Sheahan MG, III. Evaluating the prevalence of abdominal aortic aneurysms in the United States through a national screening database. *J Vasc Surg* 2021;**73**:61–8. https://doi.org10.1016/j.jvs.2020.03.046
17. Behrendt CA, Thomalla G, Rimmele DL, Petersen EL, Twerenbold R, Debus ES, *et al.* Editor's choice—prevalence of peripheral arterial disease, abdominal aortic aneurysm, and risk factors in the Hamburg city health study: a cross sectional analysis. *Eur J Vasc Endovasc Surg* 2023;**65**:590–8. https://doi.org/10.1016/j.ejvs.2023.01.002
18. Rossello X, Dorresteijn JA, Janssen A, Lambrinou E, Scherrenberg M, Bonnefoy-Cudraz E, *et al.* Risk prediction tools in cardiovascular disease prevention: a report from the ESC Prevention of CVD programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP). *Eur Heart J Acute Cardiovasc Care* 2020;**9**:522–32. https://doi.org/10.1177/2048872619858285
19. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, *et al.* 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;**42**:3227–337. https://doi.org/10.1093/eurheartj/ehab484
20. Aday AW, Matsushita K. Epidemiology of peripheral artery disease and polyvascular disease. *Circ Res* 2021;**128**:1818–32. https://doi.org/10.1161/CIRCRESAHA.121.318535
21. Pabon M, Cheng S, Altin SE, Sethi SS, Nelson MD, Moreau KL, *et al.* Sex differences in peripheral artery disease. *Circ Res* 2022;**130**:496–511. https://doi.org/10.1161/CIRCRESAHA.121.320702
22. Khawaja T, Janus SE, Tashtish N, Janko M, Baeza C, Gilkeson R, *et al.* Prevalence of thoracic aortic aneurysm in patients referred for no/low-charge coronary artery calcium scoring: insights from the CLARIFY registry. *Am J Prev Cardiol* 2022;**12**:100378. https://doi.org/10.1016/j.ajpc.2022.100378
23. Obel LM, Diederichsen AC, Steffensen FH, Frost L, Lambrechtsen J, Busk M, *et al.* Population-based risk factors for ascending, arch, descending, and abdominal aortic dilations for 60-74-year-old individuals. *J Am Coll Cardiol* 2021;**78**:201–11. https://doi.org/10.1016/j.jacc.2021.04.094
24. Bossone E, Eagle KA. Epidemiology and management of aortic disease: aortic aneurysms and acute aortic syndromes. *Nat Rev Cardiol* 2021;**18**:331–48. https://doi.org/10.1038/s41569-020-00472-6
25. Verhagen JMA, Kempers M, Cozijnsen L, Bouma BJ, Duijnhouwer AL, Post JG, *et al.* Expert consensus recommendations on the cardiogenetic care for patients with thoracic aortic disease and their first-degree relatives. *Int J Cardiol* 2018;**258**:243–8. https://doi.org/10.1016/j.ijcard.2018.01.145
26. Burger PM, Pradhan AD, Dorresteijn JAN, Koudstaal S, Teraa M, de Borst GJ, *et al.* C-reactive protein and risk of cardiovascular events and mortality in patients with various cardiovascular disease locations. *Am J Cardiol* 2023;**197**:13–23. https://doi.org/10.1016/j.amjcard.2023.03.025
27. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, *et al.* Colchicine in patients with chronic coronary disease. *N Engl J Med* 2020;**383**:1838–47. https://doi.org/10.1056/NEJMoa2021372
28. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, *et al.* Efficacy and safety of low-dose colchicine after myocardial infarction. *N Engl J Med* 2019;**381**:2497–505. https://doi.org/10.1056/NEJMoa1912388
29. Parkkila K, Kiviniemi A, Tulppo M, Perkiömäki J, Kesäniemi YA, Ukkola O. Carotid and femoral bruits as cardiovascular risk indicators in a middle-aged Finnish population: a 20-year prospective study. *PLoS One* 2022;**17**:e0278901. https://doi.org/10.1371/journal.pone.0278901
30. Pickett CA, Jackson JL, Hemann BA, Atwood JE. Carotid bruits as a prognostic indicator of cardiovascular death and myocardial infarction: a meta-analysis. *Lancet* 2008;**371**:1587–94. https://doi.org/10.1016/s0140-6736(08)60691-1
31. Charry D, Gouskova N, Meyer ML, Ring K, Nambi V, Heiss G, *et al.* Arterial stiffness and contralateral differences in blood pressure: the Atherosclerosis Risk in Communities (ARIC) study. *J Clin Hypertens (Greenwich)* 2022;**24**:878–84. https://doi.org/10.1111/jch.14493
32. Aboyans V, Criqui MH, McDermott MM, Allison MA, Denenberg JO, Shadman R, *et al.* The vital prognosis of subclavian stenosis. *J Am Coll Cardiol* 2007;**49**:1540–5. https://doi.org/10.1016/j.jacc.2006.09.055
33. Marcovina SM, Shapiro MD. Measurement of lipoprotein(a): a once in a lifetime opportunity. *J Am Coll Cardiol* 2022;**79**:629–31. https://doi.org/10.1016/j.jacc.2021.11.053
34. Arndt H, Nordanstig J, Bertges DJ, Budtz-Lilly J, Venermo M, Espada CL, *et al.* A Delphi consensus on patient reported outcomes for registries and trials including patients with intermittent claudication: recommendations and reporting standard. *Eur J Vasc Endovasc Surg* 2022;**64**:526–33. https://doi.org/10.1016/j.ejvs.2022.08.011
35. Rymer JA, Narcisse D, Cosiano M, Tanaka J, McDermott MM, Treat-Jacobson DJ, *et al.* Patient-reported outcome measures in symptomatic, non-limb-threatening peripheral artery disease: a state-of-the-art review. *Circ Cardiovasc Interv* 2022;**15**:e011320. https://doi.org/10.1161/circinterventions.121.011320
36. Raja A, Spertus J, Yeh RW, Secemsky EA. Assessing health-related quality of life among patients with peripheral artery disease: a review of the literature and focus on patient-reported outcome measures. *Vasc Med* 2021;**26**:317–25. https://doi.org/10.1177/1358863x20977016
37. Treat-Jacobson D, McDermott MM, Bronas UG, Campia U, Collins TC, Criqui MH, *et al.* Optimal exercise programs for patients with peripheral artery disease: a scientific statement from the American Heart Association. *Circulation* 2019;**139**:e10–33. https://doi.org/10.1161/cir.0000000000000623
38. Poku E, Duncan R, Keetharuth A, Essat M, Phillips P, Woods HB, *et al.* Patient-reported outcome measures in patients with peripheral arterial disease: a systematic review of

psychometric properties. *Health Qual Life Outcomes* 2016;**14**:161. https://doi.org/10.1186/s12955-016-0563-y
39. Mays RJ, Casserly IP, Kohrt WM, Ho PM, Hiatt WR, Nehler MR, *et al.* Assessment of functional status and quality of life in claudication. *J Vasc Surg* 2011;**53**:1410–21. https://doi.org/10.1016/j.jvs.2010.11.092
40. Regensteiner JG, Hiatt WR, Coll JR, Criqui MH, Treat-Jacobson D, McDermott MM, *et al.* The impact of peripheral arterial disease on health-related quality of life in the peripheral arterial disease awareness, risk, and treatment: new resources for survival (PARTNERS) program. *Vasc Med* 2008;**13**:15–24. https://doi.org/10.1177/1358863x07084911
41. Harwood AE, King S, Totty J, Smith GE, Vanicek N, Chetter IC. A systematic review of muscle morphology and function in intermittent claudication. *J Vasc Surg* 2017;**66**:1241–57. https://doi.org/10.1016/j.jvs.2017.05.106
42. Schieber MN, Hasenkamp RM, Pipinos II, Johanning JM, Stergiou N, DeSpiegelaere HK, *et al.* Muscle strength and control characteristics are altered by peripheral artery disease. *J Vasc Surg* 2017;**66**:178–86.e12. https://doi.org/10.1016/j.jvs.2017.01.051
43. Gohil RA, Mockford KA, Mazari F, Khan J, Vanicek N, Chetter IC, *et al.* Balance impairment, physical ability, and its link with disease severity in patients with intermittent claudication. *Ann Vasc Surg* 2013;**27**:68–74. https://doi.org/10.1016/j.avsg.2012.05.005
44. Mockford KA, Mazari FA, Jordan AR, Vanicek N, Chetter IC, Coughlin PA. Computerized dynamic posturography in the objective assessment of balance in patients with intermittent claudication. *Ann Vasc Surg* 2011;**25**:182–90. https://doi.org/10.1016/j.avsg.2010.07.021
45. Gardner AW, Montgomery PS. Impaired balance and higher prevalence of falls in subjects with intermittent claudication. *J Gerontol A Biol Sci Med Sci* 2001;**56**:M454–8. https://doi.org/10.1093/gerona/56.7.m454
46. McDermott MM, Ferrucci L, Liu K, Guralnik JM, Tian Lu, Liao Y, *et al.* Leg symptom categories and rates of mobility decline in peripheral arterial disease. *J Am Geriatr Soc* 2010;**58**:1256–62. https://doi.org/10.1111/j.1532-5415.2010.02941.x
47. McDermott MM, Liu K, Greenland P, Guralnik JM, Criqui MH, Chan C, *et al.* Functional decline in peripheral arterial disease: associations with the ankle brachial index and leg symptoms. *JAMA* 2004;**292**:453–61. https://doi.org/10.1001/jama.292.4.453
48. McDermott MM, Greenland P, Guralnik JM, Guralnik JM, Criqui MH, Chan C, *et al.* Depressive symptoms and lower extremity functioning in men and women with peripheral arterial disease. *J Gen Intern Med* 2003;**18**:461–7. https://doi.org/10.1046/j.1525-1497.2003.20527.x
49. Ramirez JL, Drudi LM, Grenon SM. Review of biologic and behavioral risk factors linking depression and peripheral artery disease. *Vasc Med* 2018;**23**:478–88. https://doi.org/10.1177/1358863X18773161
50. Golledge J, Leicht AS, Yip L, Rowbotham SE, Pinchbeck J, Jenkins JS, *et al.* Relationship between disease specific quality of life measures, physical performance, and activity in people with intermittent claudication caused by peripheral artery disease. *Eur J Vasc Endovasc Surg* 2020;**59**:957–64. https://doi.org/10.1016/j.ejvs.2020.02.006
51. Gardner AW, Montgomery PS, Wang M, Xu C. Predictors of health-related quality of life in patients with symptomatic peripheral artery disease. *J Vasc Surg* 2018;**68**:1126–34. https://doi.org/10.1016/j.jvs.2017.12.074
52. McDermott MM, Tian L, Liu K, Guralnik JM, Ferrucci L, Tan J, *et al.* Prognostic value of functional performance for mortality in patients with peripheral artery disease. *J Am Coll Cardiol* 2008;**51**:1482–9. https://doi.org/10.1016/j.jacc.2007.12.034
53. McDermott MM, Guralnik JM, Tian L, Ferrucci L, Liu K, Liao Y, *et al.* Baseline functional performance predicts the rate of mobility loss in persons with peripheral arterial disease. *J Am Coll Cardiol* 2007;**50**:974–82. https://doi.org/10.1016/j.jacc.2007.05.030
54. Sprengers RW, Teraa M, Moll FL, de Wit GA, van der Graaf Y, Verhaar MC. Quality of life in patients with no-option critical limb ischemia underlines the need for new effective treatment. *J Vasc Surg* 2010;**52**:843–9.e1. https://doi.org/10.1016/j.jvs.2010.04.057
55. Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ* 1962;**27**:645–58 .
56. Leng GC, Fowkes FG. The Edinburgh claudication questionnaire: an improved version of the WHO/Rose questionnaire for use in epidemiological surveys. *J Clin Epidemiol* 1992;**45**:1101–9. https://doi.org/10.1016/0895-4356(92)90150-l
57. Birkett ST, Harwood AE, Caldow E, Ibeggazene S, Ingle L, Pymer S. A systematic review of exercise testing in patients with intermittent claudication: a focus on test standardisation and reporting quality in randomised controlled trials of exercise interventions. *PLoS One* 2021;**16**:e0249277. https://doi.org/10.1371/journal.pone.0249277
58. Harwood AE, Pymer S, Ingle L, Doherty P, Chetter IC, Parmenter B. Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners. *BMJ Open Sport Exerc Med* 2020;**6**:e000897. https://doi.org/10.1136/bmjsem-2020-000897
59. Treat-Jacobson D, McDermott MM, Beckman JA, Burt MA, Creager MA, Ehrman JK, *et al.* Implementation of supervised exercise therapy for patients with symptomatic peripheral artery disease: a science advisory from the American Heart Association. *Circulation* 2019;**140**:e700–10. https://doi.org/10.1161/cir.0000000000000727
60. Hiatt WR, Rogers RK, Brass EP. The treadmill is a better functional test than the 6-minute walk test in therapeutic trials of patients with peripheral artery disease. *Circulation* 2014;**130**:69–78. https://doi.org/10.1161/circulationaha.113.007003
61. Nicolaï SP, Viechtbauer W, Kruidenier LM, Candel MJJM, Prins MH, Teijink JAW. Reliability of treadmill testing in peripheral arterial disease: a meta-regression analysis. *J Vasc Surg* 2009;**50**:322–9. https://doi.org/10.1016/j.jvs.2009.01.042
62. Mazzolai L, Belch J, Venermo M, Aboyans V, Brodmann M, Bura-Rivière A, *et al.* Exercise therapy for chronic symptomatic peripheral artery disease. *Eur Heart J* 2024;**45**:1303–21. https://doi.org/10.1093/eurheartj/ehad734
63. McDermott MM, Guralnik JM, Criqui MH, Liu K, Kibbe MR, Ferrucci L. Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. *Circulation* 2014;**130**:61–8. https://doi.org/10.1161/circulationaha.114.007002
64. McDermott MM, Ades PA, Dyer A, Guralnik JM, Kibbe M, Criqui MH. Corridor-based functional performance measures correlate better with physical activity during daily life than treadmill measures in persons with peripheral arterial disease. *J Vasc Surg* 2008;**48**:1231–7.e1. https://doi.org/10.1016/j.jvs.2008.06.050
65. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;**166**:111–7. https://doi.org/10.1164/ajrccm.166.1.at1102
66. Verdijk LB, van Loon L, Meijer K, Savelberg HH. One-repetition maximum strength test represents a valid means to assess leg strength in vivo in humans. *J Sports Sci* 2009;**27**:59–68. https://doi.org/10.1080/02640410802428089
67. Ritti-Dias RM, Basyches M, Câmara L, Puech-Leao P, Battistella L, Wolosker N. Test-retest reliability of isokinetic strength and endurance tests in patients with intermittent claudication. *Vasc Med* 2010;**15**:275–8. https://doi.org/10.1177/1358863x10371415
68. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, *et al.* A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;**49**:M85–94. https://doi.org/10.1093/geronj/49.2.m85
69. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 1995;**332**:556–62. https://doi.org/10.1056/nejm199503023320902
70. Isselbacher EM, Preventza O, Hamilton Black J III, Augoustides JG, Beck AW, Bolen MA, *et al.* 2022 ACC/AHA Guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on clinical practice guidelines. *J Am Coll Cardiol* 2022;**80**:e223–393. https://doi.org/10.1016/j.jacc.2022.08.004
71. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, *et al.* 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* 2021;**42**:17–96. https://doi.org/10.1093/eurheartj/ehaa605
72. de Heer F, Gökalp AL, Kluin J, Takkenberg JJM. Measuring what matters to the patient: health related quality of life after aortic valve and thoracic aortic surgery. *Gen Thorac Cardiovasc Surg* 2019;**67**:37–43. https://doi.org/10.1007/s11748-017-0830-9
73. Chaddha A, Kline-Rogers E, Braverman AC, Erickson SR, Jackson EA, Franklin BA, *et al.* Survivors of aortic dissection: activity, mental health, and sexual function. *Clin Cardiol* 2015;**38**:652–9. https://doi.org/10.1002/clc.22418
74. Andonian C, Freilinger S, Achenbach S, Ewert P, Gundlach U, Kaemmerer H, *et al.* Quality of life in patients with Marfan syndrome: a cross-sectional study of 102 adult patients. *Cardiovasc Diagn Ther* 2021;**11**:602–10. https://doi.org/10.21037/cdt-20-692
75. Vanem TT, Rand-Hendriksen S, Brunborg C, Geiran OR, Røe C. Health-related quality of life in Marfan syndrome: a 10-year follow-up. *Health Qual Life Outcomes* 2020;**18**:376. https://doi.org/10.1186/s12955-020-01633-4
76. Cervin A, Wanhainen A, Björck M. Popliteal aneurysms are common among men with screening detected abdominal aortic aneurysms, and prevalence correlates with the diameters of the common iliac arteries. *Eur J Vasc Endovasc Surg* 2020;**59**:67–72. https://doi.org/10.1016/j.ejvs.2019.07.042
77. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, *et al.* 2017 ESC Guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO), the task force for the diagnosis and treatment of peripheral arterial diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;**39**:763–816. https://doi.org/10.1093/eurheartj/ehx095
78. Ichihashi S, Desormais I, Hashimoto T, Magne J, Kichikawa K, Aboyans V. Accuracy and reliability of the ankle brachial index measurement using a multicuff oscillometric device versus the Doppler method. *Eur J Vasc Endovasc Surg* 2020;**60**:462–8. https://doi.org/10.1016/j.ejvs.2020.06.013
79. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, *et al.* Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation* 2012;**126**:2890–909. https://doi.org/10.1161/CIR.0b013e318276fbcb
80. Høyer C, Strandberg J, Overvad Jordansen MK, Zacho HD. The ability of the toe-brachial index to predict the outcome of treadmill exercise testing in patients with a normal resting ankle-brachial index. *Ann Vasc Surg* 2020;**64**:263–9. https://doi.org/10.1016/j.avsg.2019.10.041

81. Godet R, Bruneau A, Vielle B, Vincent F, Le Tourneau T, Carre F, *et al.* Post-exercise ankle blood pressure and ankle to brachial index after heavy load bicycle exercise. *Scand J Med Sci Sports* 2018;**28**:2144–52. https://doi.org/10.1111/sms.13234
82. van Langen H, van Gurp J, Rubbens L. Interobserver variability of ankle-brachial index measurements at rest and post exercise in patients with intermittent claudication. *Vasc Med* 2009;**14**:221–6. https://doi.org/10.1177/1358863x08101017
83. Stein R, Hriljac I, Halperin JL, Gustavson SM, Teodorescu V, Olin JW, Limitation of the resting ankle-brachial index in symptomatic patients with peripheral arterial disease. *Vasc Med* 2006;**11**:29–33. https://doi.org/10.1191/1358863x06vm663oa
84. Abraham P, Desvaux B, Saumet JL. Ankle-brachial index after maximum exercise in treadmill and cycle ergometers in athletes. *Clin Physiol* 1998;**18**:321–6. https://doi.org/10.1046/j.1365-2281.1998.00100.x
85. Stoffers HE, Kester AD, Kaiser V, Rinkens PELM, Kitslaar PJEHM, Knottnerus JA, The diagnostic value of the measurement of the ankle-brachial systolic pressure index in primary health care. *J Clin Epidemiol* 1996;**49**:1401–5. https://doi.org/10.1016/s0895-4356(96)00275-2
86. Ouriel K, McDonnell AE, Metz CE, Zarins CK. Critical evaluation of stress testing in the diagnosis of peripheral vascular disease. *Surgery* 1982;**91**:686–93 .
87. Laing S, Greenhalgh RM. The detection and progression of asymptomatic peripheral arterial disease. *Br J Surg* 2005;**70**:628–30. https://doi.org/10.1002/bjs.1800701017
88. Ankle Brachial Index Collaboration; Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, *et al.* Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality: a meta-analysis. *JAMA* 2008;**300**:197–208. https://doi.org/10.1001/jama.300.2.197
89. Criqui MH, McClelland RL, McDermott MM, McDermott MM, Allison MA, Blumenthal RS, *et al.* The ankle-brachial index and incident cardiovascular events in the MESA (multi-ethnic study of atherosclerosis). *J Am Coll Cardiol* 2010;**56**:1506–12. https://doi.org/10.1016/j.jacc.2010.04.060
90. Herraiz-Adillo Á, Cavero-Redondo I, Álvarez-Bueno C, Pozuelo-Carrascosa DP, Solera-Martínez M. The accuracy of toe brachial index and ankle brachial index in the diagnosis of lower limb peripheral arterial disease: a systematic review and meta-analysis. *Atherosclerosis* 2020;**315**:81–92. https://doi.org/10.1016/j.atherosclerosis.2020.09.026
91. Tehan PE, Santos D, Chuter VH. A systematic review of the sensitivity and specificity of the toe-brachial index for detecting peripheral artery disease. *Vasc Med* 2016;**21**:382–9. https://doi.org/10.1177/1358863x16645854
92. Fukui M, Tanaka M, Hamaguchi M, Senmaru T, Sakabe K, Asano M, *et al.* Toe-brachial index is associated more strongly with albuminuria or glomerular filtration rate than ankle-brachial index in patients with type 2 diabetes. *Hypertens Res* 2012;**35**:745–9. https://doi.org/10.1038/hr.2012.16
93. Dachun X, Jue L, Liling Z, Xu Y, Hu D, Pagoto SL, *et al.* Sensitivity and specificity of the ankle—brachial index to diagnose peripheral artery disease: a structured review. *Vasc Med* 2010;**15**:361–9. https://doi.org/10.1177/1358863x10378376
94. Morimoto S, Nakajima F, Yurugi T, Morita T, Jo F, Nishikawa M, *et al.* Risk factors of normal ankle-brachial index and low toe-brachial index in hemodialysis patients. *Ther Apher Dial* 2009;**13**:103–7. https://doi.org/10.1111/j.1744-9987.2009.00663.x
95. Young MJ, Adams JE, Anderson GF, Boulton AJ, Cavanagh PR. Medial arterial calcification in the feet of diabetic patients and matched non-diabetic control subjects. *Diabetologia* 1993;**36**:615–21. https://doi.org/10.1007/bf00404070
96. Carter SA, Lezack JD. Digital systolic pressures in the lower limb in arterial disease. *Circulation* 1971;**43**:905–14. https://doi.org/10.1161/01.cir.43.6.905
97. Watanabe Y, Masaki H, Kojima K, Tanemoto K. Toe-brachial index in the second toe: substitutability to toe-brachial index in the great toe and ankle-brachial index. *Ann Vasc Dis* 2016;**9**:300–6. https://doi.org/10.3400/avd.oa.16-00078
98. Pérez-Martin A, Meyer G, Demattei C, Böge G, Laroche J-P, Quéré I, *et al.* Validation of a fully automatic photoplethysmographic device for toe blood pressure measurement. *Eur J Vasc Endovasc Surg* 2010;**40**:515–20. https://doi.org/10.1016/j.ejvs.2010.06.008
99. Hoyer C, Sandermann J, Petersen LJ. The toe-brachial index in the diagnosis of peripheral arterial disease. *J Vasc Surg* 2013;**58**:231–8. https://doi.org/10.1016/j.jvs.2013.03.044
100. Monti M, Calanca L, Alatri A, Mazzolai L. Accuracy of in-patients ankle-brachial index measurement by medical students. *Vasa* 2016;**45**:43–8. https://doi.org/10.1024/0301-1526/a000494
101. Kaiser V, Kester AD, Stoffers HE, Kitslaar PJ, Knottnerus JA. The influence of experience on the reproducibility of the ankle-brachial systolic pressure ratio in peripheral arterial occlusive disease. *Eur J Vasc Endovasc Surg* 1999;**18**:25–9. https://doi.org/10.1053/ejvs.1999.0843
102. Ray SA, Srodon PD, Taylor RS, Dormandy JA. Reliability of ankle:brachial pressure index measurement by junior doctors. *Br J Surg* 1994;**81**:188–90. https://doi.org/10.1002/bjs.1800810208
103. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, *et al.* 2016 AHA/ACC Guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation* 2017;**135**:e726–79. https://doi.org/10.1161/CIR.0000000000000471
104. Stivalet O, Paisant A, Belabbas D, Omarjee L, Le Faucheur A, Landreau P, *et al.* Exercise testing criteria to diagnose lower extremity peripheral artery disease assessed by computed-tomography angiography. *PLoS One* 2019;**14**:e0219082. https://doi.org/10.1371/journal.pone.0219082
105. Abraham P, Picquet J, Vielle B, Sigaudo-Roussel D, Paisant-Thouveny F, Enon B, *et al.* Transcutaneous oxygen pressure measurements on the buttocks during exercise to detect proximal arterial ischemia: comparison with arteriography. *Circulation* 2003;**107**:1896–900. https://doi.org/10.1161/01.Cir.0000060500.60646.E0
106. Yamamoto K, Miyata T, Onozuka A, Koyama H, Ohtsu H, Nagawa H. Plantar flexion as an alternative to treadmill exercise for evaluating patients with intermittent claudication. *Eur J Vasc Endovasc Surg* 2007;**33**:325–9. https://doi.org/10.1016/j.ejvs.2006.10.012
107. Maufus M, Sevestre-Pietri MA, Sessa C, Pignon B, Egelhofer H, Dupas S, *et al.* Critical limb ischaemia and the response to bone marrow-derived cell therapy according to tcPO(2) measurement. *Vasa* 2017;**46**:23–8. https://doi.org/10.1024/0301-1526/a000590
108. Leenstra B, Wijnand J, Verhoeven B, Koning O, Teraa M, Verhaar MC, *et al.* Applicability of transcutaneous oxygen tension measurement in the assessment of chronic limb-threatening ischemia. *Angiology* 2020;**71**:208–16. https://doi.org/10.1177/0003319719866958
109. Ott A. Inflammation and transcutaneous measurement of oxygen pressure in dermatology. *Adv Exp Med Biol* 1987;**220**:79–82. https://doi.org/10.1007/978-1-4613-1927-6_14
110. Woo Y, Suh YJ, Lee H, Jeong E, Park SC, Yun SS, *et al.* TcPO2 value can predict wound healing time in clinical practice of CLTI patients. *Ann Vasc Surg* 2023;**91**:249–56. https://doi.org/10.1016/j.avsg.2022.11.020
111. Wang Z, Hasan R, Firwana B, Elraiyah T, Tsapas A, Prokop L, *et al.* A systematic review and meta-analysis of tests to predict wound healing in diabetic foot. *J Vasc Surg* 2016;**63**:29S–36S.e2. https://doi.org/10.1016/j.jvs.2015.10.004
112. Yamada T, Ohta T, Ishibashi H, Sugimoto I, Iwata H, Takahashi M, *et al.* Clinical reliability and utility of skin perfusion pressure measurement in ischemic limbs—comparison with other noninvasive diagnostic methods. *J Vasc Surg* 2008;**47**:318–23. https://doi.org/10.1016/j.jvs.2007.10.045
113. Noori N, Haruno L, Schroeder I, Vrahas M, Little M, Moon C, *et al.* Preoperative transcutaneous oxygen perfusion measurements in predicting atraumatic wound healing after major lower extremity amputation. *Orthopedics* 2022;**45**:174–80. https://doi.org/10.3928/01477447-20220128-05
114. Nishio H, Minakata K, Kawaguchi A, Kumagai M, Ikeda T, Shimizu A, *et al.* Transcutaneous oxygen pressure as a surrogate index of lower limb amputation. *Int Angiol* 2016;**35**:565–72.
115. Sarin S, Shami S, Shields DA, Scurr JH, Smith PD. Selection of amputation level: a review. *Eur J Vasc Surg* 1991;**5**:611–20. https://doi.org/10.1016/s0950-821x(05)80894-1
116. Abraham P, Ramondou P, Hersant J, Sempore WY, Feuilloy M, Henni S. Investigation of arterial claudication with transcutaneous oxygen pressure at exercise: interests and limits. *Trends Cardiovasc Med* 2021;**31**:218–23. https://doi.org/10.1016/j.tcm.2020.03.003
117. Abraham P, Gu Y, Guo L, Kroeger K, Ouedraogo N, Wennberg P, *et al.* Clinical application of transcutaneous oxygen pressure measurements during exercise. *Atherosclerosis* 2018;**276**:117–23. https://doi.org/10.1016/j.atherosclerosis.2018.07.023
118. Colas-Ribas C, Signolet I, Henni S, Feuillloy M, Gagnadoux F, Abraham P. High prevalence of known and unknown pulmonary diseases in patients with claudication during exercise oximetry: a retrospective analysis. *Medicine (Baltimore)* 2016;**95**:e4888. https://doi.org/10.1097/md.0000000000004888
119. Frank U, Nikol S, Belch J, Boc V, Brodmann M, Carpentier PH, *et al.* ESVM guideline on peripheral arterial disease. *Vasa* 2019;**48**:1–79. https://doi.org/10.1024/0301-1526/a000834
120. Schlager O, Francesconi M, Haumer M, Dick P, Sabeti S, Amighi J, *et al.* Duplex sonography versus angiography for assessment of femoropopliteal arterial disease in a 'real-world' setting. *J Endovasc Ther* 2007;**14**:452–9. https://doi.org/10.1177/152660280701400404
121. Collins R, Burch J, Cranny G, Aguiar-Ibáñez R, Craig D, Wright K, *et al.* Duplex ultrasonography, magnetic resonance angiography, and computed tomography angiography for diagnosis and assessment of symptomatic, lower limb peripheral arterial disease: systematic review. *BMJ* 2007;**334**:1257. https://doi.org/10.1136/bmj.39217.473275.55
122. Sprynger M, Rigo F, Moonen M, Aboyans V, Edvardsen T, de Alcantara ML, *et al.* Focus on echovascular imaging assessment of arterial disease: complement to the ESC Guidelines (PARTIM 1) in collaboration with the working group on aorta and peripheral vascular diseases. *Eur Heart J Cardiovasc Imaging* 2018;**19**:1195–221. https://doi.org/10.1093/ehjci/jey103
123. Collins R, Cranny G, Burch J, Aguiar-Ibáñez R, Craig D, Wright K, *et al.* A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease. *Health Technol Assess* 2007;**11**:iii–iv, xi-xiii, 1–184. https://doi.org/10.3310/hta11200

124. Rodway AD, Cheal D, Allan C, Pazos-Casal F, Hanna L, Field BCT, *et al.* Ankle Doppler for cuffless ankle brachial index estimation and peripheral artery disease diagnosis independent of diabetes. *J Clin Med* 2022;**12**:97. https://doi.org/10.3390/jcm12010097
125. Katsanos K, Tepe G, Tsetis D, Fanelli F. Standards of practice for superficial femoral and popliteal artery angioplasty and stenting. *Cardiovasc Intervent Radiol* 2014;**37**:592–603. https://doi.org/10.1007/s00270-014-0876-3
126. Coffi SB, Ubbink DT, Zwiers I, van Gurp JA, Legemate DA. Improved assessment of the hemodynamic significance of borderline iliac stenoses with use of hyperemic duplex scanning. *J Vasc Surg* 2002;**36**:575–80. https://doi.org/10.1067/mva.2002.126086
127. Elsman BH, Legemate DA, de Vos HJ, Mali WP, Eikelboom BC. Hyperaemic colour duplex scanning for the detection of aortoiliac stenoses. a comparative study with intra-arterial pressure measurement. *Eur J Vasc Endovasc Surg* 1997;**14**:462–7. https://doi.org/10.1016/s1078-5884(97)80125-6
128. Venermo M, Sprynger M, Desormais I, Björck M, Brodmann M, Cohnert T, *et al.* Follow-up of patients after revascularisation for peripheral arterial diseases: a consensus document from the European Society of Cardiology working group on aorta and peripheral vascular diseases and the European Society for Vascular Surgery. *Eur J Prev Cardiol* 2019;**26**:1971–84. https://doi.org/10.1177/2047487319846999
129. Golemati S, Cokkinos DD. Recent advances in vascular ultrasound imaging technology and their clinical implications. *Ultrasonics* 2022;**119**:106599. https://doi.org/10.1016/j.ultras.2021.106599
130. Itoga NK, Minami HR, Chelvakumar M, Pearson K, Mell MM, Bendavid E, *et al.* Cost-effectiveness analysis of asymptomatic peripheral artery disease screening with the ABI test. *Vasc Med* 2018;**23**:97–106. https://doi.org/10.1177/1358863X17745371
131. Xu D, Zou L, Xing Y, Hou L, Wei Y, Zhang J, *et al.* Diagnostic value of ankle-brachial index in peripheral arterial disease: a meta-analysis. *Can J Cardiol* 2013;**29**:492–8. https://doi.org/10.1016/j.cjca.2012.06.014
132. Hashimoto T, Ichihashi S, Iwakoshi S, Kichikawa K. Combination of pulse volume recording (PVR) parameters and ankle-brachial index (ABI) improves diagnostic accuracy for peripheral arterial disease compared with ABI alone. *Hypertens Res* 2016;**39**:430–4. https://doi.org/10.1038/hr.2016.13
133. Tehan PE, Bray A, Chuter VH. Non-invasive vascular assessment in the foot with diabetes: sensitivity and specificity of the ankle brachial index, toe brachial index and continuous wave Doppler for detecting peripheral arterial disease. *J Diabetes Complications* 2016;**30**:155–60. https://doi.org/10.1016/j.jdiacomp.2015.07.019
134. Loukas M, Bilinsky E, Bilinsky S, Blaak C, Tubbs RS, Anderson RH. The anatomy of the aortic root. *Clin Anat* 2014;**27**:748–56. https://doi.org/10.1002/ca.22295
135. Dagenais F. Anatomy of the thoracic aorta and of its branches. *Thorac Surg Clin* 2011;**21**:219–27, viii. https://doi.org/10.1016/j.thorsurg.2010.12.004
136. Lombardi JV, Hughes GC, Appoo JJ, Bavaria JE, Beck AW, Cambria RP, *et al.* Society for Vascular Surgery (SVS) and Society of Thoracic Surgeons (STS) reporting standards for type B aortic dissections. *Ann Thorac Surg* 2020;**109**:959–81. https://doi.org/10.1016/j.athoracsur.2019.10.005
137. Rodríguez-Palomares JF, Teixidó-Tura G, Galuppo V, Cuéllar H, Laynez A, Gutiérrez L, *et al.* Multimodality assessment of ascending aortic diameters: comparison of different measurement methods. *J Am Soc Echocardiogr* 2016;**29**:819–26.e4. https://doi.org/10.1016/j.echo.2016.04.006
138. Saura D, Dulgheru R, Caballero L, Bernard A, Kou S, Gonjilashvili N, *et al.* Two-dimensional transthoracic echocardiographic normal reference ranges for proximal aorta dimensions: results from the EACVI NORRE study. *Eur Heart J Cardiovasc Imaging* 2017;**18**:167–79. https://doi.org/10.1093/ehjci/jew053
139. Bons LR, Duijnhouwer AL, Boccalini S, van den Hoven AT, van der Vlugt MJ, Chelu RG, *et al.* Intermodality variation of aortic dimensions: how, where and when to measure the ascending aorta. *Int J Cardiol* 2019;**276**:230–5. https://doi.org/10.1016/j.ijcard.2018.08.067
140. Amsallem M, Ou P, Milleron O, Henry-Feugeas M-C, Detaint D, Arnoult F, *et al.* Comparative assessment of ascending aortic aneurysms in Marfan patients using ECG-gated computerized tomographic angiography versus trans-thoracic echocardiography. *Int J Cardiol* 2015;**184**:22–7. https://doi.org/10.1016/j.ijcard.2015.01.086
141. Matthews EO, Pinchbeck J, Elmore K, Jones RE, Moxon JV, Golledge J. The reproducibility of measuring maximum abdominal aortic aneurysm diameter from ultrasound images. *Ultrasound J* 2021;**13**:13. https://doi.org/10.1186/s13089-021-00211-z
142. Bonnafy T, Lacroix P, Desormais I, Labrunie A, Marin B, Leclerc A, *et al.* Reliability of the measurement of the abdominal aortic diameter by novice operators using a pocket-sized ultrasound system. *Arch Cardiovasc Dis* 2013;**106**:644–50. https://doi.org/10.1016/j.acvd.2013.08.004
143. Fitzgerald BT, Kwon A, Scalia GM. The new dimension in aortic measurements—use of the inner edge measurement for the thoracic aorta in Australian patients. *Heart Lung Circ* 2015;**24**:1104–10. https://doi.org/10.1016/j.hlc.2015.05.001
144. Burman ED, Keegan J, Kilner PJ. Aortic root measurement by cardiovascular magnetic resonance: specification of planes and lines of measurement and corresponding normal values. *Circ Cardiovasc Imaging* 2008;**1**:104–13. https://doi.org/10.1161/circimaging.108.768911
145. Muraru D, Maffessanti F, Kocabay G, Peluso D, Bianco LD, Piasentini E, *et al.* Ascending aorta diameters measured by echocardiography using both leading edge-to-leading edge and inner edge-to-inner edge conventions in healthy volunteers. *Eur Heart J Cardiovasc Imaging* 2014;**15**:415–22. https://doi.org/10.1093/ehjci/jet173
146. Vis JC, Rodríguez-Palomares JF, Teixidó-Tura G, Galian-Gay L, Granato C, Guala A, *et al.* Implications of asymmetry and valvular morphotype on echocardiographic measurements of the aortic root in bicuspid aortic valve. *J Am Soc Echocardiogr* 2019;**32**:105–12. https://doi.org/10.1016/j.echo.2018.08.004
147. Ghulam Ali S, Fusini L, Dalla Cia A, Tamborini G, Gripari P, Muratori M, *et al.* Technological advancements in echocardiographic assessment of thoracic aortic dilatation: head to head comparison among multidetector computed tomography, 2-dimensional, and 3-dimensional echocardiography measurements. *J Thorac Imaging* 2018;**33**:232–9. https://doi.org/10.1097/rti.0000000000000330
148. Mendoza DD, Kochar M, Devereux RB, Basson CT, Min JK, Holmes K, *et al.* Impact of image analysis methodology on diagnostic and surgical classification of patients with thoracic aortic aneurysms. *Ann Thorac Surg* 2011;**92**:904–12. https://doi.org/10.1016/j.athoracsur.2011.03.130
149. Campens L, Demulier L, De Groote K, Vandekerckhove K, De Wolf D, Roman MJ, *et al.* Reference values for echocardiographic assessment of the diameter of the aortic root and ascending aorta spanning all age categories. *Am J Cardiol* 2014;**114**:914–20. https://doi.org/10.1016/j.amjcard.2014.06.024
150. Pedersen OM, Aslaksen A, Vik-Mo H. Ultrasound measurement of the luminal diameter of the abdominal aorta and iliac arteries in patients without vascular disease. *J Vasc Surg* 1993;**17**:596–601. https://doi.org/10.1067/mva.1993.39525
151. Kim H, Kwon TW, Choi E, Jeong S, Kim H-K, Han Y, *et al.* Aortoiliac diameter and length in a healthy cohort. *PLoS One* 2022;**17**:e0268077. https://doi.org/10.1371/journal.pone.0268077
152. Evangelista A, Flachskampf FA, Erbel R, Antonini-Canterin F, Vlachopoulos C, Rocchi G, *et al.* Echocardiography in aortic diseases: EAE recommendations for clinical practice. *Eur J Echocardiogr* 2010;**11**:645–58. https://doi.org/10.1093/ejechocard/jeq056
153. Zafar MA, Li Y, Rizzo JA, Charilaou P, Saeyeldin A, Velasquez CA, *et al.* Height alone, rather than body surface area, suffices for risk estimation in ascending aortic aneurysm. *J Thorac Cardiovasc Surg* 2018;**155**:1938–50. https://doi.org/10.1016/j.jtcvs.2017.10.140
154. Masri A, Kalahasti V, Svensson LG, Roselli EE, Johnston D, Hammer D, *et al.* Aortic cross-sectional area/height ratio and outcomes in patients with a trileaflet aortic valve and a dilated aorta. *Circulation* 2016;**134**:1724–37. https://doi.org/10.1161/circulationaha.116.022995
155. Wu J, Zafar MA, Li Y, Saeyeldin A, Huang Y, Zhao R, *et al.* Ascending aortic length and risk of aortic adverse events: the neglected dimension. *J Am Coll Cardiol* 2019;**74**:1883–94. https://doi.org/10.1016/j.jacc.2019.07.078
156. Pham MHC, Ballegaard C, de Knegt MC, Sigvardsen PE, Sørgaard MH, Fuchs A, *et al.* Normal values of aortic dimensions assessed by multidetector computed tomography in the Copenhagen general population study. *Eur Heart J Cardiovasc Imaging* 2019;**20**:939–48. https://doi.org/10.1093/ehjci/jez012
157. Davis AE, Lewandowski AJ, Holloway CJ, Ntusi NAB, Banerjee R, Nethononda R, *et al.* Observational study of regional aortic size referenced to body size: production of a cardiovascular magnetic resonance nomogram. *J Cardiovasc Magn Reson* 2014;**16**:9. https://doi.org/10.1186/1532-429x-16-9
158. Braley KT, Tang X, Makil ES, Borroughs-Ray D, Collins RT. The impact of body weight on the diagnosis of aortic dilation—misdiagnosis in overweight and underweight groups. *Echocardiography* 2017;**34**:1029–34. https://doi.org/10.1111/echo.13565
159. Evangelista A, Sitges M, Jondeau G, Nijveldt R, Pepi M, Cuellar H, *et al.* Multimodality imaging in thoracic aortic diseases: a clinical consensus statement from the European Association of Cardiovascular Imaging and the European Society of Cardiology working group on aorta and peripheral vascular diseases. *Eur Heart J Cardiovasc Imaging* 2023;**24**:e65–85. https://doi.org/10.1093/ehjci/jead024
160. Macdonald DB, Hurrell C, Costa AF, McInnes MDF, O'Malley ME, Barrett B, *et al.* Canadian Association of Radiologists Guidance on contrast associated acute kidney injury. *Can Assoc Radiol J* 2022;**73**:499–514. https://doi.org/10.1177/08465371221083970
161. Committee opinion no. 723: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol* 2017;**130**:e210–6. https://doi.org/10.1097/AOG.0000000000002355
162. von Kodolitsch Y, Nienaber CA, Dieckmann C, Schwartz AG, Hofmann T, Brekenfeld C, *et al.* Chest radiography for the diagnosis of acute aortic syndrome. *Am J Med* 2004;**116**:73–7. https://doi.org/10.1016/j.amjmed.2003.08.030
163. Nazerian P, Pivetta E, Veglia S, Cavigli E, Mueller C, de Matos Soeiro A, *et al.* Integrated use of conventional chest radiography cannot rule out acute aortic syndromes in emergency department patients at low clinical probability. *Acad Emerg Med* 2019;**26**:1255–65. https://doi.org/10.1111/acem.13819
164. Hartnell GG, Wakeley CJ, Tottle A, Papouchado M, Wilde RP. Limitations of chest radiography in discriminating between aortic dissection and myocardial infarction: implications for thrombolysis. *J Thorac Imaging* 1993;**8**:152–5. https://doi.org/10.1097/00005382-199321000-00008
165. Evangelista A, Avegliano G, Aguilar R, Cuellar H, Igual A, Gonzalez-Alujas T, *et al.* Impact of contrast-enhanced echocardiography on the diagnostic algorithm of acute aortic dissection. *Eur Heart J* 2010;**31**:472–9. https://doi.org/10.1093/eurheartj/ehp505

166. Litmanovich D, Bankier AA, Cantin L, Raptopoulos V, Boiselle PM. CT and MRI in diseases of the aorta. *AJR Am J Roentgenol* 2009;**193**:928–40. https://doi.org/10.2214/ajr.08.2166
167. Pennell DJ, Sechtem UP, Higgins CB, Manning W, Pohost G, Rademakers F, *et al.* Clinical indications for cardiovascular magnetic resonance (CMR): consensus panel report. *J Cardiovasc Magn Reson* 2004;**6**:727–65. https://doi.org/10.1081/jcmr-200038581
168. Yoshioka K, Tanaka R. MRI and MRA of aortic disease. *Ann Vasc Dis* 2010;**3**:196–201. https://doi.org/10.3400/avd.sasdi10003
169. Fadel BM, Mohty D, Kazzi BE, Alamro B, Arshi F, Mustafa M, *et al.* Ultrasound imaging of the abdominal aorta: a comprehensive review. *J Am Soc Echocardiogr* 2021;**34**:1119–36. https://doi.org/10.1016/j.echo.2021.06.012
170. Bhave NM, Nienaber CA, Clough RE, Eagle KA. Multimodality imaging of thoracic aortic diseases in adults. *JACC Cardiovasc Imaging* 2018;**11**:902–19. https://doi.org/10.1016/j.jcmg.2018.03.009
171. Goldstein SA, Evangelista A, Abbara S, Arai A, Asch FM, Badano LP, *et al.* Multimodality imaging of diseases of the thoracic aorta in adults: from the American Society of Echocardiography and the European Association of Cardiovascular Imaging: endorsed by the Society of Cardiovascular Computed Tomography and Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2015;**28**:119–82. https://doi.org/10.1016/j.echo.2014.11.015
172. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, *et al.* 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The task force for the diagnosis and treatment of aortic diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2014;**35**:2873–926. https://doi.org/10.1093/eurheartj/ehu281
173. Bossone E, Czerny M, Lerakis S, Rodríguez-Palomares J, Kukar N, Ranieri B, *et al.* Imaging and biomarkers in acute aortic syndromes: diagnostic and prognostic implications. *Curr Probl Cardiol* 2021;**46**:100654. https://doi.org/10.1016/j.cpcardiol.2020.100654
174. Bossone E, LaBounty TM, Eagle KA. Acute aortic syndromes: diagnosis and management, an update. *Eur Heart J* 2018;**39**:739–49d. https://doi.org/10.1093/eurheartj/ehx319
175. Vardhanabhuti V, Nicol E, Morgan-Hughes G, Roobottom CA, Roditi G, Hamilton MCK, *et al.* Recommendations for accurate CT diagnosis of suspected acute aortic syndrome (AAS)—on behalf of the British Society of Cardiovascular Imaging (BSCI)/British Society of Cardiovascular CT (BSCCT). *Br J Radiol* 2016;**89**:20150705. https://doi.org/10.1259/bjr.20150705
176. Carstensen M, Keer D, Rempel J, Jeon P, Barrett B. Prevalence of risk factors for contrast-induced nephrotoxicity in outpatients undergoing intravenous contrast-enhanced computed tomography studies. *Can Assoc Radiol J* 2012;**63**:177–82. https://doi.org/10.1016/j.carj.2010.12.004
177. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Engl J Med* 2007;**357**:2277–84. https://doi.org/10.1056/NEJMra072149
178. Barra L, Kanji T, Malette J, Pagnoux C. Imaging modalities for the diagnosis and disease activity assessment of Takayasu's arteritis: a systematic review and meta-analysis. *Autoimmun Rev* 2018;**17**:175–87. https://doi.org/10.1016/j.autrev.2017.11.021
179. Dyverfeldt P, Bissell M, Barker AJ, Bolger AF, Carlhäll C-J, Ebbers T, *et al.* 4D flow cardiovascular magnetic resonance consensus statement. *J Cardiovasc Magn Reson* 2015;**17**:72. https://doi.org/10.1186/s12968-015-0174-5
180. Rodriguez-Palomares JF. Genetics of bicuspid aortic valve: ready for clinical use? *Heart* 2022;**108**:1078–9. https://doi.org/10.1136/heartjnl-2021-320742
181. Guala A, Teixido-Tura G, Dux-Santoy L, Granato C, Ruiz-Muñoz A, Valente F, *et al.* Decreased rotational flow and circumferential wall shear stress as early markers of descending aorta dilation in Marfan syndrome: a 4D flow CMR study. *J Cardiovasc Magn Reson* 2019;**21**:63. https://doi.org/10.1186/s12968-019-0572-1
182. Horowitz MJ, Kupsky DF, El-Said HG, Alshawabkeh L, Kligerman SJ, Hsiao A. 4D flow MRI quantification of congenital shunts: comparison to invasive catheterization. *Radiol Cardiothorac Imaging* 2021;**3**:e200446. https://doi.org/10.1148/ryct.2021200446
183. Rizk J. 4D flow MRI applications in congenital heart disease. *Eur Radiol* 2021;**31**:1160–74. https://doi.org/10.1007/s00330-020-07210-z
184. Gupta SK, Ya'qoub L, Wimmer AP, Fisher S, Saeed IM. Safety and clinical impact of MRI in patients with non-MRI-conditional cardiac devices. *Radiol Cardiothorac Imaging* 2020;**2**:e200086. https://doi.org/10.1148/ryct.2020200086
185. Munawar DA, Chan JEZ, Emami M, Kadhim K, Khokhar K, O'Shea C, *et al.* Magnetic resonance imaging in non-conditional pacemakers and implantable cardioverter-defibrillators: a systematic review and meta-analysis. *Europace* 2020;**22**:288–98. https://doi.org/10.1093/europace/euz343
186. Nienaber CA. The role of imaging in acute aortic syndromes. *Eur Heart J Cardiovasc Imaging* 2013;**14**:15–23. https://doi.org/10.1093/ehjci/jes215
187. van der Geest KSM, Treglia G, Glaudemans A, Brouwer E, Sandovici M, Jamar F, *et al.* Diagnostic value of [18F]FDG-PET/CT for treatment monitoring in large vessel vasculitis: a systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2021;**48**:3886–902. https://doi.org/10.1007/s00259-021-05362-8
188. Dejaco C, Ramiro S, Duftner C, Besson FL, Bley TA, Blockmans D, *et al.* EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. *Ann Rheum Dis* 2018;**77**:636–43. https://doi.org/10.1136/annrheumdis-2017-212649
189. Forsythe RO, Dweck MR, McBride OMB, Vesey AT, Semple SI, Shah ASV, *et al.* (18)F-sodium fluoride uptake in abdominal aortic aneurysms: the SoFIA(3) study. *J Am Coll Cardiol* 2018;**71**:513–23. https://doi.org/10.1016/j.jacc.2017.11.053
190. Roque A, Pizzi MN. (18)F-FDG PET/CT: not only a promise for complex scenarios-let's talk about aortic grafts. *J Nucl Cardiol* 2022;**29**:2949–51. https://doi.org/10.1007/s12350-021-02888-0
191. Roque A, Pizzi MN, Fernández-Hidalgo N, Permanyer E, Cuellar-Calabria H, Romero-Farina G, *et al.* Morpho-metabolic post-surgical patterns of non-infected prosthetic heart valves by [18F]FDG PET/CTA: 'normality' is a possible diagnosis. *Eur Heart J Cardiovasc Imaging* 2020;**21**:24–33. https://doi.org/10.1093/ehjci/jez222
192. Pizzi MN, Roque A, Cuéllar-Calabria H, Fernández-Hidalgo N, Ferreira-González I, González-Alujas MT, *et al.* (18)F-FDG-PET/CTA of prosthetic cardiac valves and valve-tube grafts: infective versus inflammatory patterns. *JACC Cardiovasc Imaging* 2016;**9**:1224–7. https://doi.org/10.1016/j.jcmg.2016.05.013
193. Pizzi MN, Roque A, Fernández-Hidalgo N, Cuéllar-Calabria H, Ferreira-González I, Gonzàlez-Alujas MT, *et al.* Improving the diagnosis of infective endocarditis in prosthetic valves and intracardiac devices with 18F-fluordeoxyglucose positron emission tomography/computed tomography angiography: initial results at an infective endocarditis referral center. *Circulation* 2015;**132**:1113–26. https://doi.org/10.1161/circulationaha.115.015316
194. Teraa M, Hazenberg CE, Houben IB, Trimarchi S, van Herwaarden JA. Important issues regarding planning and sizing for emergent TEVAR. *J Cardiovasc Surg (Torino)* 2020;**61**:708–12. https://doi.org/10.23736/S0021-9509.20.11571-4
195. Lindholt JS, Sogaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet* 2017;**390**:2256–65. https://doi.org/10.1016/S0140-6736(17)32250-X
196. Lin JS, Evans CV, Johnson E, Redmond N, Coppola EL, Smith N. Nontraditional risk factors in cardiovascular disease risk assessment: updated evidence report and systematic review for the US preventive services task force. *JAMA* 2018;**320**:281–97. https://doi.org/10.1001/jama.2018.4242
197. Normahani P, Burgess L, Norrie J, Epstein DM, Kandiyil N, Saratzis A, *et al.* Study protocol for a multicentre comparative diagnostic accuracy study of tools to establish the presence and severity of peripheral arterial disease in people with diabetes mellitus: the DM PAD study. *BMJ Open* 2022;**12**:e066950. https://doi.org/10.1136/bmjopen-2022-066950
198. Ueshima D, Barioli A, Nai Fovino L, D'Amico G, Fabris T, Brener SJ, *et al.* The impact of pre-existing peripheral artery disease on transcatheter aortic valve implantation outcomes: a systematic review and meta-analysis. *Catheter Cardiovasc Interv* 2020;**95**:993–1000. https://doi.org/10.1002/ccd.28335
199. de Weerd M, Greving JP, Hedblad B, Lorenz MW, Mathiesen EB, O'Leary DH, *et al.* Prevalence of asymptomatic carotid artery stenosis in the general population: an individual participant data meta-analysis. *Stroke* 2010;**41**:1294–7. https://doi.org/10.1161/STROKEAHA.110.581058
200. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, *et al.* Screening for asymptomatic carotid artery stenosis: US preventive services task force recommendation statement. *JAMA* 2021;**325**:476–81. https://doi.org/10.1001/jama.2020.26988
201. AbuRahma AF, Avgerinos ED, Chang RW, Darling RC, Duncan AA, Forbes TL, *et al.* Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease. *J Vasc Surg* 2022;**75**:4S–22S. https://doi.org/10.1016/j.jvs.2021.04.073
202. Howard DPJ, Gaziano L, Rothwell PM. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol* 2021;**20**:193–202. https://doi.org/10.1016/s1474-4422(20)30484-1
203. Paraskevas KI, Spence JD, Mikhailidis DP, Antignani PL, Gloviczki P, Eckstein H-H, *et al.* Why do guidelines recommend screening for abdominal aortic aneurysms, but not for asymptomatic carotid stenosis? A plea for a randomized controlled trial. *Int J Cardiol* 2023;**371**:406–12. https://doi.org/10.1016/j.ijcard.2022.09.045
204. Kobo O, Saada M, von Birgelen C, Tonino PAL, Íñiguez-Romo A, Fröbert O, *et al.* Impact of multisite artery disease on clinical outcomes after percutaneous coronary intervention: an analysis from the e-Ultimaster registry. *Eur Heart J Qual Care Clin Outcomes* 2023;**9**:417–26. https://doi.org/10.1093/ehjqcco/qcac043
205. Steffel J, Eikelboom JW, Anand SS, Shestakovska O, Yusuf S, Fox KAA. The COMPASS trial: net clinical benefit of low-dose rivaroxaban plus aspirin as compared with aspirin in patients with chronic vascular disease. *Circulation* 2020;**142**:40–8. https://doi.org/10.1161/CIRCULATIONAHA.120.046048
206. Del Giorno R, Reveilhac M, Stauffer I, Berthoud M, Mazzolai L, Depairon M, *et al.* A new score for improving cardiovascular risk prediction and prevention. *Nutr Metab Cardiovasc Dis* 2023;**33**:1546–55. https://doi.org/10.1016/j.numecd.2023.04.019
207. Mehta A, Rigdon J, Tattersall MC, German CA, Barringer TA, Joshi PH, *et al.* Association of carotid artery plaque with cardiovascular events and incident coronary

artery calcium in individuals with absent coronary calcification: the MESA. *Circ Cardiovasc Imaging* 2021;**14**:e011701. https://doi.org/10.1161/circimaging.120.011701
208. Gepner AD, Young R, Delaney JA, Budoff MJ, Polak JF, Blaha MJ, *et al.* Comparison of carotid plaque score and coronary artery calcium score for predicting cardiovascular disease events: the multi-ethnic study of atherosclerosis. *J Am Heart Assoc* 2017;**6**: e005179. https://doi.org/10.1161/jaha.116.005179
209. Laclaustra M, Casasnovas JA, Fernández-Ortiz A, Fuster V, León-Latre M, Jiménez-Borreguero LJ, *et al.* Femoral and carotid subclinical atherosclerosis association with risk factors and coronary calcium: the AWHS study. *J Am Coll Cardiol* 2016;**67**:1263–74. https://doi.org/10.1016/j.jacc.2015.12.056
210. Jacobowitz GR, Rockman CB, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, *et al.* A model for predicting occult carotid artery stenosis: screening is justified in a selected population. *J Vasc Surg* 2003;**38**:705–9. https://doi.org/10.1016/s0741-5214(03)00730-4
211. Rockman CB, Jacobowitz GR, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, *et al.* Focused screening for occult carotid artery disease: patients with known heart disease are at high risk. *J Vasc Surg* 2004;**39**:44–50. https://doi.org/10.1016/j.jvs.2003.07.008
212. Yuo TH, Sidaoui J, Marone LK, Makaroun MS, Chaer RA. Revascularization of asymptomatic carotid stenosis is not appropriate in patients on dialysis. *J Vasc Surg* 2015;**61**: 670–4. https://doi.org/10.1016/j.jvs.2014.10.002
213. Ramos MJ, González-Fajardo JA, Vaquero-Puerta C, Vallina-Victorero M, Vicente-Santiago M, Vaquero-Lorenzo F, *et al.* Asymptomatic carotid stenosis in patients with intermittent claudication: epidemiological study. *J Cardiovasc Surg (Torino)* 2011;**52**:761–8 .
214. Aboyans V, Lacroix P, Guilloux J, Rollé F, Le Guyader A, Cautrès M, *et al.* A predictive model for screening cerebrovascular disease in patient undergoing coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2005;**4**:90–5. https://doi.org/10.1510/icvts.2004.092262
215. Cornily JC, Le Saux D, Vinsonneau U, Bezon E, Le Ven F, Le Gal G, *et al.* Assessment of carotid artery stenosis before coronary artery bypass surgery. Is it always necessary? *Arch Cardiovasc Dis* 2011;**104**:77–83. https://doi.org/10.1016/j.acvd.2010.11.008
216. Johansson EP, Wester P. Carotid bruits as predictor for carotid stenoses detected by ultrasonography: an observational study. *BMC Neurol* 2008;**8**:23. https://doi.org/10.1186/1471-2377-8-23
217. Carmody BJ, Arora S, Avena R, Curry KM, Simpkins J, Cosby K, *et al.* Accelerated carotid artery disease after high-dose head and neck radiotherapy: is there a role for routine carotid duplex surveillance? *J Vasc Surg* 1999;**30**:1045–51. https://doi.org/10.1016/s0741-5214(99)70042-x
218. Song P, Rudan D, Zhu Y, Fowkes FJI, Rahimi K, Fowkes FGR, *et al.* Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. *Lancet Glob Health* 2019;**7**:e1020–30. https://doi.org/10.1016/s2214-109x(19)30255-4
219. Campia U, Gerhard-Herman M, Piazza G, Goldhaber SZ. Peripheral artery disease: past, present, and future. *Am J Med* 2019;**132**:1133–41. https://doi.org/10.1016/j.amjmed.2019.04.043
220. Søgaard R, Lindholt JS. Cost-effectiveness of population-based vascular disease screening and intervention in men from the Viborg Vascular (VIVA) trial. *Br J Surg* 2018;**105**: 1283–93. https://doi.org/10.1002/bjs.10872
221. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *BMJ* 2005;**330**:750. https://doi.org/10.1136/bmj.38369.620162.82
222. Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ, *et al.* Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ* 2004;**329**:1259. https://doi.org/10.1136/bmj.38272.478438.55
223. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, *et al.* The multicentre aneurysm screening study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet* 2002;**360**: 1531–9. https://doi.org/10.1016/s0140-6736(02)11522-4
224. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg* 1995;**82**:1066–70. https://doi.org/10.1002/bjs.1800820821
225. Duncan A, Maslen C, Gibson C, Hartshorne T, Farooqi A, Saratzis A, *et al.* Ultrasound screening for abdominal aortic aneurysm in high-risk women. *Br J Surg* 2021;**108**: 1192–8. https://doi.org/10.1093/bjs/znab220
226. Lindholt JS, Sogaard R, Rasmussen LM, Mejldal A, Lambrechtsen J, Steffensen FH, *et al.* Five-year outcomes of the Danish cardiovascular screening (DANCAVAS) trial. *N Engl J Med* 2022;**387**:1385–94. https://doi.org/10.1056/NEJMoa2208681
227. Howard DP, Banerjee A, Fairhead JF, Handa A, Silver LE, Rothwell PM. Population-based study of incidence of acute abdominal aortic aneurysms with projected impact of screening strategy. *J Am Heart Assoc* 2015;**4**:e001926. https://doi.org/10.1161/JAHA.115.001926
228. Howard DP, Banerjee A, Fairhead JF, Handa A, Silver LE, Rothwell PM. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *Br J Surg* 2015;**102**:907–15. https://doi.org/10.1002/bjs.9838
229. Sprynger M, Willems M, Van Damme H, Drieghe B, Wautrecht JC, Moonen M. Screening program of abdominal aortic aneurysm. *Angiology* 2019;**70**:407–13. https://doi.org/10.1177/0003319718824940
230. Larsson E, Granath F, Swedenborg J, Hultgren R. A population-based case-control study of the familial risk of abdominal aortic aneurysm. *J Vasc Surg* 2009;**49**:47–50; discussion 51. https://doi.org/10.1016/j.jvs.2008.08.012
231. Linné A, Forsberg J, Lindström D, Ideskog E, Hultgren R. Age at detection of abdominal aortic aneurysms in siblings of patients with abdominal aortic aneurysms. *J Vasc Surg* 2016;**63**:883–7. https://doi.org/10.1016/j.jvs.2015.10.057
232. Aboyans V, Bataille V, Bliscaux P, Ederhy S, Filliol D, Honton B, *et al.* Effectiveness of screening for abdominal aortic aneurysm during echocardiography. *Am J Cardiol* 2014;**114**:1100–4. https://doi.org/10.1016/j.amjcard.2014.07.024
233. Hicks CW, Al-Qunaibet A, Ding N, Kwak L, Folsom AR, Tanaka H, *et al.* Symptomatic and asymptomatic peripheral artery disease and the risk of abdominal aortic aneurysm: the Atherosclerosis Risk in Communities (ARIC) study. *Atherosclerosis* 2021;**333**:32–8. https://doi.org/10.1016/j.atherosclerosis.2021.08.016
234. Benson RA, Poole R, Murray S, Moxey P, Loftus IM. Screening results from a large United Kingdom abdominal aortic aneurysm screening center in the context of optimizing United Kingdom National Abdominal Aortic Aneurysm Screening Programme protocols. *J Vasc Surg* 2016;**63**:301–4. https://doi.org/10.1016/j.jvs.2015.08.091
235. Sciria CT, Osorio B, Wang J, Lu DY, Amin N, Vohra A, *et al.* Sex-based disparities in outcomes with abdominal aortic aneurysms. *Am J Cardiol* 2021;**155**:135–48. https://doi.org/10.1016/j.amjcard.2021.06.023
236. Carter JL, Morris DR, Sherliker P, Clack R, Lam KBH, Halliday A, *et al.* Sex-specific associations of vascular risk factors with abdominal aortic aneurysm: findings from 1.5 million women and 0.8 million men in the United States and United Kingdom. *J Am Heart Assoc* 2020;**9**:e014748. https://doi.org/10.1161/JAHA.119.014748
237. Wanhainen A, Lundkvist J, Bergqvist D, Bjorck M. Cost-effectiveness of screening women for abdominal aortic aneurysm. *J Vasc Surg* 2006;**43**:908–14; discussion 914. https://doi.org/10.1016/j.jvs.2005.12.064
238. Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. *Am J Clin Nutr* 2010;**92**:1189–96. https://doi.org/10.3945/ajcn.2010.29673
239. Mente A, Dehghan M, Rangarajan S, O'Donnell M, Hu W, Dagenais G, *et al.* Diet, cardiovascular disease, and mortality in 80 countries. *Eur Heart J* 2023;**44**:2560–79. https://doi.org/10.1093/eurheartj/ehad269
240. Wan D, Dehghan M, de Souza RJ, Ramasundarahettige C, Eikelboom JW, Bosch J, *et al.* Dietary intake and cardiovascular outcomes in patients with chronic vascular disease: insights from the COMPASS trial cohort. *Eur J Prev Cardiol* 2023;**30**:709–18. https://doi.org/10.1093/eurjpc/zwad062
241. Adegbola A, Behrendt CA, Zyriax BC, Windler E, Kreutzburg T. The impact of nutrition on the development and progression of peripheral artery disease: a systematic review. *Clin Nutr* 2022;**41**:49–70. https://doi.org/10.1016/j.clnu.2021.11.005
242. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, *et al.* 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020;**41**:111–88. https://doi.org/10.1093/eurheartj/ehz455
243. Amarenco P, Kim JS, Labreuche J, Charles H, Giroud M, Lee B-C, *et al.* Benefit of targeting a LDL (low-density lipoprotein) cholesterol <70 mg/dL during 5 years after ischemic stroke. *Stroke* 2020;**51**:1231–9. https://doi.org/10.1161/strokeaha.119.028718
244. Aung PP, Maxwell HG, Jepson RG, Price JF, Leng GC. Lipid-lowering for peripheral arterial disease of the lower limb. *Cochrane Database Syst Rev* 2007;**4**:CD000123. https://doi.org/10.1002/14651858.CD000123.pub2
245. Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg* 2007;**45**:645–54; discussion 653–644. https://doi.org/10.1016/j.jvs.2006.12.054
246. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, *et al.* Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;**366**:1267–78. https://doi.org/10.1016/S0140-6736(05)67394-1
247. Bonaca MP, Gutierrez JA, Cannon C, Giugliano R, Blazing M, Park J-G, *et al.* Polyvascular disease, type 2 diabetes, and long-term vascular risk: a secondary analysis of the IMPROVE-IT trial. *Lancet Diabetes Endocrinol* 2018;**6**:934–43. https://doi.org/10.1016/s2213-8587(18)30290-0
248. Yu E, Malik VS, Hu FB. Cardiovascular disease prevention by diet modification: JACC health promotion series. *J Am Coll Cardiol* 2018;**72**:914–26. https://doi.org/10.1016/j.jacc.2018.02.085
249. López-Laguna N, Martínez-González MA, Toledo E, Babio N, Sorlí JV, Ros E, *et al.* Risk of peripheral artery disease according to a healthy lifestyle score: the PREDIMED study. *Atherosclerosis* 2018;**275**:133–40. https://doi.org/10.1016/j.atherosclerosis.2018.05.049
250. Kaluza J, Stackelberg O, Harris HR, Akesson A, Björck M, Wolk A. Mediterranean diet is associated with reduced risk of abdominal aortic aneurysm in smokers: results of two prospective cohort studies. *Eur J Vasc Endovasc Surg* 2021;**62**:284–93. https://doi.org/10.1016/j.ejvs.2021.04.017

251. Liu L, Yang Y. Nutritional management mode of early cardiac rehabilitation in patients with Stanford type A aortic dissection. *Comput Math Methods Med* 2022;**2022**: 2124636. https://doi.org/10.1155/2022/2124636
252. Lauret GJ, Fokkenrood HJ, Bendermacher BL, Scheltinga MR, Teijink JA. Physical activity monitoring in patients with intermittent claudication. *Eur J Vasc Endovasc Surg* 2014; **47**:656–63. https://doi.org/10.1016/j.ejvs.2014.03.001
253. Gardner AW, Addison O, Katzel LI, Montgomery PS, Prior SJ, Serra MC, *et al.* Association between physical activity and mortality in patients with claudication. *Med Sci Sports Exerc* 2021;**53**:732–9. https://doi.org/10.1249/mss.0000000000002526
254. Gardner AW, Montgomery PS, Parker DE. Physical activity is a predictor of all-cause mortality in patients with intermittent claudication. *J Vasc Surg* 2008;**47**:117–22. https://doi.org/10.1016/j.jvs.2007.09.033
255. Gardner AW, Montgomery PS, Wang M, Shen B, Zhang S, Pomilla WA. Association between meeting physical activity time-intensity guidelines with ambulation, quality of life, and inflammation in claudication. *J Cardiopulm Rehabil Prev* 2022;**42**:E82–9. https://doi.org/10.1097/hcr.0000000000000686
256. Thijssen CGE, Bons LR, Gökalp AL, Van Kimmenade RRJ, Mokhles MM, Pelliccia A, *et al.* Exercise and sports participation in patients with thoracic aortic disease: a review. *Expert Rev Cardiovasc Ther* 2019;**17**:251–66. https://doi.org/10.1080/14779072.2019.1585807
257. Delsart P, Maldonado-Kauffmann P, Bic M, Boudghene-Stambouli F, Sobocinski J, Juthier F, *et al.* Post aortic dissection: gap between activity recommendation and real life patients aerobic capacities. *Int J Cardiol* 2016;**219**:271–6. https://doi.org/10.1016/j.ijcard.2016.06.026
258. Chaddha A, Eagle KA, Braverman AC, Kline-Rogers E, Hirsch AT, Brook R, *et al.* Exercise and physical activity for the post-aortic dissection patient: the clinician's conundrum. *Clin Cardiol* 2015;**38**:647–51. https://doi.org/10.1002/clc.22481
259. Chaddha A, Kline-Rogers E, Woznicki EM, Brook R, Housholder-Hughes S, Braverman AC, *et al.* Cardiology patient page. Activity recommendations for postaortic dissection patients. *Circulation* 2014;**130**:e140–2. https://doi.org/10.1161/circulationaha.113.005819
260. Katsiki N, Papadopoulou SK, Fachantidou AI, Mikhailidis DP. Smoking and vascular risk: are all forms of smoking harmful to all types of vascular disease? *Public Health* 2013; **127**:435–41. https://doi.org/10.1016/j.puhe.2012.12.021
261. Wu CW, Chuang HY, Watanabe K, Wu P-S, Pan H-C, Wang C-L, *et al.* Association between secondhand smoke and peripheral arterial disease: a meta-analysis of cross-sectional studies. *Int Arch Occup Environ Health* 2022;**95**:1091–101. https://doi.org/10.1007/s00420-022-01837-9
262. Sode BF, Nordestgaard BG, Gronbaek M, Dahl M. Tobacco smoking and aortic aneurysm: two population-based studies. *Int J Cardiol* 2013;**167**:2271–7. https://doi.org/10.1016/j.ijcard.2012.06.003
263. Altobelli E, Rapacchietta L, Profeta VF, Fagnano R. Risk factors for abdominal aortic aneurysm in population-based studies: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2018;**15**:2805. https://doi.org/10.3390/ijerph15122805
264. Lederle FA, Nelson DB, Joseph AM. Smokers' relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg* 2003;**38**: 329–34. https://doi.org/10.1016/s0741-5214(03)00136-8
265. Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, *et al.* Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006;**368**:647–58. https://doi.org/10.1016/S0140-6736(06)69249-0
266. Mahtta D, Ramsey D, Krittanawong C, Al Rifai M, Khurram N, Samad Z, *et al.* Recreational substance use among patients with premature atherosclerotic cardiovascular disease. *Heart* 2021;**107**:650–6. https://doi.org/10.1136/heartjnl-2020-318119
267. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005;**142**:233–9. https://doi.org/10.7326/0003-4819-142-4-200502150-00005
268. Suissa K, Lariviere J, Eisenberg MJ, Eberg M, Gore GC, Grad R, *et al.* Efficacy and safety of smoking cessation interventions in patients with cardiovascular disease: a network meta-analysis of randomized controlled trials. *Circ Cardiovasc Qual Outcomes* 2017;**10**: e002458. https://doi.org/10.1161/CIRCOUTCOMES.115.002458
269. Livingstone-Banks J, Fanshawe TR, Thomas KH, Theodoulou A, Hajizadeh A, Hartman L, *et al.* Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2023;**5**:CD006103. https://doi.org/10.1002/14651858.CD006103.pub8
270. Rose JJ, Krishnan-Sarin S, Exil VJ, Hamburg NM, Fetterman JL, Ichinose F, *et al.* Cardiopulmonary impact of electronic cigarettes and vaping products: a scientific statement from the American Heart Association. *Circulation* 2023;**148**:703–28. https://doi.org/10.1161/CIR.0000000000001160
271. Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Begh R, *et al.* Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2024;**1**:CD010216. https://doi.org/10.1002/14651858.CD010216.pub8
272. Travis N, Knoll M, Cadham CJ, Cook S, Warner KE, Fleischer NL, *et al.* Health effects of electronic cigarettes: an umbrella review and methodological considerations. *Int J Environ Res Public Health* 2022;**19**:9054. https://doi.org/10.3390/ijerph19159054
273. Abbott AJ, Reibel YG, Arnett MC, Marka N, Drake MA. Oral and systemic health implications of electronic cigarette usage as compared to conventional tobacco cigarettes: a review of the literature. *J Dent Hyg* 2023;**97**:21–35.
274. Hamann SL, Kungskulniti N, Charoenca N, Kasemsup V, Ruangkanchanasetr S, Jongkhajornpong P. Electronic cigarette harms: aggregate evidence shows damage to biological systems. *Int J Environ Res Public Health* 2023;**20**:6808. https://doi.org/10.3390/ijerph20196808
275. Kavousi M, Pisinger C, Barthelemy JC, De Smedt D, Koskinas K, Marques-Vidal P, *et al.* Electronic cigarettes and health with special focus on cardiovascular effects: position paper of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol* 2021;**28**:1552–66. https://doi.org/10.1177/2047487320941993
276. Goldman RE, Parker DR, Eaton CB, Borkan JM, Gramling R, Cover RT, *et al.* Patients' perceptions of cholesterol, cardiovascular disease risk, and risk communication strategies. *Ann Fam Med* 2006;**4**:205–12. https://doi.org/10.1370/afm.534
277. Howarth M, Lister C. Social prescribing in cardiology: rediscovering the nature within us. *Br J Card Nurs* 2019;**14**:1–9. https://doi.org/10.12968/bjca.2019.0036
278. Nichols LO, Martindale-Adams J, Burns R, Graney MJ, Zuber J. Translation of a dementia caregiver support program in a health care system—REACH VA. *Arch Intern Med* 2011;**171**:353–9. https://doi.org/10.1001/archinternmed.2010.548
279. Martire LM, Schulz R, Keefe FJ, Rudy TE, Starz TW. Couple-oriented education and support intervention for osteoarthritis: effects on spouses' support and responses to patient pain. *Fam Syst Health* 2008;**26**:185–95. https://doi.org/10.1037/1091-7527.26.2.185
280. Morris SM, King C, Turner M, Payne S. Family carers providing support to a person dying in the home setting: a narrative literature review. *Palliat Med* 2015;**29**:487–95. https://doi.org/10.1177/0269216314565706
281. Ventura AD, Burney S, Brooker J, Fletcher J, Ricciardelli L. Home-based palliative care: a systematic literature review of the self-reported unmet needs of patients and carers. *Palliat Med* 2014;**28**:391–402. https://doi.org/10.1177/0269216313511141
282. Reynolds CF, III, Jeste DV, Sachdev PS, Blazer DG. Mental health care for older adults: recent advances and new directions in clinical practice and research. *World Psychiatry* 2022;**21**:336–63. https://doi.org/10.1002/wps.20996
283. Katch H. The role of self-efficacy in cardiovascular disease self-management: a review of effective programs. *Patient Intelligence* 2010;**2**:33–4. doi: https://doi.org/10.2147/PI.S12624]
284. Ohman EM, Bhatt DL, Steg PG, Goto S, Hirsch AT, Liau C-S, *et al.* The REduction of Atherothrombosis for Continued Health (REACH) registry: an international, prospective, observational investigation in subjects at risk for atherothrombotic events–study design. *Am Heart J* 2006;**151**:786.e1–10. https://doi.org/10.1016/j.ahj.2005.11.004
285. Simons PC, Algra A, van de Laak MF, Grobbee DE, van der Graaf Y. Second manifestations of ARTerial disease (SMART) study: rationale and design. *Eur J Epidemiol* 1999;**15**: 773–81. https://doi.org/10.1023/a:1007621514757
286. Dorresteijn JA, Visseren FL, Wassink AM, Gondrie MJA, Steyerberg EW, Ridker PM, *et al.* Development and validation of a prediction rule for recurrent vascular events based on a cohort study of patients with arterial disease: the SMART risk score. *Heart* 2013;**99**:866–72. https://doi.org/10.1136/heartjnl-2013-303640
287. Kaasenbrood L, Bhatt DL, Dorresteijn JAN, Wilson PWF, D'Agostino RB, Massaro JM, *et al.* Estimated life expectancy without recurrent cardiovascular events in patients with vascular disease: the SMART-REACH model. *J Am Heart Assoc* 2018;**7**: e009217. https://doi.org/10.1161/JAHA.118.009217
288. Hageman SHJ, McKay AJ, Ueda P, Gunn LH, Jernberg T, Hagström E, *et al.* Estimation of recurrent atherosclerotic cardiovascular event risk in patients with established cardiovascular disease: the updated SMART2 algorithm. *Eur Heart J* 2022;**43**:1715–27. https://doi.org/10.1093/eurheartj/ehac056
289. van Trier TJ, Snaterse M, Boekholdt SM, Scholte Op Reimer WJM, Hageman SHJ, Visseren FLJ, *et al.* Validation of systematic coronary risk evaluation 2 (SCORE2) and SCORE2-older persons in the EPIC Norfolk prospective population cohort. *Eur J Prev Cardiol* 2024;**31**:182–9. https://doi.org/10.1093/eurjpc/zwad318
290. Wan D, Li V, Banfield L, Azab S, de Souza RJ, Anand SS, *et al.* Diet and nutrition in peripheral artery disease: a systematic review. *Can J Cardiol* 2022;**38**:672–80. https://doi.org/10.1016/j.cjca.2022.01.021
291. Sesso HD, Rist PM, Aragaki AK, Rautiainen S, Johnson LG, Friedenberg G, *et al.* Multivitamins in the prevention of cancer and cardiovascular disease: the COcoa Supplement and Multivitamin Outcomes Study (COSMOS) randomized clinical trial. *Am J Clin Nutr* 2022;**115**:1501–10. https://doi.org/10.1093/ajcn/nqac056
292. Bondonno NP, Murray K, Cassidy A, Bondonno CP, Lewis JR, Croft KD, *et al.* Higher habitual flavonoid intakes are associated with a lower risk of peripheral artery disease hospitalizations. *Am J Clin Nutr* 2021;**113**:187–99. https://doi.org/10.1093/ajcn/nqaa300
293. Bapir M, Untracht GR, Cooke D, McVey JH, Skene SS, Campagnolo P, *et al.* Cocoa flavanol consumption improves lower extremity endothelial function in healthy individuals and people with type 2 diabetes. *Food Funct* 2022;**13**:10439–48. https://doi.org/10.1039/d2fo02017c
294. Fassora M, Calanca L, Jaques C, Mazzolai L, Kayser B, Lanzi S. Intensity-dependent effects of exercise therapy on walking performance and aerobic fitness in

symptomatic patients with lower-extremity peripheral artery disease: a systematic review and meta-analysis. *Vasc Med* 2022;**27**:158–70. https://doi.org/10.1177/1358863x211034577
295. O'Connor EA, Evans CV, Rushkin MC, Redmond N, Lin JS. Behavioral counseling to promote a healthy diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors: updated evidence report and systematic review for the US preventive services task force. *JAMA* 2020;**324**:2076–94. https://doi.org/10.1001/jama.2020.17108
296. Hartmann-Boyce J, McRobbie H, Lindson N, Bullen C, Begh R, Theodoulou A, *et al.* Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2021;**4**:CD010216. https://doi.org/10.1002/14651858.CD010216.pub5
297. Krabbe B, Espinola-Klein C, Malyar N, Brodmann M, Mazzolai L, Belch JJF, *et al.* Health effects of e-cigarettes and their use for smoking cessation from a vascular perspective. *Vasa* 2023;**52**:81–5. https://doi.org/10.1024/0301-1526/a001056
298. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee I-M, *et al.* American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;**43**:1334–59. https://doi.org/10.1249/MSS.0b013e318213fefb
299. Twine CP, Kakkos SK, Aboyans V, Baumgartner I, Behrendt C-A, Bellmunt-Montoya S, *et al.* Editor's choice—European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on antithrombotic therapy for vascular diseases. *Eur J Vasc Endovasc Surg* 2023;**65**:627–89. https://doi.org/10.1016/j.ejvs.2023.03.042
300. McEvoy JW, Touyz RM, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, *et al.* 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J* 2024. https://doi.org/10.1093/eurheartj/ehae178
301. Blood Pressure Lowering Treatment Trialists' Collaboration. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis. *Lancet* 2021;**398**:1053–64. https://doi.org/10.1016/S0140-6736(21)01921-8
302. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al.* Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2016;**387**:957–67. https://doi.org/10.1016/s0140-6736(15)01225-8
303. Williamson JD, Supiano MA, Applegate WB, Berlowitz DR, Campbell RC, Chertow GM, *et al.* Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: a randomized clinical trial. *JAMA* 2016;**315**:2673–82. https://doi.org/10.1001/jama.2016.7050
304. Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, *et al.* Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med* 2021;**385**:1268–79. https://doi.org/10.1056/NEJMoa2111437
305. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension. 1. Overview, meta-analyses, and meta-regression analyses of randomized trials. *J Hypertens* 2014;**32**:2285–95. https://doi.org/10.1097/hjh.0000000000000378
306. Wright JT, Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, *et al.* A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;**373**:2103–16. https://doi.org/10.1056/NEJMoa1511939
307. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;**342**:145–53. https://doi.org/10.1056/nejm200001203420301
308. Bavry AA, Anderson RD, Gong Y, Denardo SJ, Cooper-DeHoff RM, Handberg EM, *et al.* Outcomes among hypertensive patients with concomitant peripheral and coronary artery disease: findings from the INternational VErapamil-SR/Trandolapril STudy. *Hypertension* 2010;**55**:48–53. https://doi.org/10.1161/hypertensionaha.109.142240
309. Fudim M, Hopley CW, Huang Z, Kavanagh S, Rockhold FW, Baumgartner I, *et al.* Association of hypertension and arterial blood pressure on limb and cardiovascular outcomes in symptomatic peripheral artery disease: the EUCLID trial. *Circ Cardiovasc Qual Outcomes* 2020;**13**:e006512. https://doi.org/10.1161/circoutcomes.120.006512
310. Thomas Manapurathe D, Krishna SM, Dewdney B, Moxon JV, Biros E, Golledge J, Effect of blood pressure lowering medications on leg ischemia in peripheral artery disease patients: a meta-analysis of randomised controlled trials. *PLoS One* 2017;**12**:e0178713. https://doi.org/10.1371/journal.pone.0178713
311. Lu Y, Ballew SH, Tanaka H, Szklo M, Heiss G, Coresh J, *et al.* 2017 ACC/AHA blood pressure classification and incident peripheral artery disease: the Atherosclerosis Risk in Communities (ARIC) study. *Eur J Prev Cardiol* 2020;**27**:51–9. https://doi.org/10.1177/2047487319865378
312. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, *et al.* Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008;**358**:1547–59. https://doi.org/10.1056/NEJMoa0801317
313. Ostergren J, Sleight P, Dagenais G, Danisa K, Bosch J, Qilong Y, *et al.* Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J* 2004;**25**:17–24. https://doi.org/10.1016/j.ehj.2003.10.033
314. Paravastu SC, Mendonca DA, Da Silva A. Beta blockers for peripheral arterial disease. *Cochrane Database Syst Rev* 2013;**9**:CD005508. https://doi.org/10.1002/14651858.CD005508.pub3
315. Kray JE, Dombrovskiy VY, Vogel TR. Use of angiotensin-converting enzyme inhibitors and freedom from amputation after lower extremity revascularization. *Vasc Health Risk Manag* 2017;**13**:269–74. https://doi.org/10.2147/vhrm.S137698
316. Høgh A, Lindholt JS, Nielsen H, Jensen LP, Johnsen SP. Use of angiotensin-converting enzyme inhibitors and cardiovascular outcomes following primary vascular surgery: a nationwide propensity score matched follow-up study. *Vasc Endovascular Surg* 2012;**46**:515–23. https://doi.org/10.1177/1538574412455229
317. Armstrong EJ, Chen DC, Singh GD, Amsterdam EA, Laird JR. Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use is associated with reduced major adverse cardiovascular events among patients with critical limb ischemia. *Vasc Med* 2015;**20**:237–44. https://doi.org/10.1177/1358863x15574321
318. Aronow WS, Ahn C. Effect of beta blockers on incidence of new coronary events in older persons with prior myocardial infarction and symptomatic peripheral arterial disease. *Am J Cardiol* 2001;**87**:1284–6. https://doi.org/10.1016/s0002-9149(01)01521-1
319. Soga Y, Iida O, Takahara M, Hirano K, Suzuki K, Kawasaki D. Beta-blocker treatment does not worsen critical limb ischemia in patients receiving endovascular therapy. *J Atheroscler Thromb* 2015;**22**:481–9. https://doi.org/10.5551/jat.27359
320. Carey RM, Wright JT, Jr, Taler SJ, Whelton PK. Guideline-driven management of hypertension: an evidence-based update. *Circ Res* 2021;**128**:827–46. https://doi.org/10.1161/circresaha.121.318083
321. Evans KL, Tuttle KR, Folt DA, Dawson T, Haller ST, Brewster PS, *et al.* Use of renin-angiotensin inhibitors in people with renal artery stenosis. *Clin J Am Soc Nephrol* 2014;**9**:1199–206. https://doi.org/10.2215/cjn.11611113
322. Hackam DG, Duong-Hua ML, Mamdani M, Li Ping, Tobe SW, Spence JD, *et al.* Angiotensin inhibition in renovascular disease: a population-based cohort study. *Am Heart J* 2008;**156**:549–55. https://doi.org/10.1016/j.ahj.2008.05.013
323. Solomon SD, Rice MM, Jablonski KA, Jose P, Domanski M, Sabatine M, *et al.* Renal function and effectiveness of angiotensin-converting enzyme inhibitor therapy in patients with chronic stable coronary disease in the Prevention of Events with ACE inhibition (PEACE) trial. *Circulation* 2006;**114**:26–31. https://doi.org/10.1161/circulationaha.105.592733
324. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, *et al.* Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med* 2014;**370**:13–22. https://doi.org/10.1056/NEJMoa1310753
325. Mayr NP, Hapfelmeier A, Martin K, Kurz A, van der Starre P, Babik B, *et al.* Comparison of sedation and general anaesthesia for transcatheter aortic valve implantation on cerebral oxygen saturation and neurocognitive outcomedagger. *Br J Anaesth* 2016;**116**:90–9. https://doi.org/10.1093/bja/aev294
326. Singh K, Bønaa KH, Jacobsen BK, Bjørk L, Solberg S. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: the Tromsø study. *Am J Epidemiol* 2001;**154**:236–44. https://doi.org/10.1093/aje/154.3.236
327. Vogel TR, Dombrovskiy VY, Galiñanes EL, Kruse RL. Preoperative statins and limb salvage after lower extremity revascularization in the Medicare population. *Circ Cardiovasc Interv* 2013;**6**:694–700. https://doi.org/10.1161/circinterventions.113.000274
328. Kumbhani DJ, Steg PG, Cannon CP, Eagle KA, Smith SC, Goto S, *et al.* Statin therapy and long-term adverse limb outcomes in patients with peripheral artery disease: insights from the REACH registry. *Eur Heart J* 2014;**35**:2864–72. https://doi.org/10.1093/eurheartj/ehu080
329. Pastori D, Farcomeni A, Milanese A, Del Sole F, Menichelli D, Hiatt WR, *et al.* Statins and major adverse limb events in patients with peripheral artery disease: a systematic review and meta-analysis. *Thromb Haemost* 2020;**120**:866–75. https://doi.org/10.1055/s-0040-1709711
330. Su Z, Guo J, Gu Y. Pharmacotherapy in clinical trials for abdominal aortic aneurysms: a systematic review and meta-analysis. *Clin Appl Thromb Hemost* 2022;**28**:10760296221120423. https://doi.org/10.1177/10760296221120423
331. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, *et al.* Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med* 2015;**372**:2387–97. https://doi.org/10.1056/NEJMoa1410489
332. Kaasenbrood L, Boekholdt SM, van der Graaf Y, Ray KK, Peters RJG, Kastelein JJP, *et al.* Distribution of estimated 10-year risk of recurrent vascular events and residual risk in a secondary prevention population. *Circulation* 2016;**134**:1419–29. https://doi.org/10.1161/CIRCULATIONAHA.116.021314
333. Clavijo LC, Caro J, Choi J, Caro JA, Tun H, Rowe V, *et al.* The addition of evolocumab to maximal tolerated statin therapy improves walking performance in patients with peripheral arterial disease and intermittent claudication (Evol-PAD study). *Cardiovasc Revasc Med* 2023;**55**:1–5. https://doi.org/10.1016/j.carrev.2023.04.020
334. Cholesterol Treatment Trialists Collaboration; Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, *et al.* Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet* 2015;**385**:1397–405. https://doi.org/10.1016/S0140-6736(14)61368-4

335. Murphy SA, Cannon CP, Blazing MA, Giugliano RP, White JA, Lokhnygina Y, *et al.* Reduction in total cardiovascular events with ezetimibe/simvastatin post-acute coronary syndrome: the IMPROVE-IT trial. *J Am Coll Cardiol* 2016;**67**:353–61. https://doi.org/10.1016/j.jacc.2015.10.077
336. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, *et al.* Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;**376**:1713–22. https://doi.org/10.1056/NEJMoa1615664
337. Westin GG, Armstrong EJ, Bang H, Yeo K-K, Anderson D, Dawson DL, *et al.* Association between statin medications and mortality, major adverse cardiovascular event, and amputation-free survival in patients with critical limb ischemia. *J Am Coll Cardiol* 2014;**63**:682–90. https://doi.org/10.1016/j.jacc.2013.09.073
338. Belch JJF, Brodmann M, Baumgartner I, Binder CJ, Casula M, Heiss C, *et al.* Lipid-lowering and anti-thrombotic therapy in patients with peripheral arterial disease. *Vasa* 2021;**50**:401–11. https://doi.org/10.1024/0301-1526/a000969
339. Momsen AH, Jensen MB, Norager CB, Madsen MR, Vestersgaard-Andersen T, Lindholt JS. Drug therapy for improving walking distance in intermittent claudication: a systematic review and meta-analysis of robust randomised controlled studies. *Eur J Vasc Endovasc Surg* 2009;**38**:463–74. https://doi.org/10.1016/j.ejvs.2009.06.002
340. Flint AC, Conell C, Ren X, Kamel H, Chan SL, Rao VA, *et al.* Statin adherence is associated with reduced recurrent stroke risk in patients with or without atrial fibrillation. *Stroke* 2017;**48**:1788–94. https://doi.org/10.1161/strokeaha.117.017343
341. Merwick Á, Albers GW, Arsava EM, Ay H, Calvet D, Coutts SB, *et al.* Reduction in early stroke risk in carotid stenosis with transient ischemic attack associated with statin treatment. *Stroke* 2013;**44**:2814–20. https://doi.org/10.1161/strokeaha.113.001576
342. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. *Lancet Neurol* 2009;**8**:453–63. https://doi.org/10.1016/s1474-4422(09)70058-4
343. Amarenco P, Bogousslavsky J, Callahan A, III, Goldstein LB, Hennerici M, Rudolph AE, *et al.* High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* 2006;**355**:549–59. https://doi.org/10.1056/NEJMoa061894
344. Hackam DG, Wu F, Li P, Austin PC, Tobe SW, Mamdani MM, *et al.* Statins and renovascular disease in the elderly: a population-based cohort study. *Eur Heart J* 2011;**32**:598–610. https://doi.org/10.1093/eurheartj/ehq452
345. Peng M, Dong H, Jiang X, Che W, Zou Y, Zhang Y, *et al.* A randomized unblinded trial to compare effects of intensive versus conventional lipid-lowering therapy in patients undergoing renal artery stenting. *J Cardiol* 2019;**74**:443–50. https://doi.org/10.1016/j.jjcc.2019.04.010
346. Vashist A, Heller EN, Brown EJ, Jr, Alhaddad IA. Renal artery stenosis: a cardiovascular perspective. *Am Heart J* 2002;**143**:559–64. https://doi.org/10.1067/mhj.2002.120769
347. Pan Z, Cui H, Wu N, Zhang H. Effect of statin therapy on abdominal aortic aneurysm growth rate and mortality: a systematic review and meta-analysis. *Ann Vasc Surg* 2020;**67**:503–10. https://doi.org/10.1016/j.avsg.2020.03.036
348. Salata K, Syed M, Hussain MA, de Mestral C, Greco E, Mamdani M, *et al.* Statins reduce abdominal aortic aneurysm growth, rupture, and perioperative mortality: a systematic review and meta-analysis. *J Am Heart Assoc* 2018;**7**:e008657. https://doi.org/10.1161/jaha.118.008657
349. Takagi H, Yamamoto H, Iwata K, Goto S, Umemoto T. Effects of statin therapy on abdominal aortic aneurysm growth: a meta-analysis and meta-regression of observational comparative studies. *Eur J Vasc Endovasc Surg* 2012;**44**:287–92. https://doi.org/10.1016/j.ejvs.2012.06.021
350. Stein LH, Berger J, Tranquilli M, Elefteraides JA. Effect of statin drugs on thoracic aortic aneurysms. *Am J Cardiol* 2013;**112**:1240–5. https://doi.org/10.1016/j.amjcard.2013.05.081
351. Jovin IS, Duggal M, Ebisu K, Paek H, Oprea AD, Tranquilli M, *et al.* Comparison of the effect on long-term outcomes in patients with thoracic aortic aneurysms of taking versus not taking a statin drug. *Am J Cardiol* 2012;**109**:1050–4. https://doi.org/10.1016/j.amjcard.2011.11.038
352. Skovbo Kristensen JS, Krasniqi L, Obel LM, Kavaliunaite E, Liisberg M, Lindholt JS. Exploring drug repurposing for treatment of abdominal aortic aneurysms: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2024;**67**:570–82. https://doi.org/10.1016/j.ejvs.2023.11.037
353. Rahman MN, Khan JA, Mazari FA, Mockford K, McCollum PT, Chetter IC. A randomized placebo controlled trial of the effect of preoperative statin use on matrix metalloproteinases and tissue inhibitors of matrix metalloproteinases in areas of low and peak wall stress in patients undergoing elective open repair of abdominal aortic aneurysm. *Ann Vasc Surg* 2011;**25**:32–8. https://doi.org/10.1016/j.avsg.2010.06.006
354. Periard D, Guessous I, Mazzolai L, Haesler E, Monney P, Hayoz D. Reduction of small infrarenal abdominal aortic aneurysm expansion rate by statins. *Vasa* 2012;**41**:35–42. https://doi.org/10.1024/0301-1526/a000161
355. Angeloni E, Vitaterna A, Pirelli M, Refice S. Effects of statin therapy on ascending aorta aneurysms growth: a propensity-matched analysis. *Int J Cardiol* 2015;**191**:52–5. https://doi.org/10.1016/j.ijcard.2015.05.001
356. Rowbotham SE, Krishna SM, Moran CS, Golledge J. Fenofibrate and telmisartan in the management of abdominal aortic aneurysm. *Curr Drug Targets* 2018;**19**:1241–6. https://doi.org/10.2174/1389450119666171227224655
357. Pinchbeck JL, Moxon JV, Rowbotham SE, Bourke M, Lazzaroni S, Morton SK, *et al.* Randomized placebo-controlled trial assessing the effect of 24-week fenofibrate therapy on circulating markers of abdominal aortic aneurysm: outcomes from the FAME-2 trial. *J Am Heart Assoc* 2018;**7**:e009866. https://doi.org/10.1161/JAHA.118.009866
358. Lamb YN. Inclisiran: first approval. *Drugs* 2021;**81**:389–95. https://doi.org/10.1007/s40265-021-01473-6
359. Ray KK, Bays HE, Catapano AL, Lalwani ND, Bloedon LT, Sterling LR, *et al.* Safety and efficacy of bempedoic acid to reduce LDL cholesterol. *N Engl J Med* 2019;**380**:1022–32. https://doi.org/10.1056/NEJMoa1803917
360. Ballantyne CM, Banach M, Mancini GBJ, Lepor NE, Hanselman JC, Zhao X, *et al.* Efficacy and safety of bempedoic acid added to ezetimibe in statin-intolerant patients with hypercholesterolemia: a randomized, placebo-controlled study. *Atherosclerosis* 2018;**277**:195–203. https://doi.org/10.1016/j.atherosclerosis.2018.06.002
361. Nissen SE, Lincoff AM, Brennan D, Ray KK, Mason D, Kastelein JJP, *et al.* Bempedoic acid and cardiovascular outcomes in statin-intolerant patients. *N Engl J Med* 2023;**388**:1353–64. https://doi.org/10.1056/NEJMoa2215024
362. Balling M, Afzal S, Davey Smith G, Varbo A, Langsted A, Kamstrup PR, *et al.* Elevated LDL triglycerides and atherosclerotic risk. *J Am Coll Cardiol* 2023;**81**:136–52. https://doi.org/10.1016/j.jacc.2022.10.019
363. Gao JW, Hao QY, Gao M, Zhang K, Li X-Z, Wang J-F, *et al.* Triglyceride-glucose index in the development of peripheral artery disease: findings from the Atherosclerosis Risk in Communities (ARIC) study. *Cardiovasc Diabetol* 2021;**20**:126. https://doi.org/10.1186/s12933-021-01319-1
364. Britton KA, Mukamal KJ, Ix JH, Siscovick DS, Newman AB, de Boer IH, *et al.* Insulin resistance and incident peripheral artery disease in the cardiovascular health study. *Vasc Med* 2012;**17**:85–93. https://doi.org/10.1177/1358863X11436195
365. Pande RL, Perlstein TS, Beckman JA, Creager MA. Association of insulin resistance and inflammation with peripheral arterial disease: the National Health and Nutrition Examination Survey, 1999 to 2004. *Circulation* 2008;**118**:33–41. https://doi.org/10.1161/CIRCULATIONAHA.107.721878
366. Wang D, Liu B, Tao W, Hao Z, Liu M. Fibrates for secondary prevention of cardiovascular disease and stroke. *Cochrane Database Syst Rev* 2015;**10**:CD009580. https://doi.org/10.1002/14651858.CD009580.pub2
367. Meade T, Zuhrie R, Cook C, Cooper J. Bezafibrate in men with lower extremity arterial disease: randomised controlled trial. *BMJ* 2002;**325**:1139. https://doi.org/10.1136/bmj.325.7373.1139
368. Bhatt DL, Steg PG, Miller M, Brinton EA, Jacobson TA, Ketchum SB, *et al.* Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. *N Engl J Med* 2019;**380**:11–22. https://doi.org/10.1056/NEJMoa1812792
369. Bhatt DS, Steg PG, Miller M, Brinton E, Jacobson T, Tardif J-C, *et al.* Abstract 10627: benefits of icosapent ethyl in patients with prior peripheral artery disease: REDUCE-IT PAD. *Circulation* 2021;**144**:A10627. https://doi.org/10.1161/circ.144.suppl_1.10627
370. Kobayashi Y, Fujikawa T, Haruna A, Kawano R, Ozawa M, Haze T, *et al.* Omega-3 fatty acids reduce remnant-like lipoprotein cholesterol and improve the ankle-brachial index of hemodialysis patients with dyslipidemia: a pilot study. *Medicina (Kaunas)* 2024;**60**:75. https://doi.org/10.3390/medicina60010075
371. Dopheide JF, Veit J, Ramadani H, Adam L, Papac L, Vonbank A, *et al.* Adherence to statin therapy favours survival of patients with symptomatic peripheral artery disease. *Eur Heart J Cardiovasc Pharmacother* 2021;**7**:263–70. https://doi.org/10.1093/ehjcvp/pvz081
372. Bonaca MP, Nault P, Giugliano RP, Keech AC, Pineda AL, Kanevsky E, *et al.* Low-density lipoprotein cholesterol lowering with evolocumab and outcomes in patients with peripheral artery disease: insights from the FOURIER trial (further cardiovascular outcomes research with PCSK9 inhibition in subjects with elevated risk). *Circulation* 2018;**137**:338–50. https://doi.org/10.1161/circulationaha.117.032235
373. Oyama K, Giugliano RP, Tang M, Bonaca MP, Saver JL, Murphy SA, *et al.* Effect of evolocumab on acute arterial events across all vascular territories: results from the FOURIER trial. *Eur Heart J* 2021;**42**:4821–9. https://doi.org/10.1093/eurheartj/ehab604
374. Marx N, Federici M, Schutt K, Müller-Wieland D, Ajjan RA, Antunes MJ, *et al.* 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J* 2023;**44**:4043–140. https://doi.org/10.1093/eurheartj/ehad192
375. Lazzarini PA, Cramb SM, Golledge J, Morton JI, Magliano DJ, Van Netten JJ. Global trends in the incidence of hospital admissions for diabetes-related foot disease and amputations: a review of national rates in the 21st century. *Diabetologia* 2023;**66**:267–87. https://doi.org/10.1007/s00125-022-05845-9
376. Armstrong PA. Visceral duplex scanning: evaluation before and after artery intervention for chronic mesenteric ischemia. *Perspect Vasc Surg Endovasc Ther* 2007;**19**:386–92; discussion 393–384. https://doi.org/10.1177/1531003507311802
377. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res* 2015;**116**:1509–26. https://doi.org/10.1161/CIRCRESAHA.116.303849
378. McGurnaghan SJ, McKeigue PM, Read SH, Franzen S, Svensson A-M, Colombo M, *et al.* Development and validation of a cardiovascular risk prediction model in type 1 diabetes. *Diabetologia* 2021;**64**:2001–11. https://doi.org/10.1007/s00125-021-05478-4

379. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med* 2017;**376**:2367–75. https://doi.org/10.1056/NEJMra1615439
380. Malyar NM, Freisinger E, Meyborg M, Lüders F, Gebauer K, Reinecke H, *et al.* Amputations and mortality in in-hospital treated patients with peripheral artery disease and diabetic foot syndrome. *J Diabetes Complications* 2016;**30**:1117–22. https://doi.org/10.1016/j.jdiacomp.2016.03.033
381. Verma S, Al-Omran M, Leiter LA, Mazer CD, Rasmussen S, Saevereid HA, *et al.* Cardiovascular efficacy of liraglutide and semaglutide in individuals with diabetes and peripheral artery disease. *Diabetes Obes Metab* 2022;**24**:1288–99. https://doi.org/10.1111/dom.14700
382. Verma S, Mazer CD, Al-Omran M, Inzucchi SE, Fitchett D, Hehnke U, *et al.* Cardiovascular outcomes and safety of empagliflozin in patients with type 2 diabetes mellitus and peripheral artery disease: a subanalysis of EMPA-REG OUTCOME. *Circulation* 2018;**137**:405–7. https://doi.org/10.1161/circulationaha.117.032031
383. American Diabetes Association. Standards of care in diabetes–2023 abridged for primary care providers. *Clin Diabetes* 2022;**41**:4–31. https://doi.org/10.2337/cd23-as01
384. Sattar N, McGuire DK. Prevention of CV outcomes in antihyperglycaemic drug-naive patients with type 2 diabetes with, or at elevated risk of, ASCVD: to start or not to start with metformin. *Eur Heart J* 2021;**42**:2574–6. https://doi.org/10.1093/eurheartj/ehaa879
385. Mahaffey KW, Neal B, Perkovic V, de Zeeuw D, Fulcher G, Erondu N, *et al.* Canagliflozin for primary and secondary prevention of cardiovascular events: results from the CANVAS program (canagliflozin cardiovascular assessment study). *Circulation* 2018;**137**:323–34. https://doi.org/10.1161/CIRCULATIONAHA.117.032038
386. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, *et al.* Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med* 2017;**377**:644–57. https://doi.org/10.1056/NEJMoa1611925
387. Goldenberg RM, Cheng AYY, Fitzpatrick T, Gilbert JD, Verma S, Hopyan JJ. Benefits of GLP-1 (glucagon-like peptide 1) receptor agonists for stroke reduction in type 2 diabetes: a call to action for neurologists. *Stroke* 2022;**53**:1813–22. https://doi.org/10.1161/STROKEAHA.121.038151
388. Malhotra K, Katsanos AH, Lambadiari V, Goyal N, Palaiodimou L, Kosmidou M, *et al.* GLP-1 receptor agonists in diabetes for stroke prevention: a systematic review and meta-analysis. *J Neurol* 2020;**267**:2117–22. https://doi.org/10.1007/s00415-020-09813-4
389. Tsai WH, Chuang SM, Liu SC, Lee C-C, Chien M-N, Leung C-H, *et al.* Effects of SGLT2 inhibitors on stroke and its subtypes in patients with type 2 diabetes: a systematic review and meta-analysis. *Sci Rep* 2021;**11**:15364. https://doi.org/10.1038/s41598-021-94945-4
390. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;**352**:854–65 .
391. Kooy A, de Jager J, Lehert P, Bets D, Wulffelé MG, Donker AJM, *et al.* Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. *Arch Intern Med* 2009;**169**:616–25. https://doi.org/10.1001/archinternmed.2009.20
392. Tan S, Goudot G, Arnoux A, Tran Y, Maissoro H, Poenou G, *et al.* Occurrence of major local lower limb events in type 2 diabetic patients with lower extremity arterial disease: impact of metformin. *Ann Vasc Surg* 2023;**90**:153–61. https://doi.org/10.1016/j.avsg.2022.09.064
393. Ferrannini G, Gerstein H, Colhoun HM, Dagenais GR, Diaz R, Dyal L, *et al.* Similar cardiovascular outcomes in patients with diabetes and established or high risk for coronary vascular disease treated with dulaglutide with and without baseline metformin. *Eur Heart J* 2021;**42**:2565–73. https://doi.org/10.1093/eurheartj/ehaa777
394. Zoungas S, Arima H, Gerstein HC, Holman RR, Woodward M, Reaven P, *et al.* Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. *Lancet Diabetes Endocrinol* 2017;**5**:431–7. https://doi.org/10.1016/S2213-8587(17)30104-3
395. Group AC, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, *et al.* Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2008;**358**:2560–72. https://doi.org/10.1056/NEJMoa0802987
396. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;**352**:837–53. https://doi.org/10.1016/S0140-6736(98)07019-6
397. Diabetes Control and Complications Trial Research Group; Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, *et al.* The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;**329**:977–86. https://doi.org/10.1056/NEJM199309303291401
398. McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZI, Dagogo-Jack S, *et al.* Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. *JAMA Cardiol* 2021;**6**:148–58. https://doi.org/10.1001/jamacardio.2020.4511
399. Bhatt DL, Szarek M, Steg PG, Cannon CP, Leiter LA, McGuire DK, *et al.* Sotagliflozin in patients with diabetes and recent worsening heart failure. *N Engl J Med* 2021;**384**:117–28. https://doi.org/10.1056/NEJMoa2030183
400. Bhatt DL, Szarek M, Pitt B, Cannon CP, Leiter LA, McGuire DK, *et al.* Sotagliflozin in patients with diabetes and chronic kidney disease. *N Engl J Med* 2021;**384**:129–39. https://doi.org/10.1056/NEJMoa2030186
401. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, *et al.* Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2019;**380**:347–57. https://doi.org/10.1056/NEJMoa1812389
402. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, *et al.* Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015;**373**:2117–28. https://doi.org/10.1056/NEJMoa1504720
403. Sattar N, Lee MMY, Kristensen SL, Branch KRH, Del Prato S, Khurmi NS, *et al.* Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. *Lancet Diabetes Endocrinol* 2021;**9**:653–62. https://doi.org/10.1016/S2213-8587(21)00203-5
404. Gerstein HC, Sattar N, Rosenstock J, Ramasundarahettige C, Pratley R, Lopes RD, *et al.* Cardiovascular and renal outcomes with efpeglenatide in type 2 diabetes. *N Engl J Med* 2021;**385**:896–907. https://doi.org/10.1056/NEJMoa2108269
405. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, *et al.* Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet* 2019;**394**:121–30. https://doi.org/10.1016/S0140-6736(19)31149-3
406. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JFE, Nauck MA, *et al.* Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;**375**:311–22. https://doi.org/10.1056/NEJMoa1603827
407. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, *et al.* Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2016;**375**:1834–44. https://doi.org/10.1056/NEJMoa1607141
408. International Hypoglycaemia Study Group. Hypoglycaemia, cardiovascular disease, and mortality in diabetes: epidemiology, pathogenesis, and management. *Lancet Diabetes Endocrinol* 2019;**7**:385–96. https://doi.org/10.1016/S2213-8587(18)30315-2
409. Zoungas S, Chalmers J, Ninomiya T, Li Q, Cooper ME, Colagiuri S, *et al.* Association of HbA1c levels with vascular complications and death in patients with type 2 diabetes: evidence of glycaemic thresholds. *Diabetologia* 2012;**55**:636–43. https://doi.org/10.1007/s00125-011-2404-1
410. Currie CJ, Peters JR, Tynan A, Evans M, Heine RJ, Bracco OL, *et al.* Survival as a function of HbA(1c) in people with type 2 diabetes: a retrospective cohort study. *Lancet* 2010;**375**:481–9. https://doi.org/10.1016/S0140-6736(09)61969-3
411. Control G, Turnbull FM, Abraira C, Anderson RJ, Byington RP, Chalmers JP, *et al.* Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia* 2009;**52**:2288–98. https://doi.org/10.1007/s00125-009-1470-0
412. Caturano A, Galiero R, Pafundi PC, Cesaro A, Vetrano E, Palmiero G, *et al.* Does a strict glycemic control during acute coronary syndrome play a cardioprotective effect? Pathophysiology and clinical evidence. *Diabetes Res Clin Pract* 2021;**178**:108959. https://doi.org/10.1016/j.diabres.2021.108959
413. Soehnlein O, Libby P. Targeting inflammation in atherosclerosis—from experimental insights to the clinic. *Nat Rev Drug Discov* 2021;**20**:589–610. https://doi.org/10.1038/s41573-021-00198-1
414. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Ballantyne C, *et al.* Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med* 2017;**377**:1119–31. https://doi.org/10.1056/NEJMoa1707914
415. Samuel M, Tardif JC, Bouabdallaoui N, Khairy P, Dubé M-P, Blondeau L, *et al.* Colchicine for secondary prevention of cardiovascular disease: a systematic review and meta-analysis of randomized controlled trials. *Can J Cardiol* 2021;**37**:776–85. https://doi.org/10.1016/j.cjca.2020.10.006
416. Antonopoulos AS, Papanikolaou E, Vogiatzi G, Oikonomou E, Tousoulis D. Anti-inflammatory agents in peripheral arterial disease. *Curr Opin Pharmacol* 2018;**39**:1–8. https://doi.org/10.1016/j.coph.2017.11.001
417. Mills JL, Sr, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy AN, *et al.* The Society for Vascular Surgery lower extremity threatened limb classification system: risk stratification based on wound, ischemia, and foot infection (WIfI). *J Vasc Surg* 2014;**59**:220–34.e1–2. https://doi.org/10.1016/j.jvs.2013.08.003
418. Fowkes FG, Aboyans V, Fowkes FJ, McDermott MM, Sampson UKA, Criqui MH, Peripheral artery disease: epidemiology and global perspectives. *Nat Rev Cardiol* 2017;**14**:156–70. https://doi.org/10.1038/nrcardio.2016.179
419. Diehm C, Allenberg JR, Pittrow D, Mahn M, Tepohl G, Haberl RL, *et al.* Mortality and vascular morbidity in older adults with asymptomatic versus symptomatic peripheral artery disease. *Circulation* 2009;**120**:2053–61. https://doi.org/10.1161/circulationaha.109.865600
420. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, *et al.* Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. *JAMA* 2001;**286**:1599–606. https://doi.org/10.1001/jama.286.13.1599
421. Sigvant B, Wiberg-Hedman K, Bergqvist D, Rolandsson O, Andersson B, Persson E, *et al.* A population-based study of peripheral arterial disease prevalence with special

focus on critical limb ischemia and sex differences. *J Vasc Surg* 2007;**45**:1185–91. https://doi.org/10.1016/j.jvs.2007.02.004
422. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR, *et al.* Inter-society consensus for the management of peripheral arterial disease (TASC II). *Eur J Vasc Endovasc Surg* 2007;**33**:S1–75. https://doi.org/10.1016/j.ejvs.2006.09.024
423. Buso G, Aboyans V, Mazzolai L. Lower extremity artery disease in patients with type 2 diabetes. *Eur J Prev Cardiol* 2019;**26**:114–24. https://doi.org/10.1177/2047487319880044
424. Porras CP, Bots ML, Teraa M, van Doorn S, Vernooij RWM. Differences in symptom presentation in women and men with confirmed lower limb peripheral artery disease: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2022;**63**:602–12. https://doi.org/10.1016/j.ejvs.2021.12.039
425. Fereydooni A, Gorecka J, Dardik A. Using the epidemiology of critical limb ischemia to estimate the number of patients amenable to endovascular therapy. *Vasc Med* 2020;**25**:78–87. https://doi.org/10.1177/1358863X19878271
426. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, *et al.* Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg* 2019;**58**:S1–109.e33. https://doi.org/10.1016/j.ejvs.2019.05.006
427. Sigvant B, Lundin F, Wahlberg E. The risk of disease progression in peripheral arterial disease is higher than expected: a meta-analysis of mortality and disease progression in peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2016;**51**:395–403. https://doi.org/10.1016/j.ejvs.2015.10.022
428. Hageman SHJ, de Borst GJ, Dorresteijn JAN, Bots ML, Westerink J, Asselbergs FW, *et al.* Cardiovascular risk factors and the risk of major adverse limb events in patients with symptomatic cardiovascular disease. *Heart* 2020;**106**:1686–92. https://doi.org/10.1136/heartjnl-2019-316088
429. Anand SS, Caron F, Eikelboom JW, Bosch J, Dyal L, Aboyans V, *et al.* Major adverse limb events and mortality in patients with peripheral artery disease: the COMPASS trial. *J Am Coll Cardiol* 2018;**71**:2306–15. https://doi.org/10.1016/j.jacc.2018.03.008
430. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, *et al.* Rivaroxaban with or without aspirin in stable cardiovascular disease. *N Engl J Med* 2017;**377**:1319–30. https://doi.org/10.1056/NEJMoa1709118
431. Agnelli G, Belch JJF, Baumgartner I, Giovas P, Hoffmann U. Morbidity and mortality associated with atherosclerotic peripheral artery disease: a systematic review. *Atherosclerosis* 2020;**293**:94–100. https://doi.org/10.1016/j.atherosclerosis.2019.09.012
432. Wijnand JGJ, van Koeverden ID, Teraa M, Spreen MI, Mali WPTM, van Overhagen H, *et al.* Validation of randomized controlled trial-derived models for the prediction of postintervention outcomes in chronic limb-threatening ischemia. *J Vasc Surg* 2020;**71**:869–79. https://doi.org/10.1016/j.jvs.2019.06.195
433. Jaramillo EA, Smith EJT, Matthay ZA, Sanders KM, Hiramoto JS, Gasper WJ, *et al.* Racial and ethnic disparities in major adverse limb events persist for chronic limb threatening ischemia despite presenting limb threat severity after peripheral vascular intervention. *J Vasc Surg* 2023;**77**:848–57.e2. https://doi.org/10.1016/j.jvs.2022.10.043
434. Brizuela Sanz JA, Gonzalez Fajardo JA, Taylor JH, Río Solá L, Muñoz Moreno MF, Vaquero Puerta C, *et al.* Design of a new risk score in critical limb ischaemia: the ERICVA model. *Eur J Vasc Endovasc Surg* 2016;**51**:90–9. https://doi.org/10.1016/j.ejvs.2015.09.025
435. Kreutzburg T, Peters F, Kuchenbecker J, Marschall U, Lee R, Kriston L, *et al.* Editor's choice—the GermanVasc score: a pragmatic risk score predicts five year amputation free survival in patients with peripheral arterial occlusive disease. *Eur J Vasc Endovasc Surg* 2021;**61**:248–56. https://doi.org/10.1016/j.ejvs.2020.11.013
436. Niazi K, Khan TH, Easley KA. Diagnostic utility of the two methods of ankle brachial index in the detection of peripheral arterial disease of lower extremities. *Catheter Cardiovasc Interv* 2006;**68**:788–92. https://doi.org/10.1002/ccd.20906
437. Crawford F, Welch K, Andras A, Chappell FM. Ankle brachial index for the diagnosis of lower limb peripheral arterial disease. *Cochrane Database Syst Rev* 2016;**9**:CD010680. https://doi.org/10.1002/14651858.CD010680.pub2
438. Aday AW, Kinlay S, Gerhard-Herman MD. Comparison of different exercise ankle pressure indices in the diagnosis of peripheral artery disease. *Vasc Med* 2018;**23**:541–8. https://doi.org/10.1177/1358863X18781723
439. Tehan PE, Barwick AL, Sebastian M, Chuter VH. Diagnostic accuracy of the postexercise ankle-brachial index for detecting peripheral artery disease in suspected claudicants with and without diabetes. *Vasc Med* 2018;**23**:116–25. https://doi.org/10.1177/1358863X17751259
440. Manu CA, Freedman B, Rashid H, Winkley K, Edmonds ME. Peripheral arterial disease located in the feet of patients with diabetes and foot ulceration demands a new approach to the assessment of ischemia. *Int J Low Extrem Wounds* 2022;**21**:397–404. https://doi.org/10.1177/1534734620947979
441. Salaun P, Desormais I, Lapébie FX, Rivière AB, Aboyans V, Lacroix P, *et al.* Comparison of ankle pressure, systolic toe pressure, and transcutaneous oxygen pressure to predict major amputation after 1 year in the copart cohort. *Angiology* 2019;**70**:229–36. https://doi.org/10.1177/0003319718793566
442. Fowkes FG, Murray GD, Butcher I, Folsom AR, Hirsch AT, Couper DJ, *et al.* Development and validation of an ankle brachial index risk model for the prediction of cardiovascular events. *Eur J Prev Cardiol* 2014;**21**:310–20. https://doi.org/10.1177/2047487313516564
443. Wang FM, Yang C, Ballew SH, Kalbaugh CA, Meyer ML, Tanaka H, *et al.* Ankle-brachial index and subsequent risk of incident and recurrent cardiovascular events in older adults: the Atherosclerosis Risk in Communities (ARIC) study. *Atherosclerosis* 2021;**336**:39–47. https://doi.org/10.1016/j.atherosclerosis.2021.09.028
444. Cull DL, Manos G, Hartley MC, Taylor SM, Langan EM, Eidt JF, *et al.* An early validation of the Society for Vascular Surgery lower extremity threatened limb classification system. *J Vasc Surg* 2014;**60**:1535–42. https://doi.org/10.1016/j.jvs.2014.08.107
445. Liette MD, Crisologo PA, Masadeh S, Yang SH, Bergmann CB, Caldwell CC, *et al.* A prospective analysis of the SVS WIfI classification system to stratify immediate and 1-year patient outcomes. *J Foot Ankle Surg* 2023;**62**:661–5. https://doi.org/10.1053/j.jfas.2023.02.003
446. van Reijen NS, Ponchant K, Ubbink DT, Koelemay MJW. Editor's choice—the prognostic value of the WIfI classification in patients with chronic limb threatening ischaemia: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2019;**58**:362–71. https://doi.org/10.1016/j.ejvs.2019.03.040
447. Eiberg JP, Gronvall Rasmussen JB, Hansen MA, Schroeder TV. Duplex ultrasound scanning of peripheral arterial disease of the lower limb. *Eur J Vasc Endovasc Surg* 2010;**40**:507–12. https://doi.org/10.1016/j.ejvs.2010.06.002
448. Met R, Bipat S, Legemate DA, Reekers JA, Koelemay MJ. Diagnostic performance of computed tomography angiography in peripheral arterial disease: a systematic review and meta-analysis. *JAMA* 2009;**301**:415–24. https://doi.org/10.1001/jama.301.4.415
449. Itoga NK, Kim T, Sailer AM, Fleischmann D, Mell MW. Lower extremity computed tomography angiography can help predict technical success of endovascular revascularization in the superficial femoral and popliteal artery. *J Vasc Surg* 2017;**66**:835–43.e1. https://doi.org/10.1016/j.jvs.2017.02.031
450. Selvin E, Hirsch AT. Contemporary risk factor control and walking dysfunction in individuals with peripheral arterial disease: NHANES 1999–2004. *Atherosclerosis* 2008;**201**:425–33. https://doi.org/10.1016/j.atherosclerosis.2008.02.002
451. Pande RL, Perlstein TS, Beckman JA, Creager MA. Secondary prevention and mortality in peripheral artery disease: National Health and Nutrition Examination Study, 1999 to 2004. *Circulation* 2011;**124**:17–23. https://doi.org/10.1161/circulationaha.110.003954
452. Krishnamurthy V, Munir K, Rectenwald JE, Mansour A, Hans S, Eliason JL, *et al.* Contemporary outcomes with percutaneous vascular interventions for peripheral critical limb ischemia in those with and without poly-vascular disease. *Vasc Med* 2014;**19**:491–9. https://doi.org/10.1177/1358863x14552013
453. Penin-Grandes S, Lopez-Ortiz S, Maroto-Izquierdo S, Menéndez H, Pinto-Fraga J, Martín-Hernández J, *et al.* Winners do what they fear: exercise and peripheral arterial disease–an umbrella review. *Eur J Prev Cardiol* 2024;**31**:380–388. https://doi.org/10.1093/eurjpc/zwad261
454. Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. *JAMA* 1995;**274**:975–80.
455. Parmenter BJ, Raymond J, Dinnen P, Singh MA. A systematic review of randomized controlled trials: walking versus alternative exercise prescription as treatment for intermittent claudication. *Atherosclerosis* 2011;**218**:1–12. https://doi.org/10.1016/j.atherosclerosis.2011.04.024
456. Fakhry F, van de Luijtgaarden KM, Bax L, den Hoed PT, Hunink MGGM, Rouwet EV, *et al.* Supervised walking therapy in patients with intermittent claudication. *J Vasc Surg* 2012;**56**:1132–42. https://doi.org/10.1016/j.jvs.2012.04.046
457. Parmenter BJ, Dieberg G, Smart NA. Exercise training for management of peripheral arterial disease: a systematic review and meta-analysis. *Sports Med* 2015;**45**:231–44. https://doi.org/10.1007/s40279-014-0261-z
458. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. *Cochrane Database Syst Rev* 2017;**12**:CD000990. https://doi.org/10.1002/14651858.CD000990.pub4
459. Parmenter BJ, Mavros Y, Ritti Dias R, King S, Fiatarone Singh M. Resistance training as a treatment for older persons with peripheral artery disease: a systematic review and meta-analysis. *Br J Sports Med* 2020;**54**:452–61. https://doi.org/10.1136/bjsports-2018-100205
460. Perks J, Zaccardi F, Paterson C, Houghton JSM, Nickinson ATO, Pepper CJ, *et al.* Effect of high-pain versus low-pain structured exercise on walking ability in people with intermittent claudication: meta-analysis. *Br J Surg* 2022;**109**:686–94. https://doi.org/10.1093/bjs/znac134
461. Guidon M, McGee H. Exercise-based interventions and health-related quality of life in intermittent claudication: a 20-year (1989–2008) review. *Eur J Cardiovasc Prev Rehabil* 2010;**17**:140–54. https://doi.org/10.1097/HJR.0b013e3283377f08
462. Parmenter BJ, Dieberg G, Phipps G, Smart NA. Exercise training for health-related quality of life in peripheral artery disease: a systematic review and meta-analysis. *Vasc Med* 2015;**20**:30–40. https://doi.org/10.1177/1358863x14559092
463. Gommans LN, Fokkenrood HJ, van Dalen HC, Scheltinga MRM, Teijink JAW, Peters RJG. Safety of supervised exercise therapy in patients with intermittent claudication. *J Vasc Surg* 2015;**61**:512–8.e2. https://doi.org/10.1016/j.jvs.2014.08.070
464. Harwood AE, Pymer S, Ibeggazene S, Ingle L, Caldow E, Birkett ST. Provision of exercise services in patients with peripheral artery disease in the United Kingdom. *Vascular* 2022;**30**:874–81. https://doi.org/10.1177/17085381211035259

465. Lanzi S, Belch J, Brodmann M, Madaric J, Bura-Riviere A, Visonà A, *et al.* Supervised exercise training in patients with lower extremity peripheral artery disease. *Vasa* 2022;**51**:267–74. https://doi.org/10.1024/0301-1526/a001024
466. Gommans LN, Saarloos R, Scheltinga MR, Houterman S, de Bie RA, Fokkenrood HJP, *et al.* Editor's choice—the effect of supervision on walking distance in patients with intermittent claudication: a meta-analysis. *Eur J Vasc Endovasc Surg* 2014;**48**:169–84. https://doi.org/10.1016/j.ejvs.2014.04.019
467. Vemulapalli S, Dolor RJ, Hasselblad V, Schmit K, Banks A, Heidenfelder B, *et al.* Supervised vs unsupervised exercise for intermittent claudication: a systematic review and meta-analysis. *Am Heart J* 2015;**169**:924–37.e3. https://doi.org/10.1016/j.ahj.2015.03.009
468. Hageman D, Fokkenrood HJ, Gommans LN, van den Houten MM, Teijink JA. Supervised exercise therapy versus home-based exercise therapy versus walking advice for intermittent claudication. *Cochrane Database Syst Rev* 2018;**4**:CD005263. https://doi.org/10.1002/14651858.CD005263.pub4
469. Pymer S, Ibeggazene S, Palmer J, Tew GA, Ingle L, Smith GE, *et al.* An updated systematic review and meta-analysis of home-based exercise programs for individuals with intermittent claudication. *J Vasc Surg* 2021;**74**:2076–85.e20. https://doi.org/10.1016/j.jvs.2021.03.063
470. Waddell A, Seed S, Broom DR, McGregor G, Birkett ST, Harwood AE. Safety of home-based exercise for people with intermittent claudication: a systematic review. *Vasc Med* 2022;**27**:186–92. https://doi.org/10.1177/1358863x211060388
471. Golledge J, Singh TP, Alahakoon C, Pinchbeck J, Yip L, Moxon JV, *et al.* Meta-analysis of clinical trials examining the benefit of structured home exercise in patients with peripheral artery disease. *Br J Surg* 2019;**106**:319–31. https://doi.org/10.1002/bjs.11101
472. Bulmer AC, Coombes JS. Optimising exercise training in peripheral arterial disease. *Sports Med* 2004;**34**:983–1003. https://doi.org/10.2165/00007256-200434140-00004
473. Ehrman JK, Gardner AW, Salisbury D, Lui K, Treat-Jacobson D. Supervised exercise therapy for symptomatic peripheral artery disease: a review of current experience and practice-based recommendations. *J Cardiopulm Rehabil Prev* 2023;**43**:15–21. https://doi.org/10.1097/hcr.0000000000000723
474. McDermott MM, Spring B, Tian L, Treat-Jacobson D, Ferrucci L, Lloyd-Jones D, *et al.* Effect of low-intensity vs high-intensity home-based walking exercise on walk distance in patients with peripheral artery disease: the LITE randomized clinical trial. *JAMA* 2021;**325**:1266–76. https://doi.org/10.1001/jama.2021.2536
475. Jansen SC, Abaraogu UO, Lauret GJ, Fakhry F, Fokkenrood HJP, Teijink JAW. Modes of exercise training for intermittent claudication. *Cochrane Database Syst Rev* 2020;**8**:CD009638. https://doi.org/10.1002/14651858.CD009638.pub3
476. Gardner AW, Parker DE, Montgomery PS, Blevins SM. Diabetic women are poor responders to exercise rehabilitation in the treatment of claudication. *J Vasc Surg* 2014;**59**:1036–43. https://doi.org/10.1016/j.jvs.2013.10.058
477. Gommans LN, Scheltinga MR, van Sambeek MR, Maas AHEM, Bendermacher BLW, Teijink JAW. Gender differences following supervised exercise therapy in patients with intermittent claudication. *J Vasc Surg* 2015;**62**:681–8. https://doi.org/10.1016/j.jvs.2015.03.076
478. Dipnarine K, Barak S, Martinez CA, Carmeli E, Stopka CB. Pain-free treadmill exercise for patients with intermittent claudication: are there gender differences? *Vascular* 2016;**24**:304–14. https://doi.org/10.1177/1708538115592800
479. Gardner AW, Parker DE, Montgomery PS. Sex-specific predictors of improved walking with step-monitored, home-based exercise in peripheral artery disease. *Vasc Med* 2015;**20**:424–31. https://doi.org/10.1177/1358863x15596237
480. Ney B, Lanzi S, Calanca L, Mazzolai L. Multimodal supervised exercise training is effective in improving long term walking performance in patients with symptomatic lower extremity peripheral artery disease. *J Clin Med* 2021;**10**:2057.https://doi.org/10.3390/jcm10102057
481. Lanzi S, Pousaz A, Calanca L, Mazzolai L. Sex-based differences in supervised exercise therapy outcomes for symptomatic peripheral artery disease. *Vasc Med* 2023;**28**:147–9. https://doi.org/10.1177/1358863x221149454
482. Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JAW, Hoffmann WH, *et al.* Endovascular revascularization and supervised exercise for peripheral artery disease and intermittent claudication: a randomized clinical trial. *JAMA* 2015;**314**:1936–44. https://doi.org/10.1001/jama.2015.14851
483. Pandey A, Banerjee S, Ngo C, Mody P, Marso SP, Brilakis ES, *et al.* Comparative efficacy of endovascular revascularization versus supervised exercise training in patients with intermittent claudication: meta-analysis of randomized controlled trials. *JACC Cardiovasc Interv* 2017;**10**:712–24. https://doi.org/10.1016/j.jcin.2017.01.027
484. Dorn A, Dorweiler B, Ahmad W, Mylonas S, Becker I, Majd P. Low and high ankle-brachial index are both associated with mortality in German nursing home residents–the five-year follow-up of the 'allo-study' Cohort. *J Clin Med* 2023;**12**:4411. https://doi.org/10.3390/jcm12134411
485. Fowkes FG, Price JF, Stewart MC, Butcher I, Leng GC, Pell AC, *et al.* Aspirin for prevention of cardiovascular events in a general population screened for a low ankle brachial index: a randomized controlled trial. *JAMA* 2010;**303**:841–8. https://doi.org/10.1001/jama.2010.221
486. Belch J, MacCuish A, Campbell I, Cobbe S, Taylor R, Prescott R, *et al.* The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ* 2008;**337**:a1840. https://doi.org/10.1136/bmj.a1840
487. Bowman L, Mafham M, Wallendszus K, Stevens W, Buck G, Barton J, *et al.* Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med* 2018;**379**:1529–39. https://doi.org/10.1056/NEJMoa1804988
488. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;**324**:71–86. https://doi.org/10.1136/bmj.324.7329.71
489. De Carlo M, Di Minno G, Sayre T, Fazeli MS, Siliman G, Cimminiello C. Efficacy and safety of antiplatelet therapies in symptomatic peripheral artery disease: a systematic review and network meta-analysis. *Curr Vasc Pharmacol* 2021;**19**:542–55. https://doi.org/10.2174/1570161118666200820141131
490. Willems LH, Maas D, Kramers K, Reijnen MMPJ, Riksen NP, Ten Cate H, *et al.* Antithrombotic therapy for symptomatic peripheral arterial disease: a systematic review and network meta-analysis. *Drugs* 2022;**82**:1287–302. https://doi.org/10.1007/s40265-022-01756-6
491. Katsanos K, Spiliopoulos S, Saha P, Diamantopoulos A, Karunanithy N, Krokidis M, *et al.* Comparative efficacy and safety of different antiplatelet agents for prevention of major cardiovascular events and leg amputations in patients with peripheral arterial disease: a systematic review and network meta-analysis. *PLoS One* 2015;**10**:e0135692. https://doi.org/10.1371/journal.pone.0135692
492. Basili S, Raparelli V, Vestri A, Di Tanna GL, Violi F. Comparison of efficacy of antiplatelet treatments for patients with claudication. A meta-analysis. *Thromb Haemost* 2010;**103**:766–73. https://doi.org/10.1160/th09-09-0635
493. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. *Lancet* 1996;**348**:1329–39. https://doi.org/10.1016/s0140-6736(96)09457-3
494. Berger JS, Krantz MJ, Kittelson JM, Hiatt WR. Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease: a meta-analysis of randomized trials. *JAMA* 2009;**301**:1909–19. https://doi.org/10.1001/jama.2009.623
495. Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, *et al.* Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. *N Engl J Med* 2017;**376**:32–40. https://doi.org/10.1056/NEJMoa1611688
496. Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, *et al.* Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med* 2006;**354**:1706–17. https://doi.org/10.1056/NEJMoa060989
497. Bhatt DL, Flather MD, Hacke W, Berger PB, Black HR, Boden WE, *et al.* Patients with prior myocardial infarction, stroke, or symptomatic peripheral arterial disease in the CHARISMA trial. *J Am Coll Cardiol* 2007;**49**:1982–8. https://doi.org/10.1016/j.jacc.2007.03.025
498. Kaplovitch E, Eikelboom JW, Dyal L, Aboyans V, Abola MT, Verhamme P, *et al.* Rivaroxaban and aspirin in patients with symptomatic lower extremity peripheral artery disease: a subanalysis of the COMPASS randomized clinical trial. *JAMA Cardiol* 2021;**6**:21–9. https://doi.org/10.1001/jamacardio.2020.4390
499. Anand SS, Bosch J, Eikelboom JW, Connolly SJ, Diaz R, Widimsky P, *et al.* Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2018;**391**:219–29. https://doi.org/10.1016/s0140-6736(17)32409-1
500. Strobl FF, Brechtel K, Schmehl J, Zeller T, Reiser MF, Claussen CD, *et al.* Twelve-month results of a randomized trial comparing mono with dual antiplatelet therapy in endovascularly treated patients with peripheral artery disease. *J Endovasc Ther* 2013;**20**:699–706. https://doi.org/10.1583/13-4275mr.1
501. Tsai SY, Li YS, Lee CH, Cha S-W, Wang Y-C, Su T-W, *et al.* Mono or dual antiplatelet therapy for treating patients with peripheral artery disease after lower extremity revascularization: a systematic review and meta-analysis. *Pharmaceuticals (Basel)* 2022;**15**:596. https://doi.org/10.3390/ph15050596
502. Thott O, Granath F, Malmstedt J, Wahlgren CM. Editor's choice—dual antiplatelet therapy improves outcome in diabetic patients undergoing endovascular femoropopliteal stenting for critical limb ischaemia. *Eur J Vasc Endovasc Surg* 2017;**53**:403–10. https://doi.org/10.1016/j.ejvs.2016.12.014
503. Cho S, Lee YJ, Ko YG, Kang TS, Lim S-H, Hong S-J, *et al.* Optimal strategy for antiplatelet therapy after endovascular revascularization for lower extremity peripheral artery disease. *JACC Cardiovasc Interv* 2019;**12**:2359–70. https://doi.org/10.1016/j.jcin.2019.08.006
504. Ipema J, Welling RHA, Bakker OJ, Bokkers RPH, de Vries J-PPM, Ünlü Ç. Short-term clinical outcomes of single versus dual antiplatelet therapy after infrainguinal endovascular treatment for peripheral arterial disease. *J Clin Med* 2020;**9**:3515. https://doi.org/10.3390/jcm9113515
505. Bonaca MP, Bauersachs RM, Anand SS, Debus ES, Nehler MR, Patel MR, *et al.* Rivaroxaban in peripheral artery disease after revascularization. *N Engl J Med* 2020;**382**:1994–2004. https://doi.org/10.1056/NEJMoa2000052
506. Hiatt WR, Bonaca MP, Patel MR, Nehler MR, Debus ES, Anand SS, *et al.* Rivaroxaban and aspirin in peripheral artery disease lower extremity revascularization: impact of concomitant clopidogrel on efficacy and safety. *Circulation* 2020;**142**:2219–30. https://doi.org/10.1161/circulationaha.120.050465

507. Duff S, Mafilios MS, Bhounsule P, Hasegawa JT. The burden of critical limb ischemia: a review of recent literature. *Vasc Health Risk Manag* 2019;**15**:187–208. https://doi.org/10.2147/VHRM.S209241
508. Sarac TP, Huber TS, Back MR, Ozaki CK, Carlton LM, Flynn TC, *et al.* Warfarin improves the outcome of infrainguinal vein bypass grafting at high risk for failure. *J Vasc Surg* 1998;**28**:446–57. https://doi.org/10.1016/s0741-5214(98)70130-2
509. Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (the Dutch bypass oral anticoagulants or aspirin study): a randomised trial. *Lancet* 2000;**355**:346–51. https://doi.org/10.1016/S0140-6736(99)07199-8
510. Belch JJ, Dormandy J, Biasi GM, Cairols M, Diehm C, Eikelboom B, *et al.* Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. *J Vasc Surg* 2010;**52**:825–33.e2. https://doi.org/10.1016/j.jvs.2010.04.027
511. Brumberg RS, Back MR, Armstrong PA, Cuthbertson D, Shames ML, Johnson BL, *et al.* The relative importance of graft surveillance and warfarin therapy in infrainguinal prosthetic bypass failure. *J Vasc Surg* 2007;**46**:1160–6. https://doi.org/10.1016/j.jvs.2007.07.046
512. Van Gelder IC, Kotecha D, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, *et al.* 2024 ESC Guidelines for the management of atrial fibrillation. *Eur Heart J* 2024. https://doi.org/10.1093/eurheartj/ehae176
513. Spiliopoulos S, Pastromas G, Katsanos K, Kitrou P, Karnabatidis D, Siablis D. Platelet responsiveness to clopidogrel treatment after peripheral endovascular procedures: the PRECLOP study: clinical impact and optimal cutoff value of on-treatment high platelet reactivity. *J Am Coll Cardiol* 2013;**61**:2428–34. https://doi.org/10.1016/j.jacc.2013.03.036
514. Busch L, Stern M, Dannenberg L, Mourikis P, Gröne M, Özaslan G, *et al.* Impact of high on-treatment platelet reactivity after angioplasty in patients with peripheral arterial disease. *Platelets* 2021;**32**:391–7. https://doi.org/10.1080/09537104.2020.1742314
515. Cosmi B, Conti E, Coccheri S. Anticoagulants (heparin, low molecular weight heparin and oral anticoagulants) for intermittent claudication. *Cochrane Database Syst Rev* 2014;**5**:CD001999. https://doi.org/10.1002/14651858.CD001999.pub2
516. Bagger JP, Helligsoe P, Randsbaek F, Kimose HH, Jensen BS. Effect of verapamil in intermittent claudication. A randomized, double-blind, placebo-controlled, cross-over study after individual dose-response assessment. *Circulation* 1997;**95**:411–4. https://doi.org/10.1161/01.cir.95.2.411
517. Gargiulo G, Giugliano G, Brevetti L, Sannino A, Schiattarella GG, Serino F, *et al.* Use of statins in lower extremity artery disease: a review. *BMC Surg* 2012;**12**:S15. https://doi.org/10.1186/1471-2482-12-s1-s15
518. McDermott MM, Guralnik JM, Greenland P, Pearce WH, Criqui MH, Liu K, *et al.* Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. *Circulation* 2003;**107**:757–61. https://doi.org/10.1161/01.cir.0000050380.64025.07
519. Robertson L, Andras A. Prostanoids for intermittent claudication. *Cochrane Database Syst Rev* 2013;**4**:CD000986. https://doi.org/10.1002/14651858.CD000986.pub3
520. Stevens JW, Simpson E, Harnan S, Squires H, Meng Y, Thomas S, *et al.* Systematic review of the efficacy of cilostazol, naftidrofuryl oxalate and pentoxifylline for the treatment of intermittent claudication. *Br J Surg* 2012;**99**:1630–8. https://doi.org/10.1002/bjs.8895
521. Bedenis R, Stewart M, Cleanthis M, Robless P, Mikhailidis DP, Stansby G. Cilostazol for intermittent claudication. *Cochrane Database Syst Rev* 2014;**10**:CD003748. https://doi.org/10.1002/14651858.CD003748.pub4
522. Hiatt WR, Money SR, Brass EP. Long-term safety of cilostazol in patients with peripheral artery disease: the CASTLE study (cilostazol: a study in long-term effects). *J Vasc Surg* 2008;**47**:330–6. https://doi.org/10.1016/j.jvs.2007.10.009
523. Iida O, Yokoi H, Soga Y, Inoue N, Suzuki K, Yokoi Y, *et al.* Cilostazol reduces angiographic restenosis after endovascular therapy for femoropopliteal lesions in the sufficient treatment of peripheral intervention by cilostazol study. *Circulation* 2013;**127**:2307–15. https://doi.org/10.1161/circulationaha.112.000711
524. de Backer TL, Vander Stichele R, Lehert P, Van Bortel L. Naftidrofuryl for intermittent claudication. *Cochrane Database Syst Rev* 2012;**12**:Cd001368. https://doi.org/10.1002/14651858.CD001368.pub4
525. Boccalon H, Lehert P, Mosnier M. Effect of naftidrofuryl on physiological walking distance in patients with intermittent claudication. *Ann Cardiol Angeiol* 2001;**50**:175–82. https://doi.org/10.1016/s0003-3928(01)00016-6
526. Broderick C, Forster R, Abdel-Hadi M, Salhiyyah K. Pentoxifylline for intermittent claudication. *Cochrane Database Syst Rev* 2020;**10**:Cd005262. https://doi.org/10.1002/14651858.CD005262.pub4
527. Nicolaï SP, Kruidenier LM, Bendermacher BL, Prins MH, Stokmans RA, Broos PPHL, *et al.* Ginkgo biloba for intermittent claudication. *Cochrane Database Syst Rev* 2013;**6**:Cd006888. https://doi.org/10.1002/14651858.CD006888.pub3
528. Premaratne S, Newman J, Hobbs S, Garnham A, Wall M. Meta-analysis of direct surgical versus endovascular revascularization for aortoiliac occlusive disease. *J Vasc Surg* 2020;**72**:726–37. https://doi.org/10.1016/j.jvs.2019.12.035
529. Aboyans V, Björck M, Brodmann M, Collet J-P, Czerny M, De Carlo M, *et al.* Questions and answers on diagnosis and management of patients with peripheral arterial diseases: a companion document of the 2017 ESC Guidelines for the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Endorsed by: the European Stroke Organisation (ESO), The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;**39**:e35–41. https://doi.org/10.1093/eurheartj/ehx499
530. McQuade K, Gable D, Pearl G, Theune B, Black S. Four-year randomized prospective comparison of percutaneous ePTFE/nitinol self-expanding stent graft versus prosthetic femoral-popliteal bypass in the treatment of superficial femoral artery occlusive disease. *J Vasc Surg* 2010;**52**:584–91.e7. https://doi.org/10.1016/j.jvs.2010.03.071
531. Bosiers M, Deloose K, Callaert J, Moreels N, Keirse K, Verbist J, *et al.* Results of the Protégé EverFlex 200-mm-long nitinol stent (ev3) in TASC C and D femoropopliteal lesions. *J Vasc Surg* 2011;**54**:1042–50. https://doi.org/10.1016/j.jvs.2011.03.272
532. Farhan S, Enzmann FK, Bjorkman P, Kamran H, Zhang Z, Sartori S, *et al.* Revascularization strategies for patients with femoropopliteal peripheral artery disease. *J Am Coll Cardiol* 2023;**81**:358–70. https://doi.org/10.1016/j.jacc.2022.10.036
533. Katsanos K, Spiliopoulos S, Kitrou P, Krokidis M, Karnabatidis D. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2018;**7**:e011245. https://doi.org/10.1161/jaha.118.011245
534. Ouriel K, Adelman MA, Rosenfield K, Scheinert D, Brodmann M, Peña C, *et al.* Safety of paclitaxel-coated balloon angioplasty for femoropopliteal peripheral artery disease. *JACC Cardiovasc Interv* 2019;**12**:2515–24. https://doi.org/10.1016/j.jcin.2019.08.025
535. Freisinger E, Koeppe J, Gerss J, Goerlich D, Malyar NM, Marschall U, *et al.* Mortality after use of paclitaxel-based devices in peripheral arteries: a real-world safety analysis. *Eur Heart J* 2020;**41**:3732–9. https://doi.org/10.1093/eurheartj/ehz698
536. Lyden SP, Brodmann M, Parikh SA, Krishnan P, Schroeder H, Werner M, *et al.* Four-year patient-level pooled mortality analysis of the ILLUMENATE US pivotal and EU randomized controlled trials. *J Vasc Surg* 2022;**75**:600–7. https://doi.org/10.1016/j.jvs.2021.07.244
537. Secemsky EA, Song Y, Schermerhorn M, Yeh RW. Update from the longitudinal assessment of safety of femoropopliteal endovascular treatment with paclitaxel-coated devices among medicare beneficiaries: the SAFE-PAD study. *Circ Cardiovasc Interv* 2022;**15**:e012074. https://doi.org/10.1161/circinterventions.122.012074
538. Nordanstig J, James S, Andersson M, Andersson M, Danielsson P, Gillgren P, *et al.* Mortality with paclitaxel-coated devices in peripheral artery disease. *N Engl J Med* 2020;**383**:2538–46. https://doi.org/10.1056/NEJMoa2005206
539. Fashandi AZ, Mehaffey JH, Hawkins RB, Kron IL, Upchurch GR, Robinson WP. Major adverse limb events and major adverse cardiac events after contemporary lower extremity bypass and infrainguinal endovascular intervention in patients with claudication. *J Vasc Surg* 2018;**68**:1817–23. https://doi.org/10.1016/j.jvs.2018.06.193
540. Koelemay MJW, van Reijen NS, van Dieren S, Frans FA, Vermeulen EJG, Buscher HCJL, *et al.* Editor's choice—randomised clinical trial of supervised exercise therapy vs. endovascular revascularisation for intermittent claudication caused by iliac artery obstruction: the SUPER study. *Eur J Vasc Endovasc Surg* 2022;**63**:421–9. https://doi.org/10.1016/j.ejvs.2021.09.042
541. Dormandy J, Mahir M, Ascady G, Balsano F, De Leeuw P, Blombery P, *et al.* Fate of the patient with chronic leg ischaemia. A review article. *J Cardiovasc Surg (Torino)* 1989;**30**:50–7.
542. Jelnes R, Gaardsting O, Hougaard Jensen K, Baekgaard N, Tonnesen KH, Schroeder T. Fate in intermittent claudication: outcome and risk factors. *BMJ* 1986;**293**:1137–40. https://doi.org/10.1136/bmj.293.6555.1137
543. Leng GC, Lee AJ, Fowkes FG, Whiteman M, Dunbar J, Housley E, *et al.* Incidence, natural history and cardiovascular events in symptomatic and asymptomatic peripheral arterial disease in the general population. *Int J Epidemiol* 1996;**25**:1172–81. https://doi.org/10.1093/ije/25.6.1172
544. Bloor K. Natural history of arteriosclerosis of the lower extremities: Hunterian lecture delivered at the Royal College of Surgeons of England on 22nd April 1960. *Ann R Coll Surg Engl* 1961;**28**:36–52.
545. Goode SD, Cleveland TJ, Gaines PA, Collaborators S. Randomized clinical trial of stents versus angioplasty for the treatment of iliac artery occlusions (STAG trial). *Br J Surg* 2013;**100**:1148–53. https://doi.org/10.1002/bjs.9197
546. Hajibandeh S, Hajibandeh S, Antoniou SA, Torella F, Antoniou GA. Covered vs uncovered stents for aortoiliac and femoropopliteal arterial disease: a systematic review and meta-analysis. *J Endovasc Ther* 2016;**23**:442–52. https://doi.org/10.1177/1526602816643834
547. Krankenberg H, Zeller T, Ingwersen M, Schmalstieg J, Gissler HM, Nikol S, *et al.* Self-expanding versus balloon-expandable stents for iliac artery occlusive disease: the randomized ICE trial. *JACC Cardiovasc Interv* 2017;**10**:1694–704. https://doi.org/10.1016/j.jcin.2017.05.015
548. Bosch JL, Hunink MG. Meta-analysis of the results of percutaneous transluminal angioplasty and stent placement for aortoiliac occlusive disease. *Radiology* 1997;**204**:87–96. https://doi.org/10.1148/radiology.204.1.9205227
549. Committee TS, Jaff MR, White CJ, Hiatt WR, Fowkes GR, Dormandy J, *et al.* An update on methods for revascularization and expansion of the TASC lesion classification to include below-the-knee arteries: a supplement to the inter-society consensus for

the management of peripheral arterial disease (TASC II). *J Endovasc Ther* 2015;**22**:663–77. https://doi.org/10.1177/1526602815592206
550. Boc V, Kozak M, Erzen B, Božič Mijovski M, Boc A, Blinc A. Prognostic factors for restenosis of superficial femoral artery after endovascular treatment. *J Clin Med* 2023;**12**:6343. https://doi.org/10.3390/jcm12196343
551. Alves-Cabratosa L, Comas-Cufi M, Ponjoan A, Garcia-Gil M, Martí-Lluch R, Blanch J, *et al.* Levels of ankle-brachial index and the risk of diabetes mellitus complications. *BMJ Open Diabetes Res Care* 2020;**8**:e000977. https://doi.org/10.1136/bmjdrc-2019-000977
552. Heiss C, Olinic DM, Belch JJF, Brodmann M, Mazzolai L, Stanek A, *et al.* Management of chronic peripheral artery disease patients with indication for endovascular revascularization. *Vasa* 2022;**51**:121–37. https://doi.org/10.1024/0301-1526/a000998
553. Hajibandeh S, Hajibandeh S, Shah S, Child E, Antoniou GA, Torella F. Prognostic significance of ankle brachial pressure index: a systematic review and meta-analysis. *Vascular* 2017;**25**:208–24. https://doi.org/10.1177/1708538116658392
554. Meza-Torres B, Cunningham SG, Heiss C, Joy M, Feher M, Leese GP, *et al.* Adherence to general diabetes and foot care processes, with prompt referral, are associated with amputation-free survival in people with type 2 diabetes and foot ulcers: a Scottish national registry analysis. *J Diabetes Res* 2022;**2022**:7414258. https://doi.org/10.1155/2022/7414258
555. Shishehbor MH, White CJ, Gray BH, Menard MT, Lookstein R, Rosenfield K, *et al.* Critical limb ischemia: an expert statement. *J Am Coll Cardiol* 2016;**68**:2002–15. https://doi.org/10.1016/j.jacc.2016.04.071
556. Misra S, Shishehbor MH, Takahashi EA, Aronow HD, Brewster LP, Bunte MC, *et al.* Perfusion assessment in critical limb ischemia: principles for understanding and the development of evidence and evaluation of devices: a scientific statement from the American Heart Association. *Circulation* 2019;**140**:e657–72. https://doi.org/10.1161/cir.0000000000000708
557. Sukul D, Grey SF, Henke PK, Gurm HS, Grossman PM. Heterogeneity of ankle-brachial indices in patients undergoing revascularization for critical limb ischemia. *JACC Cardiovasc Interv* 2017;**10**:2307–16. https://doi.org/10.1016/j.jcin.2017.08.026
558. Shishehbor MH, Hammad TA, Zeller T, Baumgartner I, Scheinert D, Rocha-Singh KJ. An analysis of IN.PACT DEEP randomized trial on the limitations of the societal guidelines–recommended hemodynamic parameters to diagnose critical limb ischemia. *J Vasc Surg* 2016;**63**:1311–7. https://doi.org/10.1016/j.jvs.2015.11.042
559. Randhawa MS, Reed GW, Grafmiller K, Gornik HL, Shishehbor MH. Prevalence of tibial artery and pedal arch patency by angiography in patients with critical limb ischemia and noncompressible ankle brachial index. *Circ Cardiovasc Interv* 2017;**10**:e004605. https://doi.org/10.1161/CIRCINTERVENTIONS.116.004605
560. Mustapha JA, Saab FA, Martinsen BJ, Pena CS, Zeller T, Driver VR, *et al.* Digital subtraction angiography prior to an amputation for critical limb ischemia (CLI): an expert recommendation statement from the CLI global society to optimize limb salvage. *J Endovasc Ther* 2020;**27**:540–6. https://doi.org/10.1177/1526602820928590
561. Menke J, Larsen J. Meta-analysis: accuracy of contrast-enhanced magnetic resonance angiography for assessing steno-occlusions in peripheral arterial disease. *Ann Intern Med* 2010;**153**:325–34. https://doi.org/10.7326/0003-4819-153-5-201009070-00007
562. Reinecke H, Unrath M, Freisinger E, Bunzemeier H, Meyborg M, Luders F, *et al.* Peripheral arterial disease and critical limb ischaemia: still poor outcomes and lack of guideline adherence. *Eur Heart J* 2015;**36**:932–8. https://doi.org/10.1093/eurheartj/ehv006
563. Hess CN, Wang TY, Weleski Fu J, Gundrum J, Allen LaPointe NM, Rogers RK, *et al.* Long-term outcomes and associations with major adverse limb events after peripheral artery revascularization. *J Am Coll Cardiol* 2020;**75**:498–508. https://doi.org/10.1016/j.jacc.2019.11.050
564. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FGR, Gillespie I, *et al.* Bypass versus angioplasty in severe ischaemia of the leg (BASIL) trial: a survival prediction model to facilitate clinical decision making. *J Vasc Surg* 2010;**51**:52s–68s. https://doi.org/10.1016/j.jvs.2010.01.077
565. Meltzer AJ, Graham A, Connolly PH, Meltzer EC, Karwowski JK, Bush HL, *et al.* The comprehensive risk assessment for bypass (CRAB) facilitates efficient perioperative risk assessment for patients with critical limb ischemia. *J Vasc Surg* 2013;**57**:1186–95. https://doi.org/10.1016/j.jvs.2012.09.083
566. van Netten JJ, Fortington LV, Hinchliffe RJ, Hijmans JM. Early post-operative mortality after major lower limb amputation: a systematic review of population and regional based studies. *Eur J Vasc Endovasc Surg* 2016;**51**:248–57. https://doi.org/10.1016/j.ejvs.2015.10.001
567. Farber A, Menard MT, Conte MS, Kaufman JA, Powell RJ, Choudhry NK, *et al.* Surgery or endovascular therapy for chronic limb-threatening ischemia. *N Engl J Med* 2022;**387**:2305–16. https://doi.org/10.1056/NEJMoa2207899
568. Meza-Torres B, Carinci F, Heiss C, Joy M, de Lusignan S. Health service organisation impact on lower extremity amputations in people with type 2 diabetes with foot ulcers: systematic review and meta-analysis. *Acta Diabetol* 2021;**58**:735–47. https://doi.org/10.1007/s00592-020-01662-x
569. Peters EJ, Lipsky BA, Berendt AR, Embil JM, Lavery LA, Senneville E, *et al.* A systematic review of the effectiveness of interventions in the management of infection in the diabetic foot. *Diabetes Metab Res Rev* 2012;**28**:142–62. https://doi.org/10.1002/dmrr.2247
570. Peters EJG, Lipsky BA, Senneville É, Abbas ZG, Aragón-Sánchez J, Diggle M, *et al.* Interventions in the management of infection in the foot in diabetes: a systematic review. *Diabetes Metab Res Rev* 2020;**36**:e3282. https://doi.org/10.1002/dmrr.3282
571. Dumville JC, Lipsky BA, Hoey C, Cruciani M, Fiscon M, Xia J. Topical antimicrobial agents for treating foot ulcers in people with diabetes. *Cochrane Database Syst Rev* 2017;**6**:CD011038. https://doi.org/10.1002/14651858.CD011038.pub2
572. Luo Y, Li L, Zhao P, Yang C, Zhang J. Effectiveness of silver dressings in the treatment of diabetic foot ulcers: a systematic review and meta-analysis. *J Wound Care* 2022;**31**:979–86. https://doi.org/10.12968/jowc.2022.31.11.979
573. Shu H, Xia Z, Qin X, Wang X, Lu W, Luo Q, *et al.* The clinical efficacy of collagen dressing on chronic wounds: a meta-analysis of 11 randomized controlled trials. *Front Surg* 2022;**9**:978407. https://doi.org/10.3389/fsurg.2022.978407
574. Zhang F, Chen Z, Su F, Zhang T. Comparison of topical honey and povidone iodine-based dressings for wound healing: a systematic review and meta-analysis. *J Wound Care* 2021;**30**:S28–s36. https://doi.org/10.12968/jowc.2021.30.Sup4.S28
575. Yin XL, Hu L, Li T, Zou Y, Li HL. A meta-analysis on the efficacy of vacuum sealing drainage combined with autologous platelet-rich plasma in the treatment of grade 2 and grade 3 diabetic foot ulcers. *Int Wound J* 2022;**20**:1033–41. https://doi.org/10.1111/iwj.13956
576. Lim K, Lim X, Hong Q, Yong E, Chandrasekar S, Tan GWL, *et al.* Use of home negative pressure wound therapy in peripheral artery disease and diabetic limb salvage. *Int Wound J* 2020;**17**:531–9. https://doi.org/10.1111/iwj.13307
577. Uddin A, Russell D, Game F, Santos D, Siddle HJ. The effectiveness of systemic antibiotics for osteomyelitis of the foot in adults with diabetes mellitus: a systematic review protocol. *J Foot Ankle Res* 2022;**15**:48. https://doi.org/10.1186/s13047-022-00554-3
578. O'Meara S, Nelson EA, Golder S, Dalton JE, Craig D, Iglesias C. Systematic review of methods to diagnose infection in foot ulcers in diabetes. *Diabet Med* 2006;**23**:341–7. https://doi.org/10.1111/j.1464-5491.2006.01830.x
579. Nelson A, Wright-Hughes A, Backhouse MR, Lipsky BA, Nixon J, Bhogal MS, *et al.* CODIFI (concordance in diabetic foot ulcer infection): a cross-sectional study of wound swab versus tissue sampling in infected diabetic foot ulcers in England. *BMJ Open* 2018;**8**:e019437. https://doi.org/10.1136/bmjopen-2017-019437
580. Gardner SE, Frantz RA. Wound bioburden and infection-related complications in diabetic foot ulcers. *Biol Res Nurs* 2008;**10**:44–53. https://doi.org/10.1177/1099800408319056
581. Selva Olid A, Solà I, Barajas-Nava LA, Gianneo OD, Bonfill Cosp X, Lipsky BA. Systemic antibiotics for treating diabetic foot infections. *Cochrane Database Syst Rev* 2015;**9**:CD009061. https://doi.org/10.1002/14651858.CD009061.pub2
582. Patton D, Avsar P, Sayeh A, Budri A, O'Connor T, Walsh S, *et al.* A meta-review of the impact of compression therapy on venous leg ulcer healing. *Int Wound J* 2023;**20**:430–47. https://doi.org/10.1111/iwj.13891
583. Lazzarini PA, Armstrong DG, Crews RT, Gooday C, Jarl G, Kirketerp-Moller K, *et al.* Effectiveness of offloading interventions for people with diabetes-related foot ulcers: a systematic review and meta-analysis. *Diabetes Metab Res Rev* 2024;**40**:e3650. https://doi.org/10.1002/dmrr.3650
584. Elraiyah T, Prutsky G, Domecq JP, Tsapas A, Nabhan M, Frykberg RG, *et al.* A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. *J Vasc Surg* 2016;**63**:59S–68S.e2. https://doi.org/10.1016/j.jvs.2015.10.006
585. Lumsden AB, Davies MG, Peden EK. Medical and endovascular management of critical limb ischemia. *J Endovasc Ther* 2009;**16**:Ii31–62. https://doi.org/10.1583/08-2657.1
586. Manzi M, Palena L, Cester G. Endovascular techniques for limb salvage in diabetics with crural and pedal disease. *J Cardiovasc Surg* 2011;**52**:485–92.
587. Dominguez A, III, Bahadorani J, Reeves R, Mahmud E, Patel M. Endovascular therapy for critical limb ischemia. *Expert Rev Cardiovasc Ther* 2015;**13**:429–44. https://doi.org/10.1586/14779072.2015.1019472
588. Abu Dabrh AM, Steffen MW, Undavalli C, Asi N, Wang Z, Elamin MB, *et al.* The natural history of untreated severe or critical limb ischemia. *J Vasc Surg* 2015;**62**:1642–51.e3. https://doi.org/10.1016/j.jvs.2015.07.065
589. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, *et al.* Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005;**366**:1925–34. https://doi.org/10.1016/s0140-6736(05)67704-5
590. Bradbury AW, Moakes CA, Popplewell M, Meecham L, Bate GR, Kelly L, *et al.* A vein bypass first versus a best endovascular treatment first revascularisation strategy for patients with chronic limb threatening ischaemia who required an infra-popliteal, with or without an additional more proximal infra-inguinal revascularisation procedure to restore limb perfusion (BASIL-2): an open-label, randomised, multicentre, phase 3 trial. *Lancet* 2023;**401**:1798–809. https://doi.org/10.1016/S0140-6736(23)00462-2
591. Popplewell MA, Davies H, Jarrett H, Bate G, Grant M, Patel S, *et al.* Bypass versus angioplasty in severe ischaemia of the leg—2 (BASIL-2) trial: study protocol for a randomised controlled trial. *Trials* 2016;**17**:11. https://doi.org/10.1186/s13063-015-1114-2
592. Patel K, Liu Y, Etaee F, Patel C, Monteleone P, Patel M, *et al.* Differences between patients with intermittent claudication and critical limb ischemia undergoing endovascular intervention: insights from the excellence in peripheral artery disease registry. *Circ*

Cardiovasc Interv 2021;**14**:e010635. https://doi.org/10.1161/CIRCINTERVENTIONS.121.010635
593. Almasri J, Adusumalli J, Asi N, Lakis S, Alsawas M, Prokop LJ, *et al.* A systematic review and meta-analysis of revascularization outcomes of infrainguinal chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg* 2019;**58**:S110–s119. https://doi.org/10.1016/j.ejvs.2019.04.013
594. Söder HK, Manninen HI, Jaakkola P, Matsi PJ, Räsänen HT, Kaukanen E, *et al.* Prospective trial of infrapopliteal artery balloon angioplasty for critical limb ischemia: angiographic and clinical results. *J Vasc Interv Radiol* 2000;**11**:1021–31. https://doi.org/10.1016/s1051-0443(07)61332-3
595. Balmer H, Mahler F, Do DD, Triller J, Baumgartner I. Balloon angioplasty in chronic critical limb ischemia: factors affecting clinical and angiographic outcome. *J Endovasc Ther* 2002;**9**:403–10. https://doi.org/10.1177/152660280200900403
596. Kudo T, Chandra FA, Kwun WH, Haas BT, Ahn SS. Changing pattern of surgical revascularization for critical limb ischemia over 12 years: endovascular vs. open bypass surgery. *J Vasc Surg* 2006;**44**:304–13. https://doi.org/10.1016/j.jvs.2006.03.040
597. Kim KG, Meshkin DH, Tirrell AR, Bekeny JC, Tefera EA, Fan KL, *et al.* A systematic review and meta-analysis of endovascular angiosomal revascularization in the setting of collateral vessels. *J Vasc Surg* 2021;**74**:1406–16.e3. https://doi.org/10.1016/j.jvs.2021.04.026
598. Shishehbor MH, Powell RJ, Montero-Baker MF, Dua A, Martínez-Trabal JL, Bunte MC, *et al.* Transcatheter arterialization of deep veins in chronic limb-threatening ischemia. *N Engl J Med* 2023;**388**:1171–80. https://doi.org/10.1056/NEJMoa2212754
599. Salem M, Hosny MS, Francia F, Sallam M, Saratzis A, Saha P, *et al.* Management of extensive aorto-iliac disease: a systematic review and meta-analysis of 9319 patients. *Cardiovasc Intervent Radiol* 2021;**44**:1518–35. https://doi.org/10.1007/s00270-021-02785-6
600. Bekken JA, Vroegindeweij D, Vos JA, de Vries J-PPM, Lardenoije JWHP, Petri B-J, *et al.* Editor's choice—two year results of the randomised DISCOVER trial comparing covered versus bare metal stents in the common iliac artery. *Eur J Vasc Endovasc Surg* 2023;**65**:359–68. https://doi.org/10.1016/j.ejvs.2022.11.008
601. Jongkind V, Akkersdijk GJ, Yeung KK, Wisselink W. A systematic review of endovascular treatment of extensive aortoiliac occlusive disease. *J Vasc Surg* 2010;**52**:1376–83. https://doi.org/10.1016/j.jvs.2010.04.080
602. Ye W, Liu CW, Ricco JB, Mani K, Zeng R, Jiang J. Early and late outcomes of percutaneous treatment of TransAtlantic inter-society consensus class C and D aorto-iliac lesions. *J Vasc Surg* 2011;**53**:1728–37. https://doi.org/10.1016/j.jvs.2011.02.005
603. Bosiers M, Deloose K, Callaert J, Maene L, Beelen R, Keirse K, *et al.* BRAVISSIMO: 12-month results from a large scale prospective trial. *J Cardiovasc Surg* 2013;**54**:235–53.
604. Danczyk RC, Mitchell EL, Petersen BD, Edwards J, Liem TK, Landry GJ, *et al.* Outcomes of open operation for aortoiliac occlusive disease after failed endovascular therapy. *Arch Surg* 2012;**147**:841–5. https://doi.org/10.1001/archsurg.2012.1649
605. Fereydooni A, Zhou B, Xu Y, Deng Y, Dardik A, Ochoa Chaar CI. Rapid increase in hybrid surgery for the treatment of peripheral artery disease in the vascular quality initiative database. *J Vasc Surg* 2020;**72**:977–86.e1. https://doi.org/10.1016/j.jvs.2019.11.041
606. Zeller T, Baumgartner I, Scheinert D, Brodmann M, Bosiers M, Micari A, *et al.* Drug-eluting balloon versus standard balloon angioplasty for infrapopliteal arterial revascularization in critical limb ischemia: 12-month results from the IN.PACT DEEP randomized trial. *J Am Coll Cardiol* 2014;**64**:1568–76. https://doi.org/10.1016/j.jacc.2014.06.1198
607. Zeller T, Micari A, Scheinert D, Baumgartner I, Bosiers M, Vermassen FEG, *et al.* The IN.PACT DEEP clinical drug-coated balloon trial: 5-year outcomes. *JACC Cardiovasc Interv* 2020;**13**:431–43. https://doi.org/10.1016/j.jcin.2019.10.059
608. Brizzi V, Caradu C, Berard X, Sassoust G, Midy D, Ducasse E. Six-year multicenter experience of standard endovascular treatment of critical limb ischemia in the era of drug-eluting devices. *J Cardiovasc Surg* 2018;**59**:707–15. https://doi.org/10.23736/S0021-9509.16.09737-8
609. Jude EB, Oyibo SO, Chalmers N, Boulton AJ. Peripheral arterial disease in diabetic and nondiabetic patients: a comparison of severity and outcome. *Diabetes Care* 2001;**24**:1433–7. https://doi.org/10.2337/diacare.24.8.1433
610. Ozkan U, Oguzkurt L, Tercan F. Atherosclerotic risk factors and segmental distribution in symptomatic peripheral artery disease. *J Vasc Interv Radiol* 2009;**20**:437–41. https://doi.org/10.1016/j.jvir.2009.01.010
611. Todd KE, Jr, Ahanchi SS, Maurer CA, Kim JH, Chipman CR, Panneton JM. Atherectomy offers no benefits over balloon angioplasty in tibial interventions for critical limb ischemia. *J Vasc Surg* 2013;**58**:941–8. https://doi.org/10.1016/j.jvs.2013.04.024
612. Teichgraber U, Lehmann T, Thieme M, Wahl K-U, Stelzner C, Bormann A, *et al.* Drug-coated balloon angioplasty of infrapopliteal lesions in patients with critical limb ischaemia: 1-year results of the APOLLO trial. *Cardiovasc Intervent Radiol* 2019;**42**:1380–90. https://doi.org/10.1007/s00270-019-02279-6
613. Yang X, Lu X, Ye K, Li X, Qin J, Jiang M. Systematic review and meta-analysis of balloon angioplasty versus primary stenting in the infrapopliteal disease. *Vasc Endovascular Surg* 2014;**48**:18–26. https://doi.org/10.1177/1538574413510626
614. Zhang J, Xu X, Kong J, Xu R, Fan X, Chen J, *et al.* Systematic review and meta-analysis of drug-eluting balloon and stent for infrapopliteal artery revascularization. *Vasc Endovascular Surg* 2017;**51**:72–83. https://doi.org/10.1177/1538574416689426
615. Matsuoka EK, Hasebe T, Ishii R, Miyazaki N, Soejima K, Iwasaki K. Comparative performance analysis of interventional devices for the treatment of ischemic disease in below-the-knee lesions: a systematic review and meta-analysis. *Cardiovasc Interv Ther* 2022;**37**:145–57. https://doi.org/10.1007/s12928-021-00758-7
616. Fong KY, Xin L, Ng J, Loh SEK, Ng JJ, Choong AMTL. A systematic review and meta-analysis of sirolimus-eluting stents for treatment of below-the-knee arterial disease. *J Vasc Surg* 2023;**77**:1264–73.e3. https://doi.org/10.1016/j.jvs.2022.09.022
617. Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. *Cochrane Database Syst Rev* 2013;**2**:CD004001. https://doi.org/10.1002/14651858.CD004001.pub3
618. Asimakidou E, Matis GK. Spinal cord stimulation in the treatment of peripheral vascular disease: a systematic review—revival of a promising therapeutic option? *Br J Neurosurg* 2022;**36**:555–63. https://doi.org/10.1080/02688697.2021.1884189
619. Nicoloff AD, Taylor LM, Jr, Sexton GJ, Schuff RA, Edwards JM, Yeager RA, *et al.* Relationship between site of initial symptoms and subsequent progression of disease in a prospective study of atherosclerosis progression in patients receiving long-term treatment for symptomatic peripheral arterial disease. *J Vasc Surg* 2002;**35**:38–46; discussion 46–37.
620. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, *et al.* International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA* 2006;**295**:180–9. https://doi.org/10.1001/jama.295.2.180
621. Wilson YG, Davies AH, Currie IC, Morgan M, McGrath C, Baird RN, *et al.* Vein graft stenosis: incidence and intervention. *Eur J Vasc Endovasc Surg* 1996;**11**:164–9. https://doi.org/10.1016/s1078-5884(96)80046-3
622. Armstrong PA, Bandyk DF, Wilson JS, Shames ML, Johnson BL, Back MR. Optimizing infrainguinal arm vein bypass patency with duplex ultrasound surveillance and endovascular therapy. *J Vasc Surg* 2004;**40**:724–31; discussion 730–721. https://doi.org/10.1016/j.jvs.2004.07.037
623. Pulli R, Dorigo W, Fargion A, Innocenti AA, Pratesi G, Marek J, *et al.* Early and long-term comparison of endovascular treatment of iliac artery occlusions and stenosis. *J Vasc Surg* 2011;**53**:92–8. https://doi.org/10.1016/j.jvs.2010.08.034
624. Lo RC, Darling J, Bensley RP, Giles KA, Dahlberg SE, Hamdan AD, *et al.* Outcomes following infrapopliteal angioplasty for critical limb ischemia. *J Vasc Surg* 2013;**57**:1455–64; discussion 1463–1454. https://doi.org/10.1016/j.jvs.2012.10.109
625. Rodway AD, Hanna L, Harris J, Jarrett R, Allan C, Pazos Casal F, *et al.* Prognostic and predictive value of ultrasound-based estimated ankle brachial pressure index at early follow-up after endovascular revascularization of chronic limb-threatening ischaemia: a prospective, single-centre, service evaluation. *EClinicalMedicine* 2024;**68**:102410. https://doi.org/10.1016/j.eclinm.2023.102410
626. Poursina O, Elizondo-Adamchik H, Montero-Baker M, Pallister ZS, Mills JL, Chung J. Safety and efficacy of an endovascular-first approach to acute limb ischemia. *J Vasc Surg* 2021;**73**:1741–9. https://doi.org/10.1016/j.jvs.2020.10.002
627. Hawkins KE, Valentine RJ, Duke JM, Wang Q, Reed AB. Ankle-brachial index use in peripheral vascular interventions for claudication. *J Vasc Surg* 2022;**76**:196–201. https://doi.org/10.1016/j.jvs.2022.02.049
628. Armstrong EJ, Chen DC, Westin GG, Singh S, McCoach CE, Bang H, *et al.* Adherence to guideline-recommended therapy is associated with decreased major adverse cardiovascular events and major adverse limb events among patients with peripheral arterial disease. *J Am Heart Assoc* 2014;**3**:e000697. https://doi.org/10.1161/jaha.113.000697
629. Araujo ST, Moreno DH, Cacione DG. Percutaneous thrombectomy or ultrasound-accelerated thrombolysis for initial management of acute limb ischaemia. *Cochrane Database Syst Rev* 2022;**1**:CD013486. https://doi.org/10.1002/14651858.CD013486.pub2
630. Kokkinidis DG, Arfaras-Melainis A, Giannopoulos S, Katsaros I, Jawaid O, Jonnalagadda AK, *et al.* Statin therapy for reduction of cardiovascular and limb-related events in critical limb ischemia: a systematic review and meta-analysis. *Vasc Med* 2020;**25**:106–17. https://doi.org/10.1177/1358863x19894055
631. Londero LS, Nørgaard B, Houlind K. Patient delay is the main cause of treatment delay in acute limb ischemia: an investigation of pre- and in-hospital time delay. *World J Emerg Surg* 2014;**9**:56. https://doi.org/10.1186/1749-7922-9-56
632. Duval S, Keo HH, Oldenburg NC, Baumgartner I, Jaff MR, Peacock JM, *et al.* The impact of prolonged lower limb ischemia on amputation, mortality, and functional status: the FRIENDS registry. *Am Heart J* 2014;**168**:577–87. https://doi.org/10.1016/j.ahj.2014.06.013
633. Kulezic A, Macek M, Acosta S. Inadequacies of physical examination in patients with acute lower limb ischemia are associated with dreadful consequences. *Ann Vasc Surg* 2022;**82**:190–6. https://doi.org/10.1016/j.avsg.2021.10.067
634. Blaisdell FW. The pathophysiology of skeletal muscle ischemia and the reperfusion syndrome: a review. *Cardiovasc Surg* 2002;**10**:620–30. https://doi.org/10.1016/s0967-2109(02)00070-4

635. Jivegård L, Bergqvist D, Holm J. When is urgent revascularization unnecessary for acute lower limb ischaemia? *Eur J Vasc Endovasc Surg* 1995;**9**:448–53. https://doi.org/10.1016/s1078-5884(05)80014-0
636. Crawford JD, Perrone KH, Jung E, Mitchell EL, Landry GJ, Moneta GL, *et al.* Arterial duplex for diagnosis of peripheral arterial emboli. *J Vasc Surg* 2016;**64**:1351–6. https://doi.org/10.1016/j.jvs.2016.04.005
637. Hemingway J, Emanuels D, Aarabi S, Quiroga E, Tran N, Starnes B, *et al.* Safety of transfer, type of procedure, and factors predictive of limb salvage in a modern series of acute limb ischemia. *J Vasc Surg* 2019;**69**:1174–9. https://doi.org/10.1016/j.jvs.2018.08.174
638. Currie IS, Wakelin SJ, Lee AJ, Chalmers RT. Plasma creatine kinase indicates major amputation or limb preservation in acute lower limb ischemia. *J Vasc Surg* 2007;**45**:733–9. https://doi.org/10.1016/j.jvs.2006.12.050
639. Brow TD, Kakkar VV, Das SK. The significance of creatine kinase in cardiac patients with acute limb ischaemia. *J Cardiovasc Surg* 1999;**40**:637–44.
640. Adiseshiah M, Round JM, Jones DA. Reperfusion injury in skeletal muscle: a prospective study in patients with acute limb ischaemia and claudicants treated by revascularization. *Br J Surg* 2005;**79**:1026–9. https://doi.org/10.1002/bjs.1800791013
641. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, *et al.* Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg* 1997;**26**:517–38. https://doi.org/10.1016/s0741-5214(97)70045-4
642. Ontario Health. Mechanical thrombectomy for acute and subacute blocked arteries and veins in the lower limbs: a health technology assessment. *Ont Health Technol Assess Ser* 2023;**23**:1–244.
643. Gong M, He X, Zhao B, Kong J, Gu J, Chen G, *et al.* Endovascular revascularization strategies using catheter-based thrombectomy versus conventional catheter-directed thrombolysis for acute limb ischemia. *Thromb J* 2021;**19**:96. https://doi.org/10.1186/s12959-021-00349-9
644. Doelare SAN, Koedam TWA, Ebben HP, Tournoij E, Hoksbergen AWJ, Yeung KK, *et al.* Catheter directed thrombolysis for not immediately threatening acute limb ischaemia: systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2023;**65**:537–45. https://doi.org/10.1016/j.ejvs.2022.12.030
645. Veenstra EB, van der Laan MJ, Zeebregts CJ, de Heide E-J, Kater M, Bokkers RPH. A systematic review and meta-analysis of endovascular and surgical revascularization techniques in acute limb ischemia. *J Vasc Surg* 2020;**71**:654–68.e3. https://doi.org/10.1016/j.jvs.2019.05.031
646. Kolte D, Kennedy KF, Shishehbor MH, Mamdani ST, Stangenberg L, Hyder ON, *et al.* Endovascular versus surgical revascularization for acute limb ischemia: a propensity-score matched analysis. *Circ Cardiovasc Interv* 2020;**13**:e008150. https://doi.org/10.1161/CIRCINTERVENTIONS.119.008150
647. Grip O, Wanhainen A, Michaelsson K, Lindhagen L, Bjorck M. Open or endovascular revascularization in the treatment of acute lower limb ischaemia. *Br J Surg* 2018;**105**:1598–606. https://doi.org/10.1002/bjs.10954
648. Darwood R, Berridge DC, Kessel DO, Robertson I, Forster R. Surgery versus thrombolysis for initial management of acute limb ischaemia. *Cochrane Database Syst Rev* 2018;**8**:CD002784. https://doi.org/10.1002/14651858.CD002784.pub3
649. Schrijver AM, van Leersum M, Fioole B, Reijnen MMPJ, Hoksbergen AWJ, Vahl AC, *et al.* Dutch randomized trial comparing standard catheter-directed thrombolysis and ultrasound-accelerated thrombolysis for arterial thromboembolic infrainguinal disease (DUET). *J Endovasc Ther* 2015;**22**:87–95. https://doi.org/10.1177/1526602814566578
650. Juneja A, Garuthara M, Talathi S, Rao A, Landis G, Etkin Y. Predictors of poor outcomes after lower extremity revascularization for acute limb ischemia. *Vascular* 2024;**32**:632–9. https://doi.org/10.1177/17085381231154290
651. Ouriel K, Veith FJ. Acute lower limb ischemia: determinants of outcome. *Surgery* 1998;**124**:336–41; discussion 341–332. https://doi.org/10.1016/S0039-6060(98)70139-4
652. Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008;**133**:815s–43s. https://doi.org/10.1378/chest.08-0686
653. Hess CN, Debus ES, Nehler MR, Anand SS, Patel MR, Szarek M, *et al.* Reduction in acute limb ischemia with rivaroxaban versus placebo in peripheral artery disease after lower extremity revascularization: insights from VOYAGER PAD. *Circulation* 2021;**144**:1831–41. https://doi.org/10.1161/circulationaha.121.055146
654. Jivegård L, Holm J, Bergqvist D, Björck CG, Björkman H, Brunius U, *et al.* Acute lower limb ischemia: failure of anticoagulant treatment to improve one-month results of arterial thromboembolectomy. A prospective randomized multi-center study. *Surgery* 1991;**109**:610–6.
655. Jivegård L, Holm J, Scherstén T. Arterial thromboembolectomy—should anticoagulants be administered? *Acta Chir Scand* 1986;**152**:493–7.
656. Campbell WB, Ridler BM, Szymanska TH. Two-year follow-up after acute thromboembolic limb ischaemia: the importance of anticoagulation. *Eur J Vasc Endovasc Surg* 2000;**19**:169–73. https://doi.org/10.1053/ejvs.1999.0999
657. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, *et al.* Heart disease and stroke statistics–2018 update: a report from the American Heart Association. *Circulation* 2018;**137**:e67–492. https://doi.org/10.1161/cir.0000000000000558
658. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, *et al.* Mannheim carotid intima-media thickness and plaque consensus (2004–2006–2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, at the 13th, 15th and 20th European Stroke Conferences, Mannheim, Germany, 2004, Brussels, Belgium, 2006, and Hamburg, Germany, 2011. *Cerebrovasc Dis* 2012;**34**:290–6. https://doi.org/10.1159/000343145
659. Johri AM, Nambi V, Naqvi TZ, Feinstein SB, Kim ESH, Park MM, *et al.* Recommendations for the assessment of carotid arterial plaque by ultrasound for the characterization of atherosclerosis and evaluation of cardiovascular risk: from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2020;**33**:917–33. https://doi.org/10.1016/j.echo.2020.04.021
660. Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, *et al.* Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;**325**:445–53. https://doi.org/10.1056/nejm199108153250701
661. Gornik HL, Rundek T, Gardener H, Benenati JF, Dahiya N, Hamburg NM, *et al.* Optimization of duplex velocity criteria for diagnosis of internal carotid artery (ICA) stenosis: a report of the Intersocietal Accreditation Commission (IAC) Vascular Testing Division Carotid Diagnostic Criteria Committee. *Vasc Med* 2021;**26**:515–25. https://doi.org/10.1177/1358863X211011253
662. Grant EG, Benson CB, Moneta GL, Alexandrov AV, Baker JD, Bluth EI, *et al.* Carotid artery stenosis: grayscale and Doppler ultrasound diagnosis—Society of Radiologists in ultrasound consensus conference. *Ultrasound Q* 2003;**19**:190–8. https://doi.org/10.1097/00013644-200312000-00005
663. Rustempasic N, Gengo M. Assesment of carotid stenosis with CT angiography and color Doppler ultrasonography. *Med Arch* 2019;**73**:321–5. https://doi.org/10.5455/medarh.2019.73.321-325
664. Clezar CN, Flumignan CD, Cassola N, Nakano LCU, Trevisani VFM, Flumignan RLG. Pharmacological interventions for asymptomatic carotid stenosis. *Cochrane Database Syst Rev* 2023;**8**:CD013573. https://doi.org/10.1002/14651858.CD013573.pub2
665. Côté R, Battista RN, Abrahamowicz M, Langlois Y, Bourque F, Mackey A. Lack of effect of aspirin in asymptomatic patients with carotid bruits and substantial carotid narrowing. The asymptomatic cervical bruit study group. *Ann Intern Med* 1995;**123**:649–55. https://doi.org/10.7326/0003-4819-123-9-199511010-00002
666. Aboyans V, Bauersachs R, Mazzolai L, Brodmann M, Palomares JFR, Debus S, *et al.* Antithrombotic therapies in aortic and peripheral arterial diseases in 2021: a consensus document from the ESC working group on aorta and peripheral vascular diseases, the ESC working group on thrombosis, and the ESC working group on cardiovascular pharmacotherapy. *Eur Heart J* 2021;**42**:4013–24. https://doi.org/10.1093/eurheartj/ehab390
667. Johnston SC, Easton JD, Farrant M, Barsan W, Conwit RA, Elm JJ, *et al.* Clopidogrel and aspirin in acute ischemic stroke and high-risk TIA. *N Engl J Med* 2018;**379**:215–25. https://doi.org/10.1056/NEJMoa1800410
668. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, *et al.* Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med* 2013;**369**:11–9. https://doi.org/10.1056/NEJMoa1215340
669. Kennedy J, Hill MD, Ryckborst KJ, Eliasziw M, Demchuk AM, Buchan AM. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. *Lancet Neurol* 2007;**6**:961–9. https://doi.org/10.1016/S1474-4422(07)70250-8
670. Murphy SJX, Naylor AR, Ricco JB, Sillesen H, Kakkos S, Halliday A, *et al.* Optimal antiplatelet therapy in moderate to severe asymptomatic and symptomatic carotid stenosis: a comprehensive review of the literature. *Eur J Vasc Endovasc Surg* 2019;**57**:199–211. https://doi.org/10.1016/j.ejvs.2018.09.018
671. King A, Shipley M, Markus H, Investigators A. The effect of medical treatments on stroke risk in asymptomatic carotid stenosis. *Stroke* 2013;**44**:542–6. https://doi.org/10.1161/STROKEAHA.112.673608
672. Endarterectomy for asymptomatic carotid artery stenosis. Executive committee for the asymptomatic carotid atherosclerosis study. *JAMA* 1995;**273**:1421–8.
673. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, *et al.* Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004;**363**:1491–502. https://doi.org/10.1016/s0140-6736(04)16146-1
674. Halliday A, Harrison M, Hayter E, Kong X, Mansfield A, Marro J, *et al.* 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. *Lancet* 2010;**376**:1074–84. https://doi.org/10.1016/s0140-6736(10)61197-x
675. Rothwell PM, Goldstein LB. Carotid endarterectomy for asymptomatic carotid stenosis: asymptomatic carotid surgery trial. *Stroke* 2004;**35**:2425–7. https://doi.org/10.1161/01.STR.0000141706.50170.a7
676. Hadar N, Raman G, Moorthy D, O'Donnell TF, Thaler DE, Feldmann E, *et al.* Asymptomatic carotid artery stenosis treated with medical therapy alone: temporal trends and implications for risk assessment and the design of future studies. *Cerebrovasc Dis* 2014;**38**:163–73. https://doi.org/10.1159/000365206
677. Reiff T, Eckstein HH, Mansmann U, Jansen O, Fraedrich G, Mudra H, *et al.* Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical

treatment: one-year interim results of SPACE-2. *Int J Stroke* 2020;**15**:638–49. https://doi.org/10.1177/1747493019833017
678. Naylor AR, Schroeder TV, Sillesen H. Clinical and imaging features associated with an increased risk of late stroke in patients with asymptomatic carotid disease. *Eur J Vasc Endovasc Surg* 2014;**48**:633–40. https://doi.org/10.1016/j.ejvs.2014.08.017
679. Paraskevas KI, Brown MM, Lal BK, Myrcha P, Lyden SP, Schneider PA, *et al.* Recent advances and controversial issues in the optimal management of asymptomatic carotid stenosis. *J Vasc Surg* 2024;**79**:695–703. https://doi.org/10.1016/j.jvs.2023.11.004
680. Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, *et al.* Editor's choice—European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease. *Eur J Vasc Endovasc Surg* 2023;**65**:7–111. https://doi.org/10.1016/j.ejvs.2022.04.011
681. Kashyap VS, Schneider PA, Foteh M, Motaganahalli R, Shah R, Eckstein H-H, *et al.* Early outcomes in the ROADSTER 2 study of transcarotid artery revascularization in patients with significant carotid artery disease. *Stroke* 2020;**51**:2620–9. https://doi.org/10.1161/strokeaha.120.030550
682. Nicolaides AN, Kakkos SK, Griffin M, Sabetai M, Dhanjil S, Tegos T, *et al.* Severity of asymptomatic carotid stenosis and risk of ipsilateral hemispheric ischaemic events: results from the ACSRS study. *Eur J Vasc Endovasc Surg* 2005;**30**:275–84. https://doi.org/10.1016/j.ejvs.2005.04.031
683. Lovett JK, Coull AJ, Rothwell PM. Early risk of recurrence by subtype of ischemic stroke in population-based incidence studies. *Neurology* 2004;**62**:569–73. https://doi.org/10.1212/01.wnl.0000110311.09970.83
684. Kakkos SK, Sabetai M, Tegos T, Stevens J, Thomas D, Griffin M, *et al.* Silent embolic infarcts on computed tomography brain scans and risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis. *J Vasc Surg* 2009;**49**:902–9. https://doi.org/10.1016/j.jvs.2008.10.059
685. Kakkos SK, Nicolaides AN, Charalambous I, Thomas D, Giannopoulos A, Naylor AR, *et al.* Predictors and clinical significance of progression or regression of asymptomatic carotid stenosis. *J Vasc Surg* 2014;**59**:956–67.e1. https://doi.org/10.1016/j.jvs.2013.10.073
686. Markus HS, King A, Shipley M, Topakian R, Cullinane M, Reihill S, *et al.* Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. *Lancet Neurol* 2010;**9**:663–71. https://doi.org/10.1016/s1474-4422(10)70120-4
687. Fields WS, Lemak NA, Frankowski RF, Hardy RJ. Controlled trial of aspirin in cerebral ischemia. *Stroke* 1977;**8**:301–14. https://doi.org/10.1161/01.str.8.3.301
688. King A, Serena J, Bornstein NM, Markus HS. Does impaired cerebrovascular reactivity predict stroke risk in asymptomatic carotid stenosis? A prospective substudy of the asymptomatic carotid emboli study. *Stroke* 2011;**42**:1550–5. https://doi.org/10.1161/strokeaha.110.609057
689. Amarenco P, Albers GW, Denison H, Easton JD, Evans SR, Held P, *et al.* Efficacy and safety of ticagrelor versus aspirin in acute stroke or transient ischaemic attack of atherosclerotic origin: a subgroup analysis of SOCRATES, a randomised, double-blind, controlled trial. *Lancet Neurol* 2017;**16**:301–10. https://doi.org/10.1016/s1474-4422(17)30038-8
690. Kakkos SK, Griffin MB, Nicolaides AN, Kyriacou E, Sabetai MM, Tegos T, *et al.* The size of juxtaluminal hypoechoic area in ultrasound images of asymptomatic carotid plaques predicts the occurrence of stroke. *J Vasc Surg* 2013;**57**:609–18.e1; discussion 617–608. https://doi.org/10.1016/j.jvs.2012.09.045
691. Gupta A, Kesavabhotla K, Baradaran H, Kamel H, Pandya A, Giambrone AE, *et al.* Plaque echolucency and stroke risk in asymptomatic carotid stenosis: a systematic review and meta-analysis. *Stroke* 2015;**46**:91–7. https://doi.org/10.1161/strokeaha.114.006091
692. Palacio S, Hart RG, Pearce LA, Anderson DC, Sharma M, Birnbaum LA, *et al.* Effect of addition of clopidogrel to aspirin on stroke incidence: meta-analysis of randomized trials. *Int J Stroke* 2015;**10**:686–91. https://doi.org/10.1111/ijs.12050
693. Gupta A, Baradaran H, Schweitzer AD, Kamel H, Pandya A, Delgado D, *et al.* Carotid plaque MRI and stroke risk: a systematic review and meta-analysis. *Stroke* 2013;**44**:3071–7. https://doi.org/10.1161/strokeaha.113.002551
694. Wong KS, Chen C, Fu J, Chang HM, Suwanwela NC, Huang YN, *et al.* Clopidogrel plus aspirin versus aspirin alone for reducing embolisation in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR study): a randomised, open-label, blinded-endpoint trial. *Lancet Neurol* 2010;**9**:489–97. https://doi.org/10.1016/s1474-4422(10)70060-0
695. Karlöf E, Buckler A, Liljeqvist ML, Lengquist M, Kronqvist M, Toonsi MA, *et al.* Carotid plaque phenotyping by correlating plaque morphology from computed tomography angiography with transcriptional profiling. *Eur J Vasc Endovasc Surg* 2021;**62**:716–26. https://doi.org/10.1016/j.ejvs.2021.07.011
696. Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, *et al.* Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke* 2011;**42**:675–80. https://doi.org/10.1161/strokeaha.110.610212
697. Baker WH, Howard VJ, Howard G, Toole JF. Effect of contralateral occlusion on long-term efficacy of endarterectomy in the asymptomatic carotid atherosclerosis study (ACAS). ACAS Investigators. *Stroke* 2000;**31**:2330–4. https://doi.org/10.1161/01.str.31.10.2330
698. Kamtchum-Tatuene J, Noubiap JJ, Wilman AH, Saqqur M, Shuaib A, Jickling GC. Prevalence of high-risk plaques and risk of stroke in patients with asymptomatic carotid stenosis: a meta-analysis. *JAMA Neurol* 2020;**77**:1524–35. https://doi.org/10.1001/jamaneurol.2020.2658
699. Saratzis A, Naylor R. 30 day outcomes after carotid interventions: an updated meta-analysis of randomised controlled trials in asymptomatic patients. *Eur J Vasc Endovasc Surg* 2022;**63**:157–8. https://doi.org/10.1016/j.ejvs.2021.10.029
700. Amarenco P, Denison H, Evans SR, Himmelmann A, James S, Knutsson M, *et al.* Ticagrelor added to aspirin in acute nonsevere ischemic stroke or transient ischemic attack of atherosclerotic origin. *Stroke* 2020;**51**:3504–13. https://doi.org/10.1161/strokeaha.120.032239
701. Halliday A, Bulbulia R, Bonati LH, Chester J, Cradduck-Bamford A, Peto R, *et al.* Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;**398**:1065–73. https://doi.org/10.1016/s0140-6736(21)01910-3
702. Rosenfield K, Matsumura JS, Chaturvedi S, Riles T, Ansel GM, Metzger DC, *et al.* Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med* 2016;**374**:1011–20. https://doi.org/10.1056/NEJMoa1515706
703. Brott TG, Howard G, Roubin GS, Meschia JF, Mackey A, Brooks W, *et al.* Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med* 2016;**374**:1021–31. https://doi.org/10.1056/NEJMoa1505215
704. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, *et al.* Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;**351**:1493–501. https://doi.org/10.1056/NEJMoa040127
705. Karpenko A, Bugurov S, Ignatenko P, Starodubtsev V, Popova I, Malinowski K, *et al.* Randomized controlled trial of conventional versus micronet-covered stent in carotid artery revascularization. *JACC Cardiovasc Interv* 2021;**14**:2377–87. https://doi.org/10.1016/j.jcin.2021.08.005
706. Karpenko A, Bugurov S, Ignatenko P, Starodubtsev V, Popova I, Malinowski K, *et al.* Randomized controlled trial of conventional versus micronet-covered stent in carotid artery revascularization: 12-month outcomes. *JACC Cardiovasc Interv* 2023;**16**:878–80. https://doi.org/10.1016/j.jcin.2023.01.369
707. Columbo JA, Martinez-Camblor P, Stone DH, Goodney PP, O'Malley AJ. Procedural safety comparison between transcarotid artery revascularization, carotid endarterectomy, and carotid stenting: perioperative and 1-year rates of stroke or death. *J Am Heart Assoc* 2022;**11**:e024964. https://doi.org/10.1161/jaha.121.024964
708. de Borst GJ. Transcarotid artery revascularization. *Br J Surg* 2023;**110**:127–8. https://doi.org/10.1093/bjs/znac421
709. Hawkins BM, Kennedy KF, Aronow HD, Nguyen LL, White CJ, Rosenfield K, *et al.* Hospital variation in carotid stenting outcomes. *JACC Cardiovasc Interv* 2015;**8**:858–63. https://doi.org/10.1016/j.jcin.2015.01.026
710. Paraskevas KI, Kalmykov EL, Naylor AR. Stroke/death rates following carotid artery stenting and carotid endarterectomy in contemporary administrative dataset registries: a systematic review. *Eur J Vasc Endovasc Surg* 2016;**51**:3–12. https://doi.org/10.1016/j.ejvs.2015.07.032
711. Brott TG, Hobson RW, II, Howard G, Roubin GS, Clark WM, Brooks W, *et al.* Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;**363**:11–23. https://doi.org/10.1056/NEJMoa0912321
712. Sacco RL, Diener HC, Yusuf S, Cotton D, Ôunpuu S, Lawton WA, *et al.* Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med* 2008;**359**:1238–51. https://doi.org/10.1056/NEJMoa0805002
713. Halkes PH, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A. Medium intensity oral anticoagulants versus aspirin after cerebral ischaemia of arterial origin (ESPRIT): a randomised controlled trial. *Lancet Neurol* 2007;**6**:115–24. https://doi.org/10.1016/s1474-4422(06)70685-8
714. Markus HS, Droste DW, Kaps M, Larrue V, Lees KR, Siebler M, *et al.* Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using Doppler embolic signal detection: the clopidogrel and aspirin for reduction of emboli in symptomatic carotid stenosis (CARESS) trial. *Circulation* 2005;**111**:2233–40. https://doi.org/10.1161/01.Cir.0000163561.90680.1c
715. Johnston SC, Amarenco P, Denison H, Evans SR, Himmelmann A, James S, *et al.* Ticagrelor and aspirin or aspirin alone in acute ischemic stroke or TIA. *N Engl J Med* 2020;**383**:207–17. https://doi.org/10.1056/NEJMoa1916870
716. Wang Y, Pan Y, Li H, Amarenco P, Denison H, Evans SR, *et al.* Efficacy and safety of ticagrelor and aspirin in patients with moderate ischemic stroke: an exploratory analysis of the THALES randomized clinical trial. *JAMA Neurol* 2021;**78**:1091–8. https://doi.org/10.1001/jamaneurol.2021.2440
717. Messas E, Goudot G, Halliday A, Sitruk J, Mirault T, Khider L, *et al.* Management of carotid stenosis for primary and secondary prevention of stroke: state-of-the-art 2020: a critical review. *Eur Heart J Suppl* 2020;**22**:M35–42. https://doi.org/10.1093/eurheartj/suaa162
718. Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, *et al.* Analysis of pooled data from the randomised controlled trials of endarterectomy for

symptomatic carotid stenosis. *Lancet* 2003;**361**:107–16. https://doi.org/10.1016/s0140-6736(03)12228-3
719. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;**351**:1379–87. https://doi.org/10.1016/S0140-6736(97)09292-1
720. Mayberg MR, Wilson SE, Yatsu F, Weiss DG, Messina L, Hershey LA, *et al.* Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. Veterans affairs cooperative studies program 309 trialist group. *JAMA* 1991;**266**:3289–94.
721. Naylor AR, Sillesen H, Schroeder TV. Clinical and imaging features associated with an increased risk of early and late stroke in patients with symptomatic carotid disease. *Eur J Vasc Endovasc Surg* 2015;**49**:513–23. https://doi.org/10.1016/j.ejvs.2015.01.011
722. Tsantilas P, Kuehnl A, König T, Breitkreuz T, Kallmayer M, Knappich C, *et al.* Short time interval between neurologic event and carotid surgery is not associated with an increased procedural risk. *Stroke* 2016;**47**:2783–90. https://doi.org/10.1161/strokeaha.116.014058
723. Loftus IM, Paraskevas KI, Johal A, Waton S, Heikkila K, Naylor AR, *et al.* Editor's choice—delays to surgery and procedural risks following carotid endarterectomy in the UK national vascular registry. *Eur J Vasc Endovasc Surg* 2016;**52**:438–43. https://doi.org/10.1016/j.ejvs.2016.05.031
724. Strömberg S, Gelin J, Osterberg T, Bergström GML, Karlström L, Österberg K, *et al.* Very urgent carotid endarterectomy confers increased procedural risk. *Stroke* 2012;**43**:1331–5. https://doi.org/10.1161/strokeaha.111.639344
725. Bush CK, Kurimella D, Cross LJ, Conner KR, Martin-Schild D, He J, *et al.* Endovascular treatment with stent-retriever devices for acute ischemic stroke: a meta-analysis of randomized controlled trials. *PLoS One* 2016;**11**:e0147287. https://doi.org/10.1371/journal.pone.0147287
726. Savardekar AR, Narayan V, Patra DP, Spetzler RF, Sun H. Timing of carotid endarterectomy for symptomatic carotid stenosis: a snapshot of current trends and systematic review of literature on changing paradigm towards early surgery. *Neurosurgery* 2019;**85**:E214–25. https://doi.org/10.1093/neuros/nyy557
727. Hill MD, Brooks W, Mackey A, Clark WM, Meschia JF, Morrish WF, *et al.* Stroke after carotid stenting and endarterectomy in the carotid revascularization endarterectomy versus stenting trial (CREST). *Circulation* 2012;**126**:3054–61. https://doi.org/10.1161/circulationaha.112.120030
728. Blackshear JL, Cutlip DE, Roubin GS, Hill MD, Leimgruber PP, Begg RJ, *et al.* Myocardial infarction after carotid stenting and endarterectomy: results from the carotid revascularization endarterectomy versus stenting trial. *Circulation* 2011;**123**:2571–8. https://doi.org/10.1161/circulationaha.110.008250
729. Howard G, Roubin GS, Jansen O, Hendrikse J, Halliday A, Fraedrich G, *et al.* Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. *Lancet* 2016;**387**:1305–11. https://doi.org/10.1016/s0140-6736(15)01309-4
730. Alamowitch S, Eliasziw M, Algra A, Meldrum H, Barnett HJ. Risk, causes, and prevention of ischaemic stroke in elderly patients with symptomatic internal-carotid-artery stenosis. *Lancet* 2001;**357**:1154–60. https://doi.org/10.1016/s0140-6736(00)04332-4
731. Bonati LH, Lyrer P, Ederle J, Featherstone R, Brown MM. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *Cochrane Database Syst Rev* 2012;**9**:CD000515. https://doi.org/10.1002/14651858.CD000515.pub4
732. Economopoulos KP, Sergentanis TN, Tsivgoulis G, Mariolis AD, Stefanadis C. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. *Stroke* 2011;**42**:687–92. https://doi.org/10.1161/strokeaha.110.606079
733. Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, *et al.* Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet* 2015;**385**:529–38. https://doi.org/10.1016/s0140-6736(14)61184-3
734. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet* 2004;**363**:915–24. https://doi.org/10.1016/s0140-6736(04)15785-1
735. Rantner B, Kollerits B, Roubin GS, Ringleb PA, Jansen O, Howard G, *et al.* Early endarterectomy carries a lower procedural risk than early stenting in patients with symptomatic stenosis of the internal carotid artery: results from 4 randomized controlled trials. *Stroke* 2017;**48**:1580–7. https://doi.org/10.1161/strokeaha.116.016233
736. Schermerhorn ML, Fokkema M, Goodney P, Dillavou ED, Jim J, Kenwood CT, *et al.* The impact of centers for medicare and medicaid services high-risk criteria on outcome after carotid endarterectomy and carotid artery stenting in the SVS vascular registry. *J Vasc Surg* 2013;**57**:1318–24. https://doi.org/10.1016/j.jvs.2012.10.107
737. Schermerhorn ML, Liang P, Eldrup-Jorgensen J, Cronenwett JL, Nolan BW, Kashyap VS, *et al.* Association of transcarotid artery revascularization vs transfemoral carotid artery stenting with stroke or death among patients with carotid artery stenosis. *JAMA* 2019;**322**:2313–22. https://doi.org/10.1001/jama.2019.18441
738. Pineau S, Fajardo A, Saqib NU, Tanaka A, Motaganahalli RL, Keyhani A, *et al.* Transcarotid revascularization timing and early postoperative outcomes in symptomatic patients. *Vasc Endovascular Surg* 2023;**57**:344–9. https://doi.org/10.1177/15385744221146678
739. Kieffer E, Praquin B, Chiche L, Koskas F, Bahnini A. Distal vertebral artery reconstruction: long-term outcome. *J Vasc Surg* 2002;**36**:549–54. https://doi.org/10.1067/mva.2002.126092
740. Berguer R, Flynn LM, Kline RA, Caplan L. Surgical reconstruction of the extracranial vertebral artery: management and outcome. *J Vasc Surg* 2000;**31**:9–18. https://doi.org/10.1016/s0741-5214(00)70063-2
741. Markus HS, Harshfield EL, Compter A, Kuker W, Kappelle LJ, Clifton A, *et al.* Stenting for symptomatic vertebral artery stenosis: a preplanned pooled individual patient data analysis. *Lancet Neurol* 2019;**18**:666–73. https://doi.org/10.1016/s1474-4422(19)30149-8
742. Hanel RA, Brasiliense LB, Spetzler RF. Microsurgical revascularization of proximal vertebral artery: a single-center, single-operator analysis. *Neurosurgery* 2009;**64**:1043–51; discussion 1051. https://doi.org/10.1227/01.Neu.0000347099.17437.64
743. Asiddao CB, Donegan JH, Whitesell RC, Kalbfleisch JH. Factors associated with perioperative complications during carotid endarterectomy. *Anesth Analg* 1982;**61**:631–7.
744. Obeid T, Arhuidese I, Gaidry A, Qazi U, Abularrage C, Goodney P, *et al.* Beta-blocker use is associated with lower stroke and death after carotid artery stenting. *J Vasc Surg* 2016;**63**:363–9. https://doi.org/10.1016/j.jvs.2015.08.108
745. Abou-Chebl A, Reginelli J, Bajzer CT, Yadav JS. Intensive treatment of hypertension decreases the risk of hyperperfusion and intracerebral hemorrhage following carotid artery stenting. *Catheter Cardiovasc Interv* 2007;**69**:690–6. https://doi.org/10.1002/ccd.20693
746. Lindblad B, Persson NH, Takolander R, Bergqvist D. Does low-dose acetylsalicylic acid prevent stroke after carotid surgery? A double-blind, placebo-controlled randomized trial. *Stroke* 1993;**24**:1125–8. https://doi.org/10.1161/01.str.24.8.1125
747. Kretschmer G, Pratschner T, Prager M, Wenzi E, Polterauer P, Schemper M, *et al.* Antiplatelet treatment prolongs survival after carotid bifurcation endarterectomy. Analysis of the clinical series followed by a controlled trial. *Ann Surg* 1990;**211**:317–22. https://doi.org/10.1097/00000658-199003000-00002
748. Dalainas I, Nano G, Bianchi P, Stegher S, Malacrida G, Tealdi DG. Dual antiplatelet regime versus acetyl-acetic acid for carotid artery stenting. *Cardiovasc Intervent Radiol* 2006;**29**:519–21. https://doi.org/10.1007/s00270-005-5288-y
749. AbuRahma AF, Avgerinos ED, Chang RW, Darling RC, Duncan AA, Forbes TL, *et al.* The Society for Vascular Surgery implementation document for management of extracranial cerebrovascular disease. *J Vasc Surg* 2022;**75**:26s–98s. https://doi.org/10.1016/j.jvs.2021.04.074
750. Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, Halliday A, *et al.* Editor's choice—management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018;**55**:3–81. https://doi.org/10.1016/j.ejvs.2017.06.021
751. Ghamraoui AK, Chang H, Maldonado TS, Ricotta JJ, II. Clopidogrel versus ticagrelor for antiplatelet therapy in transcarotid artery revascularization in the Society for Vascular Surgery vascular quality initiative. *J Vasc Surg* 2022;**75**:1652–60. https://doi.org/10.1016/j.jvs.2021.11.060
752. Marcaccio CL, Patel PB, Liang P, Rastogi V, Stangenberg L, Jim J, *et al.* Efficacy and safety of perioperative dual antiplatelet therapy with ticagrelor versus clopidogrel in carotid artery stenting. *J Vasc Surg* 2022;**75**:1293–303.e8. https://doi.org/10.1016/j.jvs.2021.09.045
753. Ghamraoui AK, Ricotta JJ, II. Outcomes and strategy of tailored antiplatelet therapy with ticagrelor in patients undergoing transcarotid artery revascularization. *J Vasc Surg* 2021;**73**:132–41. https://doi.org/10.1016/j.jvs.2020.04.518
754. Zierler RE, Jordan WD, Lal BK, Mussa F, Leers S, Fulton J, *et al.* The Society for Vascular Surgery practice guidelines on follow-up after vascular surgery arterial procedures. *J Vasc Surg* 2018;**68**:256–84. https://doi.org/10.1016/j.jvs.2018.04.018
755. Cheun TJ, Jayakumar L, Sheehan MK, Sideman MJK, Pounds LL, Davies MG. Outcomes of upper extremity interventions for chronic critical ischemia. *J Vasc Surg* 2019;**69**:120–8.e2. https://doi.org/10.1016/j.jvs.2018.04.056
756. Awad El-Karim G, Kennedy SA, Ferraresi R, Addas JAK, Oreopoulos GD, Jaberi A, *et al.* Percutaneous transluminal angioplasty for below-the-elbow critical hand ischemia: a systematic review. *J Endovasc Ther* 2022;**29**:468–77. https://doi.org/10.1177/15266028211050309
757. Raimbeau A, Pistorius MA, Goueffic Y, Connault J, Plissonneau-Duquene P, Maurel B, *et al.* Digital ischaemia aetiologies and mid-term follow-up: a cohort study of 323 patients. *Medicine* 2021;**100**:e25659. https://doi.org/10.1097/md.0000000000025659
758. Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet* 2012;**379**:905–14. https://doi.org/10.1016/s0140-6736(11)61710-8
759. Aboyans V, Kamineni A, Allison MA, McDermott MM, Crouse JR, Ni H, *et al.* The epidemiology of subclavian stenosis and its association with markers of subclinical atherosclerosis: the multi-ethnic study of atherosclerosis (MESA). *Atherosclerosis* 2010;**211**:266–70. https://doi.org/10.1016/j.atherosclerosis.2010.01.013
760. Labropoulos N, Nandivada P, Bekelis K. Prevalence and impact of the subclavian steal syndrome. *Ann Surg* 2010;**252**:166–70. https://doi.org/10.1097/SLA.0b013e3181e3375a

761. Zhang J, Wang L, Chen Y, Wang S, Xing Y, Cui L. Color Doppler ultrasonography for the evaluation of subclavian artery stenosis. *Front Neurol* 2022;**13**:804039. https://doi.org/10.3389/fneur.2022.804039
762. Harper C, Cardullo PA, Weyman AK, Patterson RB. Transcranial Doppler ultrasonography of the basilar artery in patients with retrograde vertebral artery flow. *J Vasc Surg* 2008;**48**:859–64. https://doi.org/10.1016/j.jvs.2008.05.057
763. Chidambaram PK, Swaminathan RK, Ganesan P, Mayavan M. Segmental comparison of peripheral arteries by Doppler ultrasound and CT angiography. *J Clin Diagn Res* 2016;**10**:TC12–16. https://doi.org/10.7860/JCDR/2016/17191.7242
764. Tsao TF, Cheng KL, Shen CY, Wu M-C, Huang H-H, Su C-H, *et al.* Diagnostic performance of combined contrast-enhanced magnetic resonance angiography and phase-contrast magnetic resonance imaging in suspected subclavian steal syndrome. *Can Assoc Radiol J* 2016;**67**:190–201. https://doi.org/10.1016/j.carj.2015.08.007
765. Klitfod L, Jensen LP. Treatment of chronic upper limb ischaemia is safe and results are good. *Dan Med J* 2014;**61**:A4859.
766. Duran M, Grotemeyer D, Danch MA, Grabitz K, Schelzig H, Sagban TA. Subclavian carotid transposition: immediate and long-term outcomes of 126 surgical reconstructions. *Ann Vasc Surg* 2015;**29**:397–403. https://doi.org/10.1016/j.avsg.2014.09.030
767. Daniel VT, Madenci AL, Nguyen LL, Eslami MH, Kalish JA, Farber A, *et al.* Contemporary comparison of supra-aortic trunk surgical reconstructions for occlusive disease. *J Vasc Surg* 2014;**59**:1577–82, 1582.e1–2. https://doi.org/10.1016/j.jvs.2013.12.017
768. Burihan E, Soma F, Iared W. Angioplasty versus stenting for subclavian artery stenosis. *Cochrane Database Syst Rev* 2011;**10**:CD008461. https://doi.org/10.1002/14651858.CD008461.pub2
769. Hüttl K, Nemes B, Simonffy A, Entz L, Bérczi V. Angioplasty of the innominate artery in 89 patients: experience over 19 years. *Cardiovasc Intervent Radiol* 2002;**25**:109–14. https://doi.org/10.1007/s00270-001-0074-y
770. Modarai B, Ali T, Dourado R, Reidy JF, Taylor PR, Burnand KG. Comparison of extra-anatomic bypass grafting with angioplasty for atherosclerotic disease of the supra-aortic trunks. *Br J Surg* 2004;**91**:1453–7. https://doi.org/10.1002/bjs.4751
771. Song L, Zhang J, Li J, Gu Y, Yu H, Chen B, *et al.* Endovascular stenting vs. extrathoracic surgical bypass for symptomatic subclavian steal syndrome. *J Endovasc Ther* 2012;**19**:44–51. https://doi.org/10.1583/11-3692.1
772. Owens LV, Tinsley EA, Jr, Criado E, Burnham SJ, Keagy BA. Extrathoracic reconstruction of arterial occlusive disease involving the supraaortic trunks. *J Vasc Surg* 1995;**22**:217–21; discussion 221–2. https://doi.org/10.1016/s0741-5214(95)70133-8
773. Huijben M, Meershoek AJA, de Borst GJ, Toorop RJ. Long-term outcome of axillo-axillary bypass in patients with subclavian or innominate artery stenosis. *Ann Vasc Surg* 2021;**73**:321–8. https://doi.org/10.1016/j.avsg.2020.10.029
774. Lee AD, Agarwal S, Sadhu D. A 7-year experience with thoracoscopic sympathectomy for critical upper limb ischemia. *World J Surg* 2006;**30**:1644–7. https://doi.org/10.1007/s00268-005-0559-y
775. Schillinger M, Haumer M, Schillinger S, Mlekusch W, Ahmadi R, Minar E. Outcome of conservative versus interventional treatment of subclavian artery stenosis. *J Endovasc Ther* 2002;**9**:139–46. https://doi.org/10.1177/152660280200900201
776. Ahmed AT, Mohammed K, Chehab M, Brinjikji W, Hassan Murad M, Cloft H, *et al.* Comparing percutaneous transluminal angioplasty and stent placement for treatment of subclavian arterial occlusive disease: a systematic review and meta-analysis. *Cardiovasc Intervent Radiol* 2016;**39**:652–67. https://doi.org/10.1007/s00270-015-1250-9
777. Che W, Dong H, Jiang X, Peng M, Zou Y, Song L, *et al.* Subclavian artery stenting for coronary-subclavian steal syndrome. *Catheter Cardiovasc Interv* 2017;**89**:601–8. https://doi.org/10.1002/ccd.26902
778. Hamdan R, Guilleminot P, Leclercq T, Monin A. Coronary-subclavian steal syndrome causing myocardial infarction after arteriovenous fistula creation: a case report. *ESC Heart Fail* 2023;**10**:2084–9. https://doi.org/10.1002/ehf2.14341
779. Che WQ, Dong H, Jiang XJ, Peng M, Zou Y, Qian H, *et al.* Stenting for left subclavian artery stenosis in patients scheduled for left internal mammary artery-coronary artery bypass grafting. *Catheter Cardiovasc Interv* 2016;**87**:579–88. https://doi.org/10.1002/ccd.26477
780. Muller AM, Bertram J, Bradaric C, Koppara T, Cassese S, Xhepa E, *et al.* Frequency of subclavian artery stenosis in patients with mammarian artery coronary bypass and suspected coronary artery disease progression. *Clin Res Cardiol* 2023;**112**:1204–11. https://doi.org/10.1007/s00392-022-02113-z
781. Angle JF, Matsumoto AH, McGraw JK, Spinosa DJ, Hagspiel KD, Leung DA, *et al.* Percutaneous angioplasty and stenting of left subclavian artery stenosis in patients with left internal mammary-coronary bypass grafts: clinical experience and long-term follow-up. *Vasc Endovascular Surg* 2003;**37**:89–97. https://doi.org/10.1177/153857440303700202
782. Safian RD, Textor SC. Renal-artery stenosis. *N Engl J Med* 2001;**344**:431–42. https://doi.org/10.1056/nejm200102083440607
783. Hansen KJ, Edwards MS, Craven TE, Cherr GS, Jackson SA, Appel RG, *et al.* Prevalence of renovascular disease in the elderly: a population-based study. *J Vasc Surg* 2002;**36**:443–51. https://doi.org/10.1067/mva.2002.127351
784. Aboyans V, Desormais I, Magne J, Morange G, Mohty D, Lacroix P. Renal artery stenosis in patients with peripheral artery disease: prevalence, risk factors and long-term prognosis. *Eur J Vasc Endovasc Surg* 2017;**53**:380–5. https://doi.org/10.1016/j.ejvs.2016.10.029
785. Safian RD. Renal artery stenosis. *Prog Cardiovasc Dis* 2021;**65**:60–70. https://doi.org/10.1016/j.pcad.2021.03.003
786. Messerli FH, Bangalore S, Makani H, Rimoldi SF, Allemann Y, White CJ, *et al.* Flash pulmonary oedema and bilateral renal artery stenosis: the pickering syndrome. *Eur Heart J* 2011;**32**:2231–5. https://doi.org/10.1093/eurheartj/ehr056
787. Zeller T, Bonvini RF, Sixt S. Color-coded duplex ultrasound for diagnosis of renal artery stenosis and as follow-up examination after revascularization. *Catheter Cardiovasc Interv* 2008;**71**:995–9. https://doi.org/10.1002/ccd.21525
788. Prince M, Tafur JD, White CJ. When and how should we revascularize patients with atherosclerotic renal artery stenosis? *JACC Cardiovasc Interv* 2019;**12**:505–17. https://doi.org/10.1016/j.jcin.2018.10.023
789. AbuRahma AF, Yacoub M. Renal imaging: duplex ultrasound, computed tomography angiography, magnetic resonance angiography, and angiography. *Semin Vasc Surg* 2013;**26**:134–43. https://doi.org/10.1053/j.semvascsurg.2014.06.001
790. Staub D, Canevascini R, Huegli RW, Aschwanden M, Thalhammer C, Imfeld S, *et al.* Best duplex-sonographic criteria for the assessment of renal artery stenosis—correlation with intra-arterial pressure gradient. *Ultraschall Med* 2007;**28**:45–51. https://doi.org/10.1055/s-2007-962881
791. Williams GJ, Macaskill P, Chan SF, Karplus TE, Yung W, Hodson EM, *et al.* Comparative accuracy of renal duplex sonographic parameters in the diagnosis of renal artery stenosis: paired and unpaired analysis. *AJR Am J Roentgenol* 2007;**188**:798–811. https://doi.org/10.2214/ajr.06.0355
792. Parikh SA, Shishehbor MH, Gray BH, White CJ, Jaff MR. SCAI expert consensus statement for renal artery stenting appropriate use. *Catheter Cardiovasc Interv* 2014;**84**:1163–71. https://doi.org/10.1002/ccd.25559
793. Caps MT, Perissinotto C, Zierler RE, Polissar NL, Bergelin RO, Tullis MJ, *et al.* Prospective study of atherosclerotic disease progression in the renal artery. *Circulation* 1998;**98**:2866–72. https://doi.org/10.1161/01.cir.98.25.2866
794. Amighi J, Schlager O, Haumer M, Dick P, Mlekusch W, Loewe C, *et al.* Renal artery stenosis predicts adverse cardiovascular and renal outcome in patients with peripheral artery disease. *Eur J Clin Invest* 2009;**39**:784–92. https://doi.org/10.1111/j.1365-2362.2009.02180.x
795. Fatica RA, Port FK, Young EW. Incidence trends and mortality in end-stage renal disease attributed to renovascular disease in the United States. *Am J Kidney Dis* 2001;**37**:1184–90. https://doi.org/10.1053/ajkd.2001.24521
796. Ritchie J, Green D, Alderson HV, Chrysochou C, Vassallo D, Sinha S, *et al.* Associations of antiplatelet therapy and beta blockade with patient outcomes in atherosclerotic renovascular disease. *J Am Soc Hypertens* 2016;**10**:149–58.e3. https://doi.org/10.1016/j.jash.2015.12.002
797. Raman G, Adam GP, Halladay CW, Langberg VN, Azodo IA, Balk EM. Comparative effectiveness of management strategies for renal artery stenosis: an updated systematic review. *Ann Intern Med* 2016;**165**:635–49. https://doi.org/10.7326/M16-1053
798. Bhalla V, Textor SC, Beckman JA, Casanegra AI, Cooper CJ, Kim ESH, *et al.* Revascularization for renovascular disease: a scientific statement from the American Heart Association. *Hypertension* 2022;**79**:e128–43. https://doi.org/10.1161/hyp.0000000000000217
799. Piaggio D, Bracale U, Pecchia L, Di Taranto MD, Sodo M, Bracale UM. Endovascular treatment versus medical therapy for hypertensive patients with renal artery stenosis: an updated systematic review. *Ann Vasc Surg* 2019;**61**:445–54. https://doi.org/10.1016/j.avsg.2019.04.050
800. Wheatley K, Ives N, Gray R, Kalra PA, Moss JG, Baigent C, *et al.* Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med* 2009;**361**:1953–62. https://doi.org/10.1056/NEJMoa0905368
801. Bax L, Woittiez AJ, Kouwenberg HJ, Mali WP, Buskens E, Beek FJ, *et al.* Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. *Ann Intern Med* 2009;**150**:840–8, w150–1. https://doi.org/10.7326/0003-4819-150-12-200906160-00119
802. Webster J, Marshall F, Abdalla M, Dominiczak A, Edwards R, Isles CG, *et al.* Randomised comparison of percutaneous angioplasty vs continued medical therapy for hypertensive patients with atheromatous renal artery stenosis. Scottish and Newcastle Renal Artery Stenosis Collaborative Group. *J Hum Hypertens* 1998;**12**:329–35. https://doi.org/10.1038/sj.jhh.1000599
803. van Jaarsveld BC, Krijnen P, Pieterman H, Derkx FHM, Deinum J, Postma CT, *et al.* The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch Renal Artery Stenosis Intervention Cooperative Study Group. *N Engl J Med* 2000;**342**:1007–14. https://doi.org/10.1056/nejm200004063421403
804. Plouin PF, Chatellier G, Darné B, Raynaud A. Blood pressure outcome of angioplasty in atherosclerotic renal artery stenosis: a randomized trial. Essai Multicentrique Medicaments vs Angioplastie (EMMA) Study Group. *Hypertension* 1998;**31**:823–9. https://doi.org/10.1161/01.hyp.31.3.823

805. Abela R, Ivanova S, Lidder S, Morris R, Hamilton G. An analysis comparing open surgical and endovascular treatment of atherosclerotic renal artery stenosis. *Eur J Vasc Endovasc Surg* 2009;**38**:666–75. https://doi.org/10.1016/j.ejvs.2009.08.002
806. Balzer KM, Pfeiffer T, Rossbach S, Voiculescu A, Mödder U, Godehardt E, *et al.* Prospective randomized trial of operative vs interventional treatment for renal artery ostial occlusive disease (RAOOD). *J Vasc Surg* 2009;**49**:667–75; discussion 674–665. https://doi.org/10.1016/j.jvs.2008.10.006
807. Mohler ER, III, Gornik HL, Gerhard-Herman M, Misra S, Olin JW, Zierler RE. ACCF/ACR/AIUM/ASE/ASN/ICAVL/SCAI/SCCT/SIR/SVM/SVS/SVU [corrected] 2012 appropriate use criteria for peripheral vascular ultrasound and physiological testing part I: arterial ultrasound and physiological testing: a report of the American College of Cardiology Foundation appropriate use criteria task force, American College of Radiology, American Institute of Ultrasound in Medicine, American Society of Echocardiography, American Society of Nephrology, Intersocietal Commission for the Accreditation of Vascular Laboratories, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Interventional Radiology, Society for Vascular Medicine, Society for Vascular Surgery, [corrected] and Society for Vascular Ultrasound. [corrected]. *J Am Coll Cardiol* 2012;**60**:242–76. https://doi.org/10.1016/j.jacc.2012.02.009
808. Davies MG, Saad WA, Bismuth JX, Peden EK, Naoum JJ, Lumsden AB. Outcomes of endoluminal reintervention for restenosis after percutaneous renal angioplasty and stenting. *J Vasc Surg* 2009;**49**:946–52. https://doi.org/10.1016/j.jvs.2008.11.039
809. Hicks CW, Clark TWI, Cooper CJ, de Bhailís ÁM, De Carlo M, Green D, *et al.* Atherosclerotic renovascular disease: A KDIGO (kidney disease: improving global outcomes) controversies conference. *Am J Kidney Dis* 2022;**79**:289–301. https://doi.org/10.1053/j.ajkd.2021.06.025
810. Johansen KL, Garimella PS, Hicks CW, Kalra PA, Kelly DM, Martens S, *et al.* Central and peripheral arterial diseases in chronic kidney disease: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. *Kidney Int* 2021;**100**:35–48. https://doi.org/10.1016/j.kint.2021.04.029
811. Pappaccogli M, Robberechts T, Lengele JP, Van der Niepen P, Sarafidis P, Rabbia F, *et al.* Endovascular versus medical management of atherosclerotic renovascular disease: update and emerging concepts. *Hypertension* 2023;**80**:1150–61. https://doi.org/10.1161/HYPERTENSIONAHA.122.17965
812. Tian Y, Yuan B, Zhang N, Huang Z. Outcomes following the endovascular treatment of renal artery stenosis caused by fibromuscular dysplasia: a systematic review and meta-analysis. *Ann Vasc Surg* 2022;**78**:362–72. https://doi.org/10.1016/j.avsg.2021.06.042
813. Persu A, Giavarini A, Touzé E, Januszewicz A, Sapoval M, Azizi M, *et al.* European consensus on the diagnosis and management of fibromuscular dysplasia. *J Hypertens* 2014;**32**:1367–78. https://doi.org/10.1097/hjh.0000000000000213
814. Zeller T, Krankenberg H, Erglis A, Blessing E, Fuss T, Scheinert D, *et al.* A randomized, multi-center, prospective study comparing best medical treatment versus best medical treatment plus renal artery stenting in patients with hemodynamically relevant atherosclerotic renal artery stenosis (RADAR)—one-year results of a pre-maturely terminated study. *Trials* 2017;**18**:380. https://doi.org/10.1186/s13063-017-2126-x
815. Tamme K, Reintam Blaser A, Laisaar KT, Mändul M, Kals J, Forbes A, *et al.* Incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis. *BMJ Open* 2022;**12**:e062846. https://doi.org/10.1136/bmjopen-2022-062846
816. Acosta S. Epidemiology of mesenteric vascular disease: clinical implications. *Semin Vasc Surg* 2010;**23**:4–8. https://doi.org/10.1053/j.semvascsurg.2009.12.001
817. Acosta S, Ogren M, Sternby NH, Bergqvist D, Björck M. Incidence of acute thromboembolic occlusion of the superior mesenteric artery—a population-based study. *Eur J Vasc Endovasc Surg* 2004;**27**:145–50. https://doi.org/10.1016/j.ejvs.2003.11.003
818. Carver TW, Vora RS, Taneja A. Mesenteric ischemia. *Crit Care Clin* 2016;**32**:155–71. https://doi.org/10.1016/j.ccc.2015.11.001
819. Klass AA. Embolectomy in acute mesenteric occlusion. *Ann Surg* 1951;**134**:913–7. https://doi.org/10.1097/00000658-195111000-00016
820. Acosta S, Björck M. Acute thrombo-embolic occlusion of the superior mesenteric artery: a prospective study in a well defined population. *Eur J Vasc Endovasc Surg* 2003;**26**:179–83. https://doi.org/10.1053/ejvs.2002.1893
821. Kärkkäinen JM, Acosta S. Acute mesenteric ischemia (part I)—incidence, etiologies, and how to improve early diagnosis. *Best Pract Res Clin Gastroenterol* 2017;**31**:15–25. https://doi.org/10.1016/j.bpg.2016.10.018
822. Kärkkäinen JM. Acute mesenteric ischemia: a challenge for the acute care surgeon. *Scand J Surg* 2021;**110**:150–8. https://doi.org/10.1177/14574969211007590
823. Powell A, Armstrong P. Plasma biomarkers for early diagnosis of acute intestinal ischemia. *Semin Vasc Surg* 2014;**27**:170–5. https://doi.org/10.1053/j.semvascsurg.2015.01.008
824. Block T, Nilsson TK, Björck M, Acosta S. Diagnostic accuracy of plasma biomarkers for intestinal ischaemia. *Scand J Clin Lab Invest* 2008;**68**:242–8. https://doi.org/10.1080/00365510701646264
825. Kougias P, Lau D, El Sayed HF, Zhou W, Huynh TT, Lin PH. Determinants of mortality and treatment outcome following surgical interventions for acute mesenteric ischemia. *J Vasc Surg* 2007;**46**:467–74. https://doi.org/10.1016/j.jvs.2007.04.045
826. Lehtimäki TT, Kärkkäinen JM, Saari P, Manninen H, Paajanen H, Vanninen R. Detecting acute mesenteric ischemia in CT of the acute abdomen is dependent on clinical suspicion: review of 95 consecutive patients. *Eur J Radiol* 2015;**84**:2444–53. https://doi.org/10.1016/j.ejrad.2015.09.006
827. Kirkpatrick ID, Kroeker MA, Greenberg HM. Biphasic CT with mesenteric CT angiography in the evaluation of acute mesenteric ischemia: initial experience. *Radiology* 2003;**229**:91–8. https://doi.org/10.1148/radiol.2291020991
828. Oliva IB, Davarpanah AH, Rybicki FJ, Desjardins B, Flamm SD, Francois CJ, *et al.* ACR appropriateness Criteria ® imaging of mesenteric ischemia. *Abdom Imaging* 2013;**38**:714–9. https://doi.org/10.1007/s00261-012-9975-2
829. Salsano G, Salsano A, Sportelli E, Petrocelli F, Dahmane M, Spinella G, *et al.* What is the best revascularization strategy for acute occlusive arterial mesenteric ischemia: systematic review and meta-analysis. *Cardiovasc Intervent Radiol* 2018;**41**:27–36. https://doi.org/10.1007/s00270-017-1749-3
830. El Farargy M, Abdel Hadi A, Abou Eisha M, Bashaeb K, Antoniou GA. Systematic review and meta-analysis of endovascular treatment for acute mesenteric ischaemia. *Vascular* 2017;**25**:430–8. https://doi.org/10.1177/1708538116689353
831. Kärkkäinen JM, Acosta S. Acute mesenteric ischemia (part II)—vascular and endovascular surgical approaches. *Best Pract Res Clin Gastroenterol* 2017;**31**:27–38. https://doi.org/10.1016/j.bpg.2016.11.003
832. Wyers MC, Powell RJ, Nolan BW, Cronenwett JL. Retrograde mesenteric stenting during laparotomy for acute occlusive mesenteric ischemia. *J Vasc Surg* 2007;**45**:269–75. https://doi.org/10.1016/j.jvs.2006.10.047
833. Tilsed JV, Casamassima A, Kurihara H, Mariani D, Martinez I, Pereira J, *et al.* ESTES guidelines: acute mesenteric ischaemia. *Eur J Trauma Emerg Surg* 2016;**42**:253–70. https://doi.org/10.1007/s00068-016-0634-0
834. Tallarita T, Oderich GS, Gloviczki P, Duncan AA, Kalra M, Cha S, *et al.* Patient survival after open and endovascular mesenteric revascularization for chronic mesenteric ischemia. *J Vasc Surg* 2013;**57**:747–55; discussion 754–745. https://doi.org/10.1016/j.jvs.2012.09.047
835. Alahdab F, Arwani R, Pasha AK, Razouki ZA, Prokop LJ, Huber TS, *et al.* A systematic review and meta-analysis of endovascular versus open surgical revascularization for chronic mesenteric ischemia. *J Vasc Surg* 2018;**67**:1598–605. https://doi.org/10.1016/j.jvs.2017.12.046
836. Mensink PB, Moons LM, Kuipers EJ. Chronic gastrointestinal ischaemia: shifting paradigms. *Gut* 2011;**60**:722–37. https://doi.org/10.1136/gut.2009.199695
837. Roobottom CA, Dubbins PA. Significant disease of the celiac and superior mesenteric arteries in asymptomatic patients: predictive value of Doppler sonography. *AJR Am J Roentgenol* 1993;**161**:985–8. https://doi.org/10.2214/ajr.161.5.8273642
838. Høyer C, Christensen MH, Sandermann J, Leusink R, Abrahamsen J. Chronic mesenteric ischaemia: the importance of the individual mesenteric artery. *Clin Physiol Funct Imaging* 2022;**42**:15–22. https://doi.org/10.1111/cpf.12730
839. Mensink PB, van Petersen AS, Geelkerken RH, Otte JA, Huisman AB, Kolkman JJ, *et al.* Clinical significance of splanchnic artery stenosis. *Br J Surg* 2006;**93**:1377–82. https://doi.org/10.1002/bjs.5481
840. van Noord D, Mensink PB, de Knegt RJ, Ouwendijk M, Francke J, van Vuuren AJ, *et al.* Serum markers and intestinal mucosal injury in chronic gastrointestinal ischemia. *Dig Dis Sci* 2011;**56**:506–12. https://doi.org/10.1007/s10620-010-1303-5
841. Mensink PB, Hol L, Borghuis-Koertshuis N, Geelkerken RH, Huisman AB, Doelman CJA, *et al.* Transient postprandial ischemia is associated with increased intestinal fatty acid binding protein in patients with chronic gastrointestinal ischemia. *Eur J Gastroenterol Hepatol* 2009;**21**:278–82. https://doi.org/10.1097/MEG.0b013e32832183a7
842. van Noord D, Kolkman JJ. Functional testing in the diagnosis of chronic mesenteric ischemia. *Best Pract Res Clin Gastroenterol* 2017;**31**:59–68. https://doi.org/10.1016/j.bpg.2016.12.002
843. van Petersen AS, Meerwaldt R, Kolkman JJ, Huisman AB, van der Palen J, van Bockel JH, *et al.* The influence of respiration on criteria for transabdominal duplex examination of the splanchnic arteries in patients with suspected chronic splanchnic ischemia. *J Vasc Surg* 2013;**57**:1603–11, 1611.e1–10. https://doi.org/10.1016/j.jvs.2012.11.120
844. Zwolak RM, Fillinger MF, Walsh DB, LaBombard FA, Musson A, Darling CE, *et al.* Mesenteric and celiac duplex scanning: a validation study. *J Vasc Surg* 1998;**27**:1078–88; discussion 1088. https://doi.org/10.1016/s0741-5214(98)60010-0
845. Schaefer PJ, Pfarr J, Trentmann J, Wulff A, Langer C, Siggelkow M, *et al.* Comparison of noninvasive imaging modalities for stenosis grading in mesenteric arteries. *Rofo* 2013;**185**:628–34. https://doi.org/10.1055/s-0033-1335212
846. Cademartiri F, Palumbo A, Maffei E, Martini C, Malagò R, Belgrano M, *et al.* Noninvasive evaluation of the celiac trunk and superior mesenteric artery with multislice CT in patients with chronic mesenteric ischaemia. *Radiol Med* 2008;**113**:1135–42. https://doi.org/10.1007/s11547-008-0330-1
847. Pecoraro F, Rancic Z, Lachat M, Mayer D, Amann-Vesti B, Pfammatter T, *et al.* Chronic mesenteric ischemia: critical review and guidelines for management. *Ann Vasc Surg* 2013;**27**:113–22. https://doi.org/10.1016/j.avsg.2012.05.012
848. Gupta PK, Horan SM, Turaga KK, Miller WJ, Pipinos II. Chronic mesenteric ischemia: endovascular versus open revascularization. *J Endovasc Ther* 2010;**17**:540–9. https://doi.org/10.1583/09-2935.1

849. Huber TS, Björck M, Chandra A, Clouse WD, Dalsing MC, Oderich GS, *et al.* Chronic mesenteric ischemia: clinical practice guidelines from the society for vascular surgery. *J Vasc Surg* 2021;**73**:87s–115s. https://doi.org/10.1016/j.jvs.2020.10.029
850. Fernández-Friera L, Fuster V, López-Melgar B, Oliva B, Sánchez-González J, Macías A, *et al.* Vascular inflammation in subclinical atherosclerosis detected by hybrid PET/MRI. *J Am Coll Cardiol* 2019;**73**:1371–82. https://doi.org/10.1016/j.jacc.2018.12.075
851. Meissner I, Whisnant JP, Khandheria BK, Spittell PC, O'Fallon WM, Pascoe RD, *et al.* Prevalence of potential risk factors for stroke assessed by transesophageal echocardiography and carotid ultrasonography: the SPARC study. Stroke prevention: assessment of risk in a community. *Mayo Clin Proc* 1999;**74**:862–9. https://doi.org/10.4065/74.9.862
852. Russo C, Jin Z, Rundek T, Homma S, Sacco RL, Di Tullio MR. Atherosclerotic disease of the proximal aorta and the risk of vascular events in a population-based cohort: the Aortic Plaques and Risk of Ischemic Stroke (APRIS) study. *Stroke* 2009;**40**:2313–8. https://doi.org/10.1161/strokeaha.109.548313
853. Oyama N, Gona P, Salton CJ, Chuang ML, Jhaveri RR, Blease SJ, *et al.* Differential impact of age, sex, and hypertension on aortic atherosclerosis: the Framingham heart study. *Arterioscler Thromb Vasc Biol* 2008;**28**:155–9. https://doi.org/10.1161/atvbaha.107.153544
854. Montgomery DH, Ververis JJ, McGorisk G, Frohwein S, Martin RP, Taylor WR. Natural history of severe atheromatous disease of the thoracic aorta: a transesophageal echocardiographic study. *J Am Coll Cardiol* 1996;**27**:95–101. https://doi.org/10.1016/0735-1097(95)00431-9
855. Amarenco P, Cohen A, Hommel M, Moulin T, Leys D, Bousser M-G. Atherosclerotic disease of the aortic arch as a risk factor for recurrent ischemic stroke. *N Engl J Med* 1996;**334**:1216–21. https://doi.org/10.1056/nejm199605093341902
856. Fujimoto S, Yasaka M, Otsubo R, Oe H, Nagatsuka K, Minematsu K. Aortic arch atherosclerotic lesions and the recurrence of ischemic stroke. *Stroke* 2004;**35**:1426–9. https://doi.org/10.1161/01.STR.0000127788.32550.d4
857. Koren MJ, Bryant B, Hilton TC. Atherosclerotic disease of the aortic arch and the risk of ischemic stroke. *N Engl J Med* 1995;**332**:1237–8. author reply 1237-1238. https://doi.org/10.1056/NEJM199505043321815
858. Meissner I, Khandheria BK, Sheps SG, Schwartz GL, Wiebers DO, Whisnant JP, *et al.* Atherosclerosis of the aorta: risk factor, risk marker, or innocent bystander? A prospective population-based transesophageal echocardiography study. *J Am Coll Cardiol* 2004;**44**:1018–24. https://doi.org/10.1016/j.jacc.2004.05.075
859. Mitusch R, Doherty C, Wucherpfennig H, Memmesheimer C, Tepe C, Stierle U, *et al.* Vascular events during follow-up in patients with aortic arch atherosclerosis. *Stroke* 1997;**28**:36–9. https://doi.org/10.1161/01.str.28.1.36
860. Tunick PA, Rosenzweig BP, Katz ES, Freedberg RS, Perez JL, Kronzon I. High risk for vascular events in patients with protruding aortic atheromas: a prospective study. *J Am Coll Cardiol* 1994;**23**:1085–90. https://doi.org/10.1016/0735-1097(94)90595-9
861. Di Tullio MR, Russo C, Jin Z, Sacco RL, Mohr JP, Homma S. Aortic arch plaques and risk of recurrent stroke and death. *Circulation* 2009;**119**:2376–82. https://doi.org/10.1161/circulationaha.108.811935
862. Tunick PA, Nayar AC, Goodkin GM, Mirchandani S, Francescone S, Rosenzweig BP, *et al.* Effect of treatment on the incidence of stroke and other emboli in 519 patients with severe thoracic aortic plaque. *Am J Cardiol* 2002;**90**:1320–5. https://doi.org/10.1016/s0002-9149(02)02870-9
863. Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, *et al.* Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet* 2004;**364**:331–7. https://doi.org/10.1016/s0140-6736(04)16721-4
864. Bowdish ME, Weaver FA, Liebman HA, Rowe VL, Hood DB. Anticoagulation is an effective treatment for aortic mural thrombi. *J Vasc Surg* 2002;**36**:713–9.
865. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, *et al.* 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke* 2021;**52**:e364–467. https://doi.org/10.1161/str.0000000000000375
866. Amarenco P, Davis S, Jones EF, Cohen AA, Heiss W-D, Kaste M, *et al.* Clopidogrel plus aspirin versus warfarin in patients with stroke and aortic arch plaques. *Stroke* 2014;**45**:1248–57. https://doi.org/10.1161/strokeaha.113.004251
867. Benavente OR, Hart RG, McClure LA, Szychowski JM, Coffey CS, Pearce LA. Effects of clopidogrel added to aspirin in patients with recent lacunar stroke. *N Engl J Med* 2012;**367**:817–25. https://doi.org/10.1056/NEJMoa1204133
868. Amarenco P, Kim JS, Labreuche J, Charles H, Abtan J, Béjot Y, *et al.* A comparison of two LDL cholesterol targets after ischemic stroke. *N Engl J Med* 2020;**382**:9. https://doi.org/10.1056/NEJMoa1910355
869. Devereux RB, de Simone G, Arnett DK, Best LG, Boerwinkle E, Howard BV, *et al.* Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons ≥15 years of age. *Am J Cardiol* 2012;**110**:1189–94. https://doi.org/10.1016/j.amjcard.2012.05.063
870. van Kimmenade RR, Kempers M, de Boer MJ, Loeys BL, Timmermans J. A clinical appraisal of different Z-score equations for aortic root assessment in the diagnostic evaluation of Marfan syndrome. *Genet Med* 2013;**15**:528–32. https://doi.org/10.1038/gim.2012.172
871. Davies RR, Gallo A, Coady MA, Tellides G, Botta DM, Burke B, *et al.* Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. *Ann Thorac Surg* 2006;**81**:169–77. https://doi.org/10.1016/j.athoracsur.2005.06.026
872. Hannawa KK, Eliason JL, Upchurch GR, Jr. Gender differences in abdominal aortic aneurysms. *Vascular* 2009;**17**:30–9. https://doi.org/10.2310/6670.2008.00092
873. Boczar KE, Cheung K, Boodhwani M, Beauchesne L, Dennie C, Nagpal S, *et al.* Sex differences in thoracic aortic aneurysm growth. *Hypertension* 2019;**73**:190–6. https://doi.org/10.1161/hypertensionaha.118.11851
874. Hultgren R, Larsson E, Wahlgren CM, Swedenborg J. Female and elderly abdominal aortic aneurysm patients more commonly have concurrent thoracic aortic aneurysm. *Ann Vasc Surg* 2012;**26**:918–23. https://doi.org/10.1016/j.avsg.2012.01.023
875. Chaer RA, Vasoncelos R, Marone LK, Al-Khoury G, Rhee RY, Cho JS, *et al.* Synchronous and metachronous thoracic aneurysms in patients with abdominal aortic aneurysms. *J Vasc Surg* 2012;**56**:1261–5. https://doi.org/10.1016/j.jvs.2012.04.056
876. Olsen PS, Schroeder T, Agerskov K, Agerskov K, Røder O, Sørensen S, *et al.* Surgery for abdominal aortic aneurysms. A survey of 656 patients. *J Cardiovasc Surg* 1991;**32**:636–42.
877. Tuveson V, Löfdahl HE, Hultgren R. Patients with abdominal aortic aneurysm have a high prevalence of popliteal artery aneurysms. *Vasc Med* 2016;**21**:369–75. https://doi.org/10.1177/1358863x16648404
878. Brunkwall J, Hauksson H, Bengtsson H, Bergqvist D, Takolander R, Bergentz S-E. Solitary aneurysms of the iliac arterial system: an estimate of their frequency of occurrence. *J Vasc Surg* 1989;**10**:381–4. https://doi.org/10.1067/mva.1989.13733
879. Bickerstaff LK, Pairolero PC, Hollier LH, Melton LJ, Van Peenen HJ, Cherry KJ, *et al.* Thoracic aortic aneurysms: a population-based study. *Surgery* 1982;**92**:1103–8.
880. Coady MA, Rizzo JA, Goldstein LJ, Elefteriades JA. Natural history, pathogenesis, and etiology of thoracic aortic aneurysms and dissections. *Cardiol Clin* 1999;**17**:615–35; vii. https://doi.org/10.1016/s0733-8651(05)70105-3
881. Diwan A, Sarkar R, Stanley JC, Zelenock GB, Wakefield TW. Incidence of femoral and popliteal artery aneurysms in patients with abdominal aortic aneurysms. *J Vasc Surg* 2000;**31**:863–9. https://doi.org/10.1067/mva.2000.105955
882. Brown LC, Thompson SG, Greenhalgh RM, Powell JT. Incidence of cardiovascular events and death after open or endovascular repair of abdominal aortic aneurysm in the randomized EVAR trial 1. *Br J Surg* 2011;**98**:935–42. https://doi.org/10.1002/bjs.7485
883. Hammo S, Grannas D, Wahlgren CM. High risk of early and late cardiovascular events after endovascular aortic aneurysm repair. *Ann Vasc Surg* 2022;**86**:320–7. https://doi.org/10.1016/j.avsg.2022.04.028
884. Kuzmik GA, Sang AX, Elefteriades JA. Natural history of thoracic aortic aneurysms. *J Vasc Surg* 2012;**56**:565–71. https://doi.org/10.1016/j.jvs.2012.04.053
885. Olsson C, Thelin S, Ståhle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. *Circulation* 2006;**114**:2611–8. https://doi.org/10.1161/circulationaha.106.630400
886. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE, *et al.* 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation* 2010;**121**:e266–369. https://doi.org/10.1161/CIR.0b013e3181d4739e
887. Goldfinger JZ, Halperin JL, Marin ML, Stewart AS, Eagle KA, Fuster V. Thoracic aortic aneurysm and dissection. *J Am Coll Cardiol* 2014;**64**:1725–39. https://doi.org/10.1016/j.jacc.2014.08.025
888. Caruana M, Baars MJ, Bashiardes E, Benke K, Björck E, Codreanu A, *et al.* HTAD patient pathway: strategy for diagnostic work-up of patients and families with (suspected) heritable thoracic aortic diseases (HTAD). A statement from the HTAD working group of VASCERN. *Eur J Med Genet* 2023;**66**:104673. https://doi.org/10.1016/j.ejmg.2022.104673
889. Patel HJ, Deeb GM. Ascending and arch aorta: pathology, natural history, and treatment. *Circulation* 2008;**118**:188–95. https://doi.org/10.1161/circulationaha.107.690933
890. Boodhwani M, de Kerchove L, Glineur D, Poncelet A, Rubay J, Astarci P, *et al.* Repair-oriented classification of aortic insufficiency: impact on surgical techniques and clinical outcomes. *J Thorac Cardiovasc Surg* 2009;**137**:286–94. https://doi.org/10.1016/j.jtcvs.2008.08.054
891. Ganapathi AM, Ranney DN, Peterson MD, Lindsay ME, Patel HJ, Pyeritz RE, *et al.* Location of aortic enlargement and risk of type A dissection at smaller diameters. *J Am Coll Cardiol* 2022;**79**:1890–7. https://doi.org/10.1016/j.jacc.2022.02.053
892. Kalogerakos PD, Zafar MA, Li Y, Mukherjee SK, Ziganshin BA, Rizzo JA, *et al.* Root dilatation is more malignant than ascending aortic dilation. *J Am Heart Assoc* 2021;**10**:e020645. https://doi.org/10.1161/jaha.120.020645

893. Della Corte A, Bancone C, Buonocore M, Dialetto G, Covino FE, Manduca S, *et al.* Pattern of ascending aortic dimensions predicts the growth rate of the aorta in patients with bicuspid aortic valve. *JACC Cardiovasc Imaging* 2013;**6**:1301–10. https://doi.org/10.1016/j.jcmg.2013.07.009
894. Kim JB, Spotnitz M, Lindsay ME, MacGillivray TE, Isselbacher EM, Sundt TM. Risk of aortic dissection in the moderately dilated ascending aorta. *J Am Coll Cardiol* 2016;**68**:1209–19. https://doi.org/10.1016/j.jacc.2016.06.025
895. Saeyeldin A, Zafar MA, Velasquez CA, Ip K, Gryaznov A, Brownstein AJ, *et al.* Natural history of aortic root aneurysms in Marfan syndrome. *Ann Cardiothorac Surg* 2017;**6**:625–32. https://doi.org/10.21037/acs.2017.11.10
896. Cheung K, Boodhwani M, Chan KL, Beauchesne L, Dick A, Coutinho T. Thoracic aortic aneurysm growth: role of sex and aneurysm etiology. *J Am Heart Assoc* 2017;**6**:e003792. https://doi.org/10.1161/jaha.116.003792
897. Nataf P, Lansac E. Dilation of the thoracic aorta: medical and surgical management. *Heart* 2006;**92**:1345–52. https://doi.org/10.1136/hrt.2005.074781
898. Yiu RS, Cheng SW. Natural history and risk factors for rupture of thoracic aortic arch aneurysms. *J Vasc Surg* 2016;**63**:1189–94. https://doi.org/10.1016/j.jvs.2015.12.043
899. Coady MA, Rizzo JA, Hammond GL, Mandapati D, Darr U, Kopf GS, *et al.* What is the appropriate size criterion for resection of thoracic aortic aneurysms? *J Thorac Cardiovasc Surg* 1997;**113**:476–91; discussion 489–491. https://doi.org/10.1016/s0022-5223(97)70360-x
900. Safi HJ, Winnerkvist A, Miller CC, III, Iliopoulos DC, Reardon MJ, Espada R, *et al.* Effect of extended cross-clamp time during thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 1998;**66**:1204–8. https://doi.org/10.1016/s0003-4975(98)00781-4
901. Isselbacher EM. Thoracic and abdominal aortic aneurysms. *Circulation* 2005;**111**:816–28. https://doi.org/10.1161/01.Cir.0000154569.08857.7a
902. Zafar MA, Chen JF, Wu J, Li Y, Papanikolaou D, Abdelbaky M, *et al.* Natural history of descending thoracic and thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg* 2021;**161**:498–511.e1. https://doi.org/10.1016/j.jtcvs.2019.10.125
903. Oladokun D, Patterson BO, Sobocinski J, Karthikesalingam A, Loftus I, Thompson MM, *et al.* Systematic review of the growth rates and influencing factors in thoracic aortic aneurysms. *Eur J Vasc Endovasc Surg* 2016;**51**:674–81. https://doi.org/10.1016/j.ejvs.2016.01.017
904. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, *et al.* Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg* 2002;**73**:17–28; discussion 27–18. https://doi.org/10.1016/s0003-4975(01)03236-2
905. Verloes A, Sakalihasan N, Koulischer L, Limet R. Aneurysms of the abdominal aorta: familial and genetic aspects in three hundred thirteen pedigrees. *J Vasc Surg* 1995;**21**:646–55. https://doi.org/10.1016/s0741-5214(95)70196-6
906. Thompson SG, Brown LC, Sweeting MJ, Bown MJ, Kim LG, Glover MJ, *et al.* Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: implications for surveillance intervals and their cost-effectiveness. *Health Technol Assess* 2013;**17**:1–118. https://doi.org/10.3310/hta17410
907. Sakalihasan N, Defraigne JO, Kerstenne MA, Cheramy-Bien J-P, Smelser DT, Tromp G, *et al.* Family members of patients with abdominal aortic aneurysms are at increased risk for aneurysms: analysis of 618 probands and their families from the Liege AAA family study. *Ann Vasc Surg* 2014;**28**:787–97. https://doi.org/10.1016/j.avsg.2013.11.005
908. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK small aneurysm trial participants. *Ann Surg* 1999;**230**:289–96; discussion 296–287. https://doi.org/10.1097/00000658-199909000-00002
909. Mani K, Wanhainen A. Accurate and reproducible diameter measurement is essential in surveillance and treatment of thoracic aortic aneurysms. *Eur J Vasc Endovasc Surg* 2014;**47**:27. https://doi.org/10.1016/j.ejvs.2013.10.004
910. Isselbacher EM, Preventza O, Hamilton Black J, III, Augoustides JG, Beck AW, Bolen MA, *et al.* 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology joint committee on clinical practice guidelines. *Circulation* 2022;**146**:e334-482. https://doi.org/10.1161/cir.0000000000001106
911. Booher AM, Eagle KA. Diagnosis and management issues in thoracic aortic aneurysm. *Am Heart J* 2011;**162**:38–46.e1. https://doi.org/10.1016/j.ahj.2011.04.010
912. Wang TKM, Desai MY. Thoracic aortic aneurysm: optimal surveillance and treatment. *Cleve Clin J Med* 2020;**87**:557–68. https://doi.org/10.3949/ccjm.87a.19140-1
913. Roberts DA. Magnetic resonance imaging of thoracic aortic aneurysm and dissection. *Semin Roentgenol* 2001;**36**:295–308. https://doi.org/10.1053/sroe.2001.26938
914. Rajiah P. CT and MRI in the evaluation of thoracic aortic diseases. *Int J Vasc Med* 2013;**2013**:797189. https://doi.org/10.1155/2013/797189
915. Lin FY, Devereux RB, Roman MJ, Meng J, Jow VM, Jacobs A, *et al.* Assessment of the thoracic aorta by multidetector computed tomography: age- and sex-specific reference values in adults without evident cardiovascular disease. *J Cardiovasc Comput Tomogr* 2008;**2**:298–308. https://doi.org/10.1016/j.jcct.2008.08.002
916. McPhee JT, Hill JS, Eslami MH. The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001–2004. *J Vasc Surg* 2007;**45**:891–9. https://doi.org/10.1016/j.jvs.2007.01.043
917. Forsdahl SH, Singh K, Solberg S, Jacobsen BK. Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromsø study, 1994–2001. *Circulation* 2009;**119**:2202–8. https://doi.org/10.1161/circulationaha.108.817619
918. Jahangir E, Lipworth L, Edwards TL, Kabagambe EK, Mumma MT, Mensah GA, *et al.* Smoking, sex, risk factors and abdominal aortic aneurysms: a prospective study of 18 782 persons aged above 65 years in the southern community cohort study. *J Epidemiol Community Health* 2015;**69**:481–8. https://doi.org/10.1136/jech-2014-204920
919. Strachan DP. Predictors of death from aortic aneurysm among middle-aged men: the Whitehall study. *Br J Surg* 2005;**78**:401–4. https://doi.org/10.1002/bjs.1800780407
920. Wanhainen A, Bergqvist D, Boman K, Nilsson TK, Rutegård J, Björck M. Risk factors associated with abdominal aortic aneurysm: a population-based study with historical and current data. *J Vasc Surg* 2005;**41**:390–6. https://doi.org/10.1016/j.jvs.2005.01.002
921. Kent KC, Zwolak RM, Egorova NN, Riles TS, Manganaro A, Moskowitz AJ, *et al.* Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg* 2010;**52**:539–48. https://doi.org/10.1016/j.jvs.2010.05.090
922. Raffort J, Lareyre F, Clément M, Hassen-Khodja R, Chinetti G, Mallat Z. Diabetes and aortic aneurysm: current state of the art. *Cardiovasc Res* 2018;**114**:1702–13. https://doi.org/10.1093/cvr/cvy174
923. Avdic T, Franzén S, Zarrouk M, Acosta S, Nilsson P, Gottsäter A, *et al.* Reduced long-term risk of aortic aneurysm and aortic dissection among individuals with type 2 diabetes mellitus: a nationwide observational study. *J Am Heart Assoc* 2018;**7**:e007618. https://doi.org/10.1161/jaha.117.007618
924. Nordness MJ, Baxter BT, Matsumura J, Terrin M, Zhang K, Ye F, *et al.* The effect of diabetes on abdominal aortic aneurysm growth over 2 years. *J Vasc Surg* 2022;**75**:1211–22.e1. https://doi.org/10.1016/j.jvs.2021.10.019
925. Yusuf K, Murat B, Unal A, Ulku K, Taylan K, Ozerdem O, *et al.* Inflammatory abdominal aortic aneurysm: predictors of long-term outcome in a case-control study. *Surgery* 2007;**141**:83–9. https://doi.org/10.1016/j.surg.2006.04.007
926. Oliver-Williams C, Sweeting MJ, Turton G, Parkin D, Cooper D, Rodd C, *et al.* Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. *Br J Surg* 2018;**105**:68–74. https://doi.org/10.1002/bjs.10715
927. Golledge J, Tsao PS, Dalman RL, Norman PE. Circulating markers of abdominal aortic aneurysm presence and progression. *Circulation* 2008;**118**:2382–92. https://doi.org/10.1161/circulationaha.108.802074
928. Vermeulen JJM, Meijer M, de Vries FBG, Reijnen MMPJ, Holewijn S, Thijssen DHJ, *et al.* A systematic review summarizing local vascular characteristics of aneurysm wall to predict for progression and rupture risk of abdominal aortic aneurysms. *J Vasc Surg* 2023;**77**:288–98.e2. https://doi.org/10.1016/j.jvs.2022.07.008
929. Brady AR, Thompson SG, Fowkes FG, Greenhalgh RM, Powell JT. Abdominal aortic aneurysm expansion: risk factors and time intervals for surveillance. *Circulation* 2004;**110**:16–21. https://doi.org/10.1161/01.Cir.0000133279.07468.9f
930. Malayala SV, Raza A, Vanaparthy R. Gender-based differences in abdominal aortic aneurysm rupture: a retrospective study. *J Clin Med Res* 2020;**12**:794–802. https://doi.org/10.14740/jocmr4376
931. Skibba AA, Evans JR, Hopkins SP, Yoon HR, Katras T, Kalbfleisch JH, *et al.* Reconsidering gender relative to risk of rupture in the contemporary management of abdominal aortic aneurysms. *J Vasc Surg* 2015;**62**:1429–36. https://doi.org/10.1016/j.jvs.2015.07.079
932. Catalano O, Siani A. Ruptured abdominal aortic aneurysm: categorization of sonographic findings and report of 3 new signs. *J Ultrasound Med* 2005;**24**:1077–83. https://doi.org/10.7863/jum.2005.24.8.1077
933. Schermerhorn ML, Bensley RP, Giles KA, Hurks R, O'Malley AJ, Cotterill P, *et al.* Changes in abdominal aortic aneurysm rupture and short-term mortality, 1995-2008: a retrospective observational study. *Ann Surg* 2012;**256**:651–8. https://doi.org/10.1097/SLA.0b013e31826b4f91
934. Rakita D, Newatia A, Hines JJ, Siegel DN, Friedman B. Spectrum of CT findings in rupture and impending rupture of abdominal aortic aneurysms. *Radiographics* 2007;**27**:497–507. https://doi.org/10.1148/rg.272065026
935. Schwartz SA, Taljanovic MS, Smyth S, O'Brien MJ, Rogers LF. CT findings of rupture, impending rupture, and contained rupture of abdominal aortic aneurysms. *AJR Am J Roentgenol* 2007;**188**:W57–62. https://doi.org/10.2214/ajr.05.1554
936. Tomee SM, Bulder RMA, Meijer CA, van Berkum I, Hinnen J-W, Schoones JW, *et al.* Excess mortality for abdominal aortic aneurysms and the potential of strict implementation of cardiovascular risk management: a multifaceted study integrating meta-analysis, national registry, and PHAST and TEDY trial data. *Eur J Vasc Endovasc Surg* 2023;**65**:348–57. https://doi.org/10.1016/j.ejvs.2022.11.019
937. Freiberg MS, Arnold AM, Newman AB, Edwards MS, Kraemer KL, Kuller LH. Abdominal aortic aneurysms, increasing infrarenal aortic diameter, and risk of total mortality and incident cardiovascular disease events: 10-year follow-up data from the cardiovascular health study. *Circulation* 2008;**117**:1010–7. https://doi.org/10.1161/circulationaha.107.720219
938. Bown MJ, Sweeting MJ, Brown LC, Powell JT, Thompson SG. Surveillance intervals for small abdominal aortic aneurysms: a meta-analysis. *JAMA* 2013;**309**:806–13. https://doi.org/10.1001/jama.2013.950

939. Dugas A, Therasse E, Kauffmann C, Tang A, Elkouri S, Nozza A, *et al.* Reproducibility of abdominal aortic aneurysm diameter measurement and growth evaluation on axial and multiplanar computed tomography reformations. *Cardiovasc Intervent Radiol* 2012;**35**:779–87. https://doi.org/10.1007/s00270-011-0259-y
940. Kontopodis N, Metaxa E, Gionis M, Papaharilaou Y, Ioannou CV. Discrepancies in determination of abdominal aortic aneurysms maximum diameter and growth rate, using axial and orhtogonal computed tomography measurements. *Eur J Radiol* 2013;**82**:1398–403. https://doi.org/10.1016/j.ejrad.2013.04.031
941. Foo FJ, Hammond CJ, Goldstone AR, Abuhamdiah M, Rashid ST, West RM, *et al.* Agreement between computed tomography and ultrasound on abdominal aortic aneurysms and implications on clinical decisions. *Eur J Vasc Endovasc Surg* 2011;**42**:608–14. https://doi.org/10.1016/j.ejvs.2011.07.003
942. Zhu C, Tian B, Leach JR, Liu Q, Lu J, Chen L, *et al.* Non-contrast 3D black blood MRI for abdominal aortic aneurysm surveillance: comparison with CT angiography. *Eur Radiol* 2017;**27**:1787–94. https://doi.org/10.1007/s00330-016-4559-0
943. Sakalihasan N, Michel JB, Katsargyris A, Kuivaniemi H, Defraigne J-O, Nchimi A, *et al.* Abdominal aortic aneurysms. *Nat Rev Dis Primers* 2018;**4**:34. https://doi.org/10.1038/s41572-018-0030-7
944. Wemmelund H, Jørgensen TM, Høgh A, Behr-Rasmussen C, Johnsen SP, Lindholt JS, *et al.* Low-dose aspirin and rupture of abdominal aortic aneurysm. *J Vasc Surg* 2017;**65**:616–5.e4. https://doi.org/10.1016/j.jvs.2016.04.061
945. Wanhainen A, Mani K, Kullberg J, Svensjö S, Bersztel A, Karlsson L, *et al.* The effect of ticagrelor on growth of small abdominal aortic aneurysms–a randomized controlled trial. *Cardiovasc Res* 2020;**116**:450–6. https://doi.org/10.1093/cvr/cvz133
946. Golledge J, Thanigaimani S, Powell JT, Tsao PS. Pathogenesis and management of abdominal aortic aneurysm. *Eur Heart J* 2023;**44**:2682–97. https://doi.org/10.1093/eurheartj/ehad386
947. Sweeting MJ, Thompson SG, Brown LC, Powell JT, Collaborators R. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg* 2012;**99**:655–65. https://doi.org/10.1002/bjs.8707
948. Golledge J, Moxon J, Pinchbeck J, Anderson G, Rowbotham S, Jenkins J, *et al.* Association between metformin prescription and growth rates of abdominal aortic aneurysms. *Br J Surg* 2017;**104**:1486–93. https://doi.org/10.1002/bjs.10587
949. Thanigaimani S, Singh TP, Unosson J, Phie J, Moxon J, Wanhainen A, *et al.* Editor's choice—association between metformin prescription and abdominal aortic aneurysm growth and clinical events: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2021;**62**:747–56. https://doi.org/10.1016/j.ejvs.2021.06.013
950. Wong KHF, Zlatanovic P, Bosanquet DC, Saratzis A, Kakkos SK, Aboyans V, *et al.* Antithrombotic therapy for aortic aneurysms: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2022;**64**:544–56. https://doi.org/10.1016/j.ejvs.2022.07.008
951. Newton ER, Akerman AW, Strassle PD, Kibbe MR. Association of fluoroquinolone use with short-term risk of development of aortic aneurysm. *JAMA Surg* 2021;**156**:264–72. https://doi.org/10.1001/jamasurg.2020.6165
952. Wee I, Chin B, Syn N, Lee KS, Ng JJ, Choong AMTL. The association between fluoroquinolones and aortic dissection and aortic aneurysms: a systematic review and meta-analysis. *Sci Rep* 2021;**11**:11073. https://doi.org/10.1038/s41598-021-90692-8
953. Pasternak B, Inghammar M, Svanström H. Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study. *BMJ* 2018;**360**:k678. https://doi.org/10.1136/bmj.k678
954. Garg M, Venugopalan V, Vouri SM, Diaby V, Iovine NM, Park H, *et al.* Oral fluoroquinolones and risk of aortic aneurysm or dissection: a nationwide population-based propensity score-matched cohort study. *Pharmacotherapy* 2023;**43**:883–93. https://doi.org/10.1002/phar.2841
955. Fatima K, Uzair SU, Salman A, Jawed A, Husain MA, Shah MG, *et al.* Fluoroquinolones and the risk of aortic aneurysm or aortic dissection: an updated systematic review and meta-analysis including 53,651,283 patients. *Minerva Cardiol Angiol* 2023;**71**:485–93. https://doi.org/10.23736/S2724-5683.22.06124-5
956. LeMaire SA, Zhang L, Luo W, Ren P, Azares AR, Wang Y, *et al.* Effect of ciprofloxacin on susceptibility to aortic dissection and rupture in mice. *JAMA Surg* 2018;**153**:e181804. https://doi.org/10.1001/jamasurg.2018.1804
957. Brown JP, Wing K, Leyrat C, Evans SJ, Mansfield KE, Wong AYS, *et al.* Association between fluoroquinolone use and hospitalization with aortic aneurysm or aortic dissection. *JAMA Cardiol* 2023;**8**:865. https://doi.org/10.1001/jamacardio.2023.2418
958. Gopalakrishnan C, Bykov K, Fischer MA, Connolly JG, Gagne JJ, Fralick M. Association of fluoroquinolones with the risk of aortic aneurysm or aortic dissection. *JAMA Intern Med* 2020;**180**:1596–605. https://doi.org/10.1001/jamainternmed.2020.4199
959. Lee CC, Lee MT, Chen YS, Lee S-H, Chen Y-S, Chen S-C, *et al.* Risk of aortic dissection and aortic aneurysm in patients taking oral fluoroquinolone. *JAMA Intern Med* 2015;**175**:1839–47. https://doi.org/10.1001/jamainternmed.2015.5389
960. Huh K, Kang M, Jung J. Lack of association between fluoroquinolone and aortic aneurysm or dissection. *Eur Heart J* 2023;**44**:4476–84. https://doi.org/10.1093/eurheartj/ehad627
961. Klotz S, Stock S, Sievers HH, Diwoky M, Petersen M, Stierle U, *et al.* Survival and reoperation pattern after 20 years of experience with aortic valve-sparing root replacement in patients with tricuspid and bicuspid valves. *J Thorac Cardiovasc Surg* 2018;**155**:1403–11.e1. https://doi.org/10.1016/j.jtcvs.2017.12.039
962. Lee H, Cho YH, Sung K, Kim WS, Park K-H, Jeong DS, *et al.* Clinical outcomes of root reimplantation and Bentall procedure: propensity score matching analysis. *Ann Thorac Surg* 2018;**106**:539–47. https://doi.org/10.1016/j.athoracsur.2018.02.057
963. Mastrobuoni S, de Kerchove L, Navarra E, Watremez C, Vancraeynest D, Rubay J, *et al.* Long-term experience with valve-sparing reimplantation technique for the treatment of aortic aneurysm and aortic regurgitation. *J Thorac Cardiovasc Surg* 2019;**158**:14–23. https://doi.org/10.1016/j.jtcvs.2018.10.155
964. Leontyev S, Schamberger L, Davierwala PM, Von Aspern K, Etz C, Lehmann S, *et al.* Early and late results after David vs Bentall procedure: a propensity matched analysis. *Ann Thorac Surg* 2020;**110**:120–6. https://doi.org/10.1016/j.athoracsur.2019.10.020
965. Elbatarny M, Tam DY, Edelman JJ, Rocha RV, Chu MWA, Peterson MD, *et al.* Valve-sparing root replacement versus composite valve grafting in aortic root dilation: a meta-analysis. *Ann Thorac Surg* 2020;**110**:296–306. https://doi.org/10.1016/j.athoracsur.2019.11.054
966. Leyh RG, Fischer S, Kallenbach K, Kofidis T, Pethig K, Harringer W, *et al.* High failure rate after valve-sparing aortic root replacement using the "remodeling technique" in acute type A aortic dissection. *Circulation* 2002;**106**:I229–33.
967. Schäfers H, Fries R, Langer F, Nikoloudakis N, Graeter T, Grundmann U. Valve-preserving replacement of the ascending aorta: remodeling versus reimplantation. *J Thorac Cardiovasc Surg* 1998;**116**:990–6. https://doi.org/10.1016/s0022-5223(98)70051-0
968. Rahnavardi M, Yan TD, Bannon PG, Wilson MK. Aortic valve-sparing operations in aortic root aneurysms: remodeling or reimplantation? *Interact Cardiovasc Thorac Surg* 2011;**13**:189–97. https://doi.org/10.1510/icvts.2011.267401
969. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, *et al.* 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022;**43**:561–632. https://doi.org/10.1093/eurheartj/ehab395
970. Mok CK, Boey J, Wang R, Chan TK, Cheung KL, Lee PK, *et al.* Warfarin versus dipyridamole-aspirin and pentoxifylline-aspirin for the prevention of prosthetic heart valve thromboembolism: a prospective randomized clinical trial. *Circulation* 1985;**72**:1059–63. https://doi.org/10.1161/01.cir.72.5.1059
971. Cannegieter SC, Rosendaal FR, Briët E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. *Circulation* 1994;**89**:635–41. https://doi.org/10.1161/01.cir.89.2.635
972. Brennan JM, Edwards FH, Zhao Y, O'Brien S, Booth ME, Dokholyan RS, *et al.* Early anticoagulation of bioprosthetic aortic valves in older patients: results from the Society of Thoracic Surgeons Adult Cardiac Surgery National Database. *J Am Coll Cardiol* 2012;**60**:971–7. https://doi.org/10.1016/j.jacc.2012.05.029
973. Rafiq S, Steinbrüchel DA, Lilleør NB, Møller CH, Lund JT, Thiis JJ, *et al.* Antithrombotic therapy after bioprosthetic aortic valve implantation: warfarin versus aspirin, a randomized controlled trial. *Thromb Res* 2017;**150**:104–10. https://doi.org/10.1016/j.thromres.2016.11.021
974. Czerny M, Rylski B, Della Corte A, Krüger T. Decision-making to perform elective surgery for patients with proximal thoracic aortic pathology: a European perspective. *J Thorac Cardiovasc Surg* 2022;**163**:2025–30. https://doi.org/10.1016/j.jtcvs.2021.01.141
975. Vorp DA, Schiro BJ, Ehrlich MP, Juvonen TS, Ergin MA, Griffith BP. Effect of aneurysm on the tensile strength and biomechanical behavior of the ascending thoracic aorta. *Ann Thorac Surg* 2003;**75**:1210–4. https://doi.org/10.1016/s0003-4975(02)04711-2
976. Della Corte A, Lo Presti F, Saade W, Rubino AS, Palmieri L, Patanè F, *et al.* Acute type A aortic dissection in bicuspid versus tricuspid aortic valve patients: focus on geometrical features of the aorta. *Eur J Cardiothorac Surg* 2023;**63**:ezac576. https://doi.org/10.1093/ejcts/ezac576
977. Mullan CW, Mori M, Bin Mahmood SU, Yousef S, Mangi AA, Elefteriades JA, *et al.* Incidence and characteristics of hospitalization for proximal aortic surgery for acute syndromes and for aneurysms in the USA from 2005 to 2014. *Eur J Cardiothorac Surg* 2020;**58**:583–9. https://doi.org/10.1093/ejcts/ezaa067
978. Williams JB, Peterson ED, Zhao Y, O'Brien SM, Andersen ND, Miller DC, *et al.* Contemporary results for proximal aortic replacement in North America. *J Am Coll Cardiol* 2012;**60**:1156–62. https://doi.org/10.1016/j.jacc.2012.06.023
979. Wallen T, Habertheuer A, Bavaria JE, Hughes GC, Badhwar V, Jacobs JP, *et al.* Elective aortic root replacement in North America: analysis of STS adult cardiac surgery database. *Ann Thorac Surg* 2019;**107**:1307–12. https://doi.org/10.1016/j.athoracsur.2018.12.039
980. Mori M, Shioda K, Wang X, Mangi AA, Yun JJ, Darr U, *et al.* Perioperative risk profiles and volume-outcome relationships in proximal thoracic aortic surgery. *Ann Thorac Surg* 2018;**106**:1095–104. https://doi.org/10.1016/j.athoracsur.2018.05.081
981. Wojnarski CM, Svensson LG, Roselli EE, Idrees JJ, Lowry AM, Ehrlinger J, *et al.* Aortic dissection in patients with bicuspid aortic valve-associated aneurysms. *Ann Thorac Surg* 2015;**100**:1666–73; discussion 1673–74. https://doi.org/10.1016/j.athoracsur.2015.04.126
982. Wu J, Zafar MA, Liu Y, Chen JF, Li Y, Ziganshin BA, *et al.* Fate of the unoperated ascending thoracic aortic aneurysm: three-decade experience from the Aortic Institute at Yale University. *Eur Heart J* 2023;**44**:4579–88. https://doi.org/10.1093/eurheartj/ehad148

983. Ziganshin BA, Zafar MA, Elefteriades JA. Descending threshold for ascending aortic aneurysmectomy: is it time for a "left-shift" in guidelines? *J Thorac Cardiovasc Surg* 2019;**157**:37–42. https://doi.org/10.1016/j.jtcvs.2018.07.114
984. Rylski B, Branchetti E, Bavaria JE, Vallabhajosyula P, Szeto WY, Milewski RK, *et al.* Modeling of predissection aortic size in acute type A dissection: more than 90% fail to meet the guidelines for elective ascending replacement. *J Thorac Cardiovasc Surg* 2014;**148**:944–8.e1. https://doi.org/10.1016/j.jtcvs.2014.05.050
985. Mansour AM, Peterss S, Zafar MA, Rizzo JA, Fang H, Charilaou P, *et al.* Prevention of aortic dissection suggests a diameter shift to a lower aortic size threshold for intervention. *Cardiology* 2018;**139**:139–46. https://doi.org/10.1159/000481930
986. Masri A, Kalahasti V, Alkharabsheh S, Svensson LG, Sabik JF, Roselli EE, *et al.* Characteristics and long-term outcomes of contemporary patients with bicuspid aortic valves. *J Thorac Cardiovasc Surg* 2016;**151**:1650–9.e1. https://doi.org/10.1016/j.jtcvs.2015.12.019
987. Winkler A, Puiu P, Krombholz-Reindl P, Vötsch A, Steindl J, Neuner M, *et al.* Impact of concomitant replacement of the ascending aorta in patients undergoing aortic valve replacement on operative morbidity and mortality. *Eur J Cardiothorac Surg* 2022;**61**:587–93. https://doi.org/10.1093/ejcts/ezab420
988. Peterss S, Charilaou P, Dumfarth J, Li Y, Bhandari R, Tranquilli M, *et al.* Aortic valve disease with ascending aortic aneurysm: impact of concomitant root-sparing (supracoronary) aortic replacement in nonsyndromic patients. *J Thorac Cardiovasc Surg* 2016;**152**:791–8.e1. https://doi.org/10.1016/j.jtcvs.2016.05.020
989. Lim JY, Jung SH, Kim JB, Kim DK, Chung CH, Song H, *et al.* Concomitant replacement of the dilated ascending aorta during aortic valve replacement; does it increase the perioperative morbidity and mortality risks? *J Card Surg* 2013;**28**:285–90. https://doi.org/10.1111/jocs.12111
990. Idrees JJ, Roselli EE, Lowry AM, Reside JM, Javadikasgari H, Johnson DJ, *et al.* Outcomes after elective proximal aortic replacement: a matched comparison of isolated versus multicomponent operations. *Ann Thorac Surg* 2016;**101**:2185–92. https://doi.org/10.1016/j.athoracsur.2015.12.026
991. Idrees JJ, Roselli EE, Blackstone EH, Lowry AM, Soltesz EG, Johnston DR, *et al.* Risk of adding prophylactic aorta replacement to a cardiac operation. *J Thorac Cardiovasc Surg* 2020;**159**:1669–78.e10. https://doi.org/10.1016/j.jtcvs.2019.05.001
992. Grabenwöger M, Alfonso F, Bachet J, Bonser R, Czerny M, Eggebrecht H, *et al.* Thoracic Endovascular Aortic Repair (TEVAR) for the treatment of aortic diseases: a position statement from the European Association for Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2012;**33**:1558–63. https://doi.org/10.1093/eurheartj/ehs074
993. Eggebrecht H, Thompson M, Rousseau H, Czerny M, Lönn L, Mehta RH, *et al.* Retrograde ascending aortic dissection during or after thoracic aortic stent graft placement: insight from the European registry on endovascular aortic repair complications. *Circulation* 2009;**120**:S276–281. https://doi.org/10.1161/circulationaha.108.835926
994. Zerwes S, Leissner G, Gosslau Y, Jakob R, Bruijnen H-K, Oertl F, *et al.* Clinical outcomes in hybrid repair procedures for pathologies involving the aortic arch. *Vascular* 2015;**23**:9–16. https://doi.org/10.1177/1708538114525608
995. Czerny M, Weigang E, Sodeck G, Schmidli J, Antona C, Gelpi G, *et al.* Targeting landing zone 0 by total arch rerouting and TEVAR: midterm results of a transcontinental registry. *Ann Thorac Surg* 2012;**94**:84–9. https://doi.org/10.1016/j.athoracsur.2012.03.024
996. Chiesa R, Melissano G, Tshomba Y, Civilini E, Marone EM, Bertoglio L, *et al.* Ten years of endovascular aortic arch repair. *J Endovasc Ther* 2010;**17**:1–11. https://doi.org/10.1583/09-2884.1
997. Shrestha M, Bachet J, Bavaria J, Carrel TP, De Paulis R, Di Bartolomeo R, *et al.* Current status and recommendations for use of the frozen elephant trunk technique: a position paper by the vascular domain of EACTS. *Eur J Cardiothorac Surg* 2015;**47**:759–69. https://doi.org/10.1093/ejcts/ezv085
998. Czerny M, Schmidli J, Adler S, van den Berg JC, Bertoglio L, Carrel T, *et al.* Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic arch: an expert consensus document of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Society for Vascular Surgery (ESVS). *Eur J Cardiothorac Surg* 2019;**55**:133–62. https://doi.org/10.1093/ejcts/ezy313
999. Abjigitova D, Veen KM, van Tussenbroek G, Mokhles MM, Bekkers JA, Takkenberg JJM, *et al.* Cerebral protection in aortic arch surgery: systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg* 2022;**35**:ivac270. https://doi.org/10.1093/icvts/ivac128
1000. Malaisrie SC, Duncan BF, Mehta CK, Badiwala MV, Rinewalt D, Kruse J, *et al.* The addition of hemiarch replacement to aortic root surgery does not affect safety. *J Thorac Cardiovasc Surg* 2015;**150**:118–24.e2. https://doi.org/10.1016/j.jtcvs.2015.03.020
1001. Borger MA, Fedak PWM, Stephens EH, Gleason TG, Girdauskas E, Ikonomidis JS, *et al.* The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve-related aortopathy: full online-only version. *J Thorac Cardiovasc Surg* 2018;**156**:e41–74. https://doi.org/10.1016/j.jtcvs.2018.02.115
1002. Kim JB, Kim K, Lindsay ME, MacGillivray T, Isselbacher EM, Cambria RP, *et al.* Risk of rupture or dissection in descending thoracic aortic aneurysm. *Circulation* 2015;**132**:1620–9. https://doi.org/10.1161/circulationaha.114.015177
1003. Chen JF, Zafar MA, Wu J, Li Y, Rizzo JA, Papanikolaou D, *et al.* Increased virulence of descending thoracic and thoracoabdominal aortic aneurysms in women. *Ann Thorac Surg* 2021;**112**:45–52. https://doi.org/10.1016/j.athoracsur.2020.08.026
1004. Lobato AC, Puech-Leão P. Predictive factors for rupture of thoracoabdominal aortic aneurysm. *J Vasc Surg* 1998;**27**:446–53. https://doi.org/10.1016/s0741-5214(98)70319-2
1005. Harris DG, Olson SL, Panthofer AM, Matsumura JS, DiMusto PD. A frailty-based risk score predicts morbidity and mortality after elective endovascular repair of descending thoracic aortic aneurysms. *Ann Vasc Surg* 2020;**67**:90–9. https://doi.org/10.1016/j.avsg.2019.10.090
1006. Goodney PP, Travis L, Lucas FL, Fillinger MF, Goodman DC, Cronenwett JL, *et al.* Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the Medicare population. *Circulation* 2011;**124**:2661–9. https://doi.org/10.1161/circulationaha.111.033944
1007. Grausgruber W, Scharfen E. Problems of the fight against zoonoses in Austria. *Wien Tierarztl Monatsschr* 1968;**55**:625–36.
1008. Chiu P, Goldstone AB, Schaffer JM, Lingala B, Miller DC, Mitchell RS, *et al.* Endovascular versus open repair of intact descending thoracic aortic aneurysms. *J Am Coll Cardiol* 2019;**73**:643–51. https://doi.org/10.1016/j.jacc.2018.10.086
1009. Fairman RM, Criado F, Farber M, Kwolek C, Mehta M, White R, *et al.* Pivotal results of the medtronic vascular talent thoracic stent graft system: the VALOR trial. *J Vasc Surg* 2008;**48**:546–54.e2. https://doi.org/10.1016/j.jvs.2008.03.061
1010. Matsumura JS, Cambria RP, Dake MD, Moore RD, Svensson LG, Snyder S. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. *J Vasc Surg* 2008;**47**:247–57; discussion 257. https://doi.org/10.1016/j.jvs.2007.10.032
1011. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. *Ann Thorac Surg* 2007;**83**:S862–4; discussion S890–862. https://doi.org/10.1016/j.athoracsur.2006.10.088
1012. Coselli JS, Green SY, Price MD, Hash JA, Ouyang Y, Volguina IV, *et al.* Results of open surgical repair in patients with Marfan syndrome and distal aortic dissection. *Ann Thorac Surg* 2016;**101**:2193–201. https://doi.org/10.1016/j.athoracsur.2015.11.008
1013. Tong MZ, Eagleton MJ, Roselli EE, Blackstone EH, Xiang F, Ibrahim M, *et al.* Outcomes of open versus endovascular repair of descending thoracic and thoracoabdominal aortic aneurysms. *Ann Thorac Surg* 2022;**113**:1144–52. https://doi.org/10.1016/j.athoracsur.2021.04.100
1014. Goldstein LJ, Davies RR, Rizzo JA, Davila JJ, Cooperberg MR, Shaw RK, *et al.* Stroke in surgery of the thoracic aorta: incidence, impact, etiology, and prevention. *J Thorac Cardiovasc Surg* 2001;**122**:935–45. https://doi.org/10.1067/mtc.2001.117276
1015. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Experience with 1509 patients undergoing thoracoabdominal aortic operations. *J Vasc Surg* 1993;**17**:357–68; discussion 368–70.
1016. Schermerhorn ML, Giles KA, Hamdan AD, Dalhberg SE, Hagberg R, Pomposelli F. Population-based outcomes of open descending thoracic aortic aneurysm repair. *J Vasc Surg* 2008;**48**:821–7. https://doi.org/10.1016/j.jvs.2008.05.022
1017. Yamauchi T, Takano H, Nishimura M, Matsumiya G, Sawa Y. Paraplegia and paraparesis after descending thoracic aortic aneurysm repair: a risk factor analysis. *Ann Thorac Cardiovasc Surg* 2006;**12**:179–83.
1018. Patel VI, Mukhopadhyay S, Ergul E, Aranson N, Conrad MF, LaMuraglia GM, *et al.* Impact of hospital volume and type on outcomes of open and endovascular repair of descending thoracic aneurysms in the United States Medicare population. *J Vasc Surg* 2013;**58**:346–54. https://doi.org/10.1016/j.jvs.2013.01.035
1019. Cheng D, Martin J, Shennib H, Dunning J, Muneretto C, Schueler S, *et al.* Endovascular aortic repair versus open surgical repair for descending thoracic aortic disease a systematic review and meta-analysis of comparative studies. *J Am Coll Cardiol* 2010;**55**:986–1001. https://doi.org/10.1016/j.jacc.2009.11.047
1020. Harky A, Kai Chan JS, Ming Wong CH, Bashir M. Open versus endovascular repair of descending thoracic aortic aneurysm disease: a systematic review and meta-analysis. *Ann Vasc Surg* 2019;**54**:304–15.e5. https://doi.org/10.1016/j.avsg.2018.05.043
1021. Ranney DN, Cox ML, Yerokun BA, Benrashid E, McCann RL, Hughes GC. Long-term results of endovascular repair for descending thoracic aortic aneurysms. *J Vasc Surg* 2018;**67**:363–8. https://doi.org/10.1016/j.jvs.2017.06.094
1022. Biancari F, Mariscalco G, Mariani S, Saari P, Satta J, Juvonen T. Endovascular treatment of degenerative aneurysms involving only the descending thoracic aorta: systematic review and meta-analysis. *J Endovasc Ther* 2016;**23**:387–92. https://doi.org/10.1177/1526602815626560
1023. Mousa AY, Morcos R, Broce M, Bates MC, AbuRahma AF. New preoperative spinal cord ischemia risk stratification model for patients undergoing thoracic endovascular aortic repair. *Vasc Endovascular Surg* 2020;**54**:487–96. https://doi.org/10.1177/1538574420929135
1024. Walsh SR, Tang TY, Sadat U, Naik J, Gaunt ME, Boyle JR, *et al.* Endovascular stenting versus open surgery for thoracic aortic disease: systematic review and meta-analysis of perioperative results. *J Vasc Surg* 2008;**47**:1094–8.e3. https://doi.org/10.1016/j.jvs.2007.09.062
1025. Kotelis D, Geisbüsch P, Hinz U, Hyhlik-Dürr A, von Tengg-Kobligk H, Allenberg JR, *et al.* Short and midterm results after left subclavian artery coverage during

endovascular repair of the thoracic aorta. *J Vasc Surg* 2009;**50**:1285–92. https://doi.org/10.1016/j.jvs.2009.07.106
1026. Cooper DG, Walsh SR, Sadat U, Noorani A, Hayes PD, Boyle JR, *et al.* Neurological complications after left subclavian artery coverage during thoracic endovascular aortic repair: a systematic review and meta-analysis. *J Vasc Surg* 2009;**49**:1594–601. https://doi.org/10.1016/j.jvs.2008.12.075
1027. Buth J, Harris PL, Hobo R, van Eps R, Cuypers P, Duijm L, *et al.* Neurologic complications associated with endovascular repair of thoracic aortic pathology: incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. *J Vasc Surg* 2007;**46**:1103–10; discussion 1110–1. https://doi.org/10.1016/j.jvs.2007.08.020
1028. Teixeira PG, Woo K, Beck AW, Scali ST, Weaver FA. Association of left subclavian artery coverage without revascularization and spinal cord ischemia in patients undergoing thoracic endovascular aortic repair: a Vascular Quality Initiative® analysis. *Vascular* 2017;**25**:587–97. https://doi.org/10.1177/1708538116681910
1029. Chen X, Wang J, Premaratne S, Zhao J, Zhang WW. Meta-analysis of the outcomes of revascularization after intentional coverage of the left subclavian artery for thoracic endovascular aortic repair. *J Vasc Surg* 2019;**70**:1330–40. https://doi.org/10.1016/j.jvs.2019.03.022
1030. Banno H, Ikeda S, Kawai Y, Meshii K, Takahashi N, Sugimoto M, *et al.* Early and mid-term outcomes of celiac artery coverage during thoracic endovascular aortic repair. *J Vasc Surg* 2020;**72**:1552–7. https://doi.org/10.1016/j.jvs.2020.02.025
1031. Argyriou C, Spiliopoulos S, Katsanos K, Papatheodorou N, Lazarides MK, Georgiadis GS. Safety and efficacy of intentional celiac artery coverage in endovascular management of thoracoabdominal aortic diseases: a systematic review and meta-analysis. *J Endovasc Ther* 2022;**29**:646–58. https://doi.org/10.1177/15266028211059451
1032. Hanna L, Lam K, Agbeko AE, Amoako JK, Ashrafian H, Sounderajah V, *et al.* Coverage of the coeliac artery during thoracic endovascular aortic repair: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2022;**63**:828–37. https://doi.org/10.1016/j.ejvs.2022.02.026
1033. Cambria RA, Gloviczki P, Stanson AW, Cherry KJ, Bower TC, Hallett JW, *et al.* Outcome and expansion rate of 57 thoracoabdominal aortic aneurysms managed nonoperatively. *Am J Surg* 1995;**170**:213–7. https://doi.org/10.1016/s0002-9610(99)80289-x
1034. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg* 2002;**74**:S1877–80; discussion S1892–8. https://doi.org/10.1016/s0003-4975(02)04147-4
1035. Girardi LN, Ohmes LB, Lau C, Di Franco A, Gambardella I, Elsayed M, *et al.* Open repair of descending thoracic and thoracoabdominal aortic aneurysms in patients with preoperative renal failure. *Eur J Cardiothorac Surg* 2017;**51**:971–7. https://doi.org/10.1093/ejcts/ezx007
1036. LeMaire SA, Miller CC, III, Conklin LD, Schmittling ZC, Köksoy C, Coselli JS, *et al.* A new predictive model for adverse outcomes after elective thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2001;**71**:1233–8. https://doi.org/10.1016/s0003-4975(00)02678-3
1037. Suzuki S, Davis CA, III, Miller CC, III, Huynh TT, Estrera AL, Porat EE, *et al.* Cardiac function predicts mortality following thoracoabdominal and descending thoracic aortic aneurysm repair. *Eur J Cardiothorac Surg* 2003;**24**:119–24; discussion 124. https://doi.org/10.1016/s1010-7940(03)00170-2
1038. Mohebali J, Carvalho S, Lancaster RT, Ergul EA, Conrad MF, Clouse WD, *et al.* Use of extracorporeal bypass is associated with improved outcomes in open thoracic and thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2018;**68**:941–7. https://doi.org/10.1016/j.jvs.2017.12.072
1039. Coselli JS, LeMaire SA, Preventza O, de la Cruz KI, Cooley DA, Price MD, *et al.* Outcomes of 3309 thoracoabdominal aortic aneurysm repairs. *J Thorac Cardiovasc Surg* 2016;**151**:1323–38. https://doi.org/10.1016/j.jtcvs.2015.12.050
1040. Drinkwater SL, Goebells A, Haydar A, Bourke P, Brown L, Hamady M, *et al.*. The incidence of spinal cord ischaemia following thoracic and thoracoabdominal aortic endovascular intervention. *Eur J Vasc Endovasc Surg* 2010;**40**:729–35. https://doi.org/10.1016/j.ejvs.2010.08.013
1041. Bicknell CD, Riga CV, Wolfe JH. Prevention of paraplegia during thoracoabdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2009;**37**:654–60. https://doi.org/10.1016/j.ejvs.2009.02.008
1042. Von Aspern K, Luehr M, Mohr FW, Etz CD. Spinal cord protection in open- and endovascular thoracoabdominal aortic aneurysm repair: critical review of current concepts and future perspectives. *J Cardiovasc Surg (Torino)* 2015;**56**:745–9.
1043. Hsu CC, Kwan GN, van Driel ML, Rophael JA. Distal aortic perfusion during thoracoabdominal aneurysm repair for prevention of paraplegia. *Cochrane Database Syst Rev* 2012;**3**:CD008197. https://doi.org/10.1002/14651858.CD008197.pub2
1044. Bischoff MS, Di Luozzo G, Griepp EB, Griepp RB. Spinal cord preservation in thoracoabdominal aneurysm repair. *Perspect Vasc Surg Endovasc Ther* 2011;**23**:214–22. https://doi.org/10.1177/1531003511400622
1045. Cowan JA, Jr, Dimick JB, Henke PK, Huber TS, Stanley JC, Upchurch GR. Surgical treatment of intact thoracoabdominal aortic aneurysms in the United States: hospital and surgeon volume-related outcomes. *J Vasc Surg* 2003;**37**:1169–74. https://doi.org/10.1016/s0741-5214(03)00085-5
1046. Rigberg DA, McGory ML, Zingmond DS, Maggard MA, Agustin M, Lawrence PF, *et al.* Thirty-day mortality statistics underestimate the risk of repair of thoracoabdominal aortic aneurysms: a statewide experience. *J Vasc Surg* 2006;**43**:217–22; discussion 223. https://doi.org/10.1016/j.jvs.2005.10.070
1047. Pomy BJ, Rosenfeld ES, Lala S, Lee KB, Sparks AD, Amdur RL, *et al.* Fenestrated endovascular aneurysm repair affords fewer renal complications than open surgical repair for juxtarenal abdominal aortic aneurysms in patients with chronic renal insufficiency. *Ann Vasc Surg* 2021;**75**:349–57. https://doi.org/10.1016/j.avsg.2021.03.026
1048. Varkevisser RRB, O'Donnell TFX, Swerdlow NJ, Liang P, Li C, Ultee KHJ, *et al.* Fenestrated endovascular aneurysm repair is associated with lower perioperative morbidity and mortality compared with open repair for complex abdominal aortic aneurysms. *J Vasc Surg* 2019;**69**:1670–8. https://doi.org/10.1016/j.jvs.2018.08.192
1049. Gallitto E, Faggioli G, Melissano G, Fargion A, Isernia G, Lenti M, *et al.* Preoperative and postoperative predictors of clinical outcome of fenestrated and branched endovascular repair for complex abdominal and thoracoabdominal aortic aneurysms in an Italian multicenter registry. *J Vasc Surg* 2021;**74**:1795–806.e6. https://doi.org/10.1016/j.jvs.2021.04.072
1050. Silverberg D, Bar-Dayan A, Hater H, Khaitovich B, Halak M. Short-term outcomes of inner branches for endovascular repair of complex abdominal and thoracoabdominal aortic aneurysms. *Vascular* 2021;**29**:644–51. https://doi.org/10.1177/1708538120977279
1051. Hu Z, Li Y, Peng R, Liu J, Jia X, Liu X, *et al.* Multibranched stent-grafts for the treatment of thoracoabdominal aortic aneurysms: a systematic review and meta-analysis. *J Endovasc Ther* 2016;**23**:626–33. https://doi.org/10.1177/1526602816647723
1052. Simonte G, Isernia G, Gatta E, Neri E, Parlani G, Candeloro L, *et al.* Inner branched complex aortic repair outcomes from a national multicenter registry using the E-xtra design platform. *J Vasc Surg* 2023;**77**:338–46. https://doi.org/10.1016/j.jvs.2022.08.034
1053. Gallitto E, Faggioli G, Pini R, Logiacco A, Mascoli C, Fenelli C, *et al.* Proximal aortic coverage and clinical results of the endovascular repair of juxta-/para-renal and type IV thoracoabdominal aneurysm with custom-made fenestrated endografts. *Ann Vasc Surg* 2021;**73**:397–406. https://doi.org/10.1016/j.avsg.2020.12.008
1054. Sultan S, Concannon J, Veerasingam D, Tawfick W, McHugh P, Jordan F, *et al.* Endovascular versus conventional open surgical repair for thoracoabdominal aortic aneurysms. *Cochrane Database Syst Rev* 2022;**4**:CD012926. https://doi.org/10.1002/14651858.CD012926.pub2
1055. Kölbel T, Spanos K, Jama K, Behrendt CA, Panuccio G, Eleshra A, *et al.* Early outcomes of the t-Branch off-the-shelf multi-branched stent graft in 542 patients for elective and urgent aortic pathologies: a retrospective observational study. *J Vasc Surg* 2021;**74**:1817–24. https://doi.org/10.1016/j.jvs.2021.05.041
1056. Oderich GS, Ribeiro M, Hofer J, Wigham J, Cha S, Chini J, *et al.* Prospective, nonrandomized study to evaluate endovascular repair of pararenal and thoracoabdominal aortic aneurysms using fenestrated-branched endografts based on supraceliac sealing zones. *J Vasc Surg* 2017;**65**:1249–59.e10. https://doi.org/10.1016/j.jvs.2016.09.038
1057. Oderich GS, Tenorio ER, Mendes BC, Lima GBB, Marcondes GB, Saqib N, *et al.* Midterm outcomes of a prospective, nonrandomized study to evaluate endovascular repair of complex aortic aneurysms using fenestrated-branched endografts. *Ann Surg* 2021;**274**:491–9. https://doi.org/10.1097/sla.0000000000004982
1058. Konstantinou N, Antonopoulos CN, Jerkku T, Banafsche R, Kölbel T, Fiorucci B, *et al.* Systematic review and meta-analysis of published studies on endovascular repair of thoracoabdominal aortic aneurysms with the t-Branch off-the-shelf multibranched endograft. *J Vasc Surg* 2020;**72**:716–25.e1. https://doi.org/10.1016/j.jvs.2020.01.049
1059. Ellahi A, Shaikh FN, Kashif H, Khan H, Ali E, Nasim B, *et al.* Effectiveness of endovascular repair versus open surgery for the treatment of thoracoabdominal aneurysm: a systematic review and meta analysis. *Ann Med Surg* 2022;**81**:104477. https://doi.org/10.1016/j.amsu.2022.104477
1060. Hongku K, Sonesson B, Bjorses K, Holst J, Resch T, Dias NV, *et al.* Mid-term Outcomes of Endovascular Repair of Ruptured Thoraco-abdominal Aortic Aneurysms with Off the Shelf Branched Stent Grafts. *Eur J Vasc Endovasc Surg* 2018;**55**:377–84. https://doi.org/10.1016/j.ejvs.2017.11.021
1061. Youssef M, Deglise S, Szopinski P, Jost-Philipp S, Jomha A, Vahl CF, *et al.* A multicenter experience with a new fenestrated-branched device for endovascular repair of thoracoabdominal aortic aneurysms. *J Endovasc Ther* 2018;**25**:209–19. https://doi.org/10.1177/1526602817752147
1062. Ouzounian M, Tadros RO, Svensson LG, Lyden SP, Oderich GS, Coselli JS Thoracoabdominal aortic disease and repair: JACC focus seminar, part 3. *J Am Coll Cardiol* 2022;**80**:845–56. https://doi.org/10.1016/j.jacc.2021.05.056
1063. Hofmann Bowman MA, Eagle KA, Milewicz DM. Update on clinical trials of losartan with and without β-blockers to block aneurysm growth in patients with Marfan syndrome: a review. *JAMA Cardiol* 2019;**4**:702–7. https://doi.org/10.1001/jamacardio.2019.1176
1064. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *Lancet* 1998;**352**:1649–55.

1065. Powell JT, Brady AR, Brown LC, Fowkes FG, Greenhalgh RM, Ruckley CV, *et al.* Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;**346**:1445–52. https://doi.org/10.1056/NEJMoa013527
1066. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, *et al.* Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;**346**:1437–44. https://doi.org/10.1056/NEJMoa012573
1067. Shirasu T, Takagi H, Yasuhara J, Kuno T, Kent KC, Clouse WD. Smaller size is more suitable for pharmacotherapy among undersized abdominal aortic aneurysm: a systematic review and meta-analysis. *Vasc Med* 2022;**27**:261–8. https://doi.org/10.1177/1358863x211061603
1068. Ouriel K, Clair DG, Kent KC, Zarins CK. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg* 2010;**51**:1081–7. https://doi.org/10.1016/j.jvs.2009.10.113
1069. Golledge J, Parr A, Boult M, Maddern G, Fitridge R. The outcome of endovascular repair of small abdominal aortic aneurysms. *Ann Surg* 2007;**245**:326–33. https://doi.org/10.1097/01.sla.0000253965.95368.52
1070. Filardo G, Powell JT, Martinez MA, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev* 2015;**2**:CD001835. https://doi.org/10.1002/14651858.CD001835.pub4
1071. Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial. *Eur J Vasc Endovasc Surg* 2011;**41**:13–25. https://doi.org/10.1016/j.ejvs.2010.08.026
1072. Lo RC, Lu B, Fokkema MT, Conrad M, Patel VI, Fillinger M, *et al.* Relative importance of aneurysm diameter and body size for predicting abdominal aortic aneurysm rupture in men and women. *J Vasc Surg* 2014;**59**:1209–16. https://doi.org/10.1016/j.jvs.2013.10.104
1073. Bath MF, Gokani VJ, Sidloff DA, Jones LR, Choke E, Sayers RD, *et al.* Systematic review of cardiovascular disease and cardiovascular death in patients with a small abdominal aortic aneurysm. *Br J Surg* 2015;**102**:866–72. https://doi.org/10.1002/bjs.9837
1074. Kristensen SD, Knuuti J. New ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management. *Eur Heart J* 2014;**35**:2344–5. https://doi.org/10.1093/eurheartj/ehu285
1075. Devereaux PJ, Chan MT, Alonso-Coello P, Walsh M, Berwanger O, Villar JC, *et al.* Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012;**307**:2295–304. https://doi.org/10.1001/jama.2012.5502
1076. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;**365**:2179–86. https://doi.org/10.1016/s0140-6736(05)66627-5
1077. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT, Jr, Matsumura JS, Kohler TR, *et al.* Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA* 2009;**302**:1535–42. https://doi.org/10.1001/jama.2009.1426
1078. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, *et al.* A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 2011;**53**:1167–73.e1. https://doi.org/10.1016/j.jvs.2010.10.124
1079. Antoniou GA, Antoniou SA, Torella F. Editor's choice—endovascular vs. open repair for abdominal aortic aneurysm: systematic review and meta-analysis of updated peri-operative and long term data of randomised controlled trials. *Eur J Vasc Endovasc Surg* 2020;**59**:385–97. https://doi.org/10.1016/j.ejvs.2019.11.030
1080. Halvorsen S, Mehilli J, Cassese S, Hall TS, Abdelhamid M, Barbato E, *et al.* 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. *Eur Heart J* 2022;**43**:3826–924. https://doi.org/10.1093/eurheartj/ehac270
1081. McFalls EO, Ward HB, Moritz TE, Goldman S, Krupski WC, Littooy F, *et al.* Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med* 2004;**351**:2795–804. https://doi.org/10.1056/NEJMoa041905
1082. Saida T, Mori K, Sato F, Shindo M, Takahashi H, Takahashi N, *et al.* Prospective intraindividual comparison of unenhanced magnetic resonance imaging vs contrast-enhanced computed tomography for the planning of endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2012;**55**:679–87. https://doi.org/10.1016/j.jvs.2011.09.091
1083. Parker MV, O'Donnell SD, Chang AS, Johnson CA, Gillespie DL, Goff JM, *et al.* What imaging studies are necessary for abdominal aortic endograft sizing? A prospective blinded study using conventional computed tomography, aortography, and three-dimensional computed tomography. *J Vasc Surg* 2005;**41**:199–205. https://doi.org/10.1016/j.jvs.2004.12.010
1084. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, *et al.* Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation* 2011;**123**:2848–55. https://doi.org/10.1161/circulationaha.110.014902
1085. Protto S, Hahl T, Koskinen KJA, Järvenpää V, Uurto I, Väärämäki S, *et al.* Endovascular repair of abdominal aortic aneurysms is a valid alternative to open repair also in patients treated outside of instructions for use criteria. *Cardiovasc Intervent Radiol* 2022;**45**:1765–73. https://doi.org/10.1007/s00270-022-03297-7
1086. Charbonneau P, Hongku K, Herman CR, Habib M, Girsowicz E, Doonan RJ, *et al.* Long-term survival after endovascular and open repair in patients with anatomy outside instructions for use criteria for endovascular aneurysm repair. *J Vasc Surg* 2019;**70**:1823–30. https://doi.org/10.1016/j.jvs.2019.01.081
1087. O'Donnell TFX, McElroy IE, Boitano LT, Mohebali J, Lamuraglia GM, Kwolek CJ, *et al.* Comparison of treatment options for aortic necks outside standard endovascular aneurysm repair instructions for use. *J Vasc Surg* 2021;**74**:1548–57. https://doi.org/10.1016/j.jvs.2021.04.052
1088. Antoniou GA, Juszczak MT, Nasr H, Narlawar R, Antoniou SA, Matsagkas M, *et al.* Prognosis review and time-to-event data meta-analysis of endovascular aneurysm repair outside versus within instructions for use of aortic endograft devices. *J Vasc Surg* 2020;**71**:1415–31.e15. https://doi.org/10.1016/j.jvs.2019.08.247
1089. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, *et al.* Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002;**35**:1048–60. https://doi.org/10.1067/mva.2002.123763
1090. Falster MO, Garland SK, Jorm LR, Beiles CB, Freeman AJ, Sedrakyan A, *et al.* Editor's choice—comparison of outcomes for major contemporary endograft devices used for endovascular repair of intact abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2023;**65**:272–80. https://doi.org/10.1016/j.ejvs.2022.11.005
1091. van Laarhoven C, Jorritsma NKN, Balderston J, Brinjikji W, Björck M, van Herwaarden JA, *et al.* Systematic review of the co-prevalence of arterial aneurysms within the vasculature. *Eur J Vasc Endovasc Surg* 2021;**61**:473–83. https://doi.org/10.1016/j.ejvs.2020.10.002
1092. Hohneck A, Keese M, Ruemenapf G, Amendt K, Muertz H, Janda K, *et al.* Prevalence of abdominal aortic aneurysm and associated lower extremity artery aneurysm in men hospitalized for suspected or known cardiopulmonary disease. *BMC Cardiovasc Disord* 2019;**19**:284. https://doi.org/10.1186/s12872-019-1265-2
1093. D'Oria M, Scali S, Mao J, Szeberin Z, Thomson I, Beiles B, *et al.* Association between hospital volume and failure to rescue after open or endovascular repair of intact abdominal aortic aneurysms in the vascunet and international consortium of vascular registries. *Ann Surg* 2021;**274**:e452–9. https://doi.org/10.1097/sla.0000000000005044
1094. Scali ST, Columbo JA, Suckow BD, D'Oria M, Neal D, Goodney PP, *et al.* Center volume is associated with diminished failure to rescue and improved outcomes following elective open abdominal aortic aneurysm repair. *J Vasc Surg* 2022;**76**:400–8.e2. https://doi.org/10.1016/j.jvs.2021.12.076
1095. Eid MA, Barnes JA, Mehta K, Wanken Z, Columbo J, Kang R, *et al.* Factors associated with preference of choice of aortic aneurysm repair in the PReference for Open Versus Endovascular repair of AAA (PROVE-AAA) study. *J Vasc Surg* 2022;**76**:1556–64. https://doi.org/10.1016/j.jvs.2022.06.018
1096. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, *et al.* Editor's choice—European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg* 2019;**57**:8–93. https://doi.org/10.1016/j.ejvs.2018.09.020
1097. Reise JA, Sheldon H, Earnshaw J, Naylor AR, Dick F, Powell JT, *et al.* Patient preference for surgical method of abdominal aortic aneurysm repair: postal survey. *Eur J Vasc Endovasc Surg* 2010;**39**:55–61. https://doi.org/10.1016/j.ejvs.2009.08.008
1098. EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. *Lancet* 2005;**365**:2187–92. https://doi.org/10.1016/s0140-6736(05)66628-7
1099. Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010;**362**:1872–80. https://doi.org/10.1056/NEJMoa0911056
1100. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet* 2016;**388**:2366–74. https://doi.org/10.1016/s0140-6736(16)31135-7
1101. Lederle FA, Kyriakides TC, Stroupe KT, Freischlag JA, Padberg FT, Matsumura JS, *et al.* Open versus endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2019;**380**:2126–35. https://doi.org/10.1056/NEJMoa1715955
1102. Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT, Kohler TR, *et al.* Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med* 2012;**367**:1988–97. https://doi.org/10.1056/NEJMoa1207481
1103. Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, *et al.* Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med* 2015;**373**:328–38. https://doi.org/10.1056/NEJMoa1405778
1104. Nana P, Dakis K, Brodis A, Spanos K, Kouvelos G, Eckstein H-H, *et al.* A systematic review and meta-analysis on early mortality after abdominal aortic aneurysm repair in females in urgent and elective settings. *J Vasc Surg* 2022;**75**:1082–8.e6. https://doi.org/10.1016/j.jvs.2021.10.040
1105. Böckler D, Power AH, Bouwman LH, van Sterkenburg S, Bosiers M, Peeters P, *et al.* Improvements in patient outcomes with next generation endovascular aortic repair devices in the ENGAGE global registry and the EVAR-1 clinical trial. *J Cardiovasc Surg* 2020;**61**:604–9. https://doi.org/10.23736/s0021-9509.19.11021-x

1106. Teijink JAW, Power AH, Böckler D, Peeters P, van Sterkenburg S, Bouwman LH, *et al.* Editor's choice—five year outcomes of the endurant stent graft for endovascular abdominal aortic aneurysm repair in the ENGAGE registry. *Eur J Vasc Endovasc Surg* 2019;**58**:175–81. https://doi.org/10.1016/j.ejvs.2019.01.008
1107. Oliveira-Pinto J, Oliveira NFG, Bastos-Gonçalves FM, Hoeks S, Rijn MJV, Raa ST, *et al.* Long-term results after standard endovascular aneurysm repair with the endurant and excluder stent grafts. *J Vasc Surg* 2020;**71**:64–74. https://doi.org/10.1016/j.jvs.2019.03.039
1108. Deery SE, Shean KE, Pothof AB, O'Donnell TFX, Dalebout BA, Darling JD, *et al.* Three-Year Results of the Endurant Stent Graft System Post Approval Study. *Ann Vasc Surg* 2018;**50**:202–8. https://doi.org/10.1016/j.avsg.2017.12.017
1109. Prinssen M, Verhoeven EL, Buth J, Cuypers PWM, van Sambeek MRHM, Balm R, *et al.* A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;**351**:1607–18. https://doi.org/10.1056/NEJMoa042002
1110. Dakour-Aridi H, Paracha NZ, Locham S, Nejim B, Malas MB. Assessment of failure to rescue after abdominal aortic aneurysm repair using the National Surgical Quality Improvement Program procedure-targeted data set. *J Vasc Surg* 2018;**68**:1335–44.e1. https://doi.org/10.1016/j.jvs.2018.01.059
1111. Scali ST, Giles KA, Kubilis P, Beck AW, Crippen CJ, Hughes SJ, *et al.* Impact of hospital volume on patient safety indicators and failure to rescue following open aortic aneurysm repair. *J Vasc Surg* 2020;**71**:1135–46.e4. https://doi.org/10.1016/j.jvs.2019.06.194
1112. Ma B, Wang YN, Chen KY, Zhang Y, Pan H, Yang K. Transperitoneal versus retroperitoneal approach for elective open abdominal aortic aneurysm repair. *Cochrane Database Syst Rev* 2016;**2**:CD010373. https://doi.org/10.1002/14651858.CD010373.pub2
1113. Camazine M, Bath J, Singh P, Kruse RL, Vogel TR. Characteristics associated with failure to rescue after open abdominal aortic aneurysm repair. *J Surg Res* 2023;**283**:683–9. https://doi.org/10.1016/j.jss.2022.11.018
1114. Blair R, Harkin D, Johnston D, Lim A, McFetridge L, Mitchell H. Open surgery for abdominal aortic aneurysm: 980 consecutive patient outcomes from a high-volume centre in the United Kingdom. *Vasc Endovascular Surg* 2023;**57**:463–70. https://doi.org/10.1177/15385744221149585
1115. Hoornweg LL, Storm-Versloot MN, Ubbink DT, Koelemay MJW, Legemate DA, Balm R, *et al.* Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2008;**35**:558–70. https://doi.org/10.1016/j.ejvs.2007.11.019
1116. Kontopodis N, Galanakis N, Antoniou SA, Tsetis D, Ioannou CV, Veith FJ, *et al.* Meta-analysis and meta-regression analysis of outcomes of endovascular and open repair for ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2020;**59**:399–410. https://doi.org/10.1016/j.ejvs.2019.12.023
1117. Wang LJ, Locham S, Al-Nouri O, Eagleton MJ, Clouse WD, Malas MB. Endovascular repair of ruptured abdominal aortic aneurysm is superior to open repair: propensity-matched analysis in the vascular quality initiative. *J Vasc Surg* 2020;**72**:498–507. https://doi.org/10.1016/j.jvs.2019.11.063
1118. Tan TW, Eslami M, Rybin D, Doros G, Zhang WW, Farber A. Outcomes of endovascular and open surgical repair of ruptured abdominal aortic aneurysms in elderly patients. *J Vasc Surg* 2017;**66**:64–70. https://doi.org/10.1016/j.jvs.2016.10.119
1119. Dewulf M, Muysoms F, Vierendeels T, Huyghe M, Miserez M, Ruppert M, *et al.* Prevention of incisional hernias by prophylactic mesh-augmented reinforcement of midline laparotomies for abdominal aortic aneurysm treatment: five-year follow-up of a randomized controlled trial. *Ann Surg* 2022;**276**:e217–22. https://doi.org/10.1097/sla.0000000000005545
1120. Honig S, Diener H, Kölbel T, Reinpold W, Zapf A, Bibiza-Freiwald E, *et al.* Abdominal incision defect following AAA-surgery (AIDA): 2-year results of prophylactic onlay-mesh augmentation in a multicentre, double-blind, randomised controlled trial. *Updates Surg* 2022;**74**:1105–16. https://doi.org/10.1007/s13304-021-01125-0
1121. Indrakusuma R, Jalalzadeh H, van der Meij JE, Balm R, Koelemay MJW. Prophylactic mesh reinforcement versus sutured closure to prevent incisional hernias after open abdominal aortic aneurysm repair via midline laparotomy: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2018;**56**:120–8. https://doi.org/10.1016/j.ejvs.2018.03.021
1122. van Keulen JW, de Vries JP, Dekker H, Gonçalves FB, Moll FL, Verhagen HJ, *et al.* One-year multicenter results of 100 abdominal aortic aneurysm patients treated with the endurant stent graft. *J Vasc Surg* 2011;**54**:609–15. https://doi.org/10.1016/j.jvs.2011.02.053
1123. Piazza M, Squizzato F, Suominen V, Grego F, Trimarchi S, Antonello M, *et al.* Early and long-term outcomes of endovascular aortic repair in young and low surgical risk patients in the global registry for endovascular aortic treatment. *J Endovasc Ther* 2022;**29**:248–57. https://doi.org/10.1177/15266028211045703
1124. Paravastu SC, Jayarajasingam R, Cottam R, Palfreyman SJ, Michaels JA, Thomas SM. Endovascular repair of abdominal aortic aneurysm. *Cochrane Database Syst Rev* 2014;**1**:CD004178. https://doi.org/10.1002/14651858.CD004178.pub2
1125. Dosluoglu HH, Lall P, Blochle R, Harris LM, Dryjski ML. Ambulatory percutaneous endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2014;**59**:58–64. https://doi.org/10.1016/j.jvs.2013.06.076
1126. Geragotellis A, Cox K, Yip HCA, Jubouri M, Williams IM, Bailey DM, *et al.* Renal outcomes of suprarenal vs. infrarenal endograft fixation in endovascular abdominal aortic aneurysm repair: a narrative review. *Cardiovasc Diagn Ther* 2022;**12**:531–44. https://doi.org/10.21037/cdt-22-196
1127. Verhoeven EL, Katsargyris A, Bachoo P, Larzon T, Fisher R, Ettles D, *et al.* Real-world performance of the new C3 gore excluder stent-graft: 1-year results from the European C3 module of the global registry for endovascular aortic treatment (GREAT). *Eur J Vasc Endovasc Surg* 2014;**48**:131–7. https://doi.org/10.1016/j.ejvs.2014.04.009
1128. Torsello G, Scheinert D, Brunkwall JS, Chiesa R, Coppi G, Pratesi C. Safety and effectiveness of the INCRAFT AAA stent graft for endovascular repair of abdominal aortic aneurysms. *J Vasc Surg* 2015;**61**:1–8. https://doi.org/10.1016/j.jvs.2014.06.007
1129. Kontopodis N, Galanakis N, Tzartzalou I, Tavlas E, Georgakarakos E, Dimopoulos I, *et al.* An update on the improvement of patient eligibility with the use of new generation endografts for the treatment of abdominal aortic aneurysms. *Expert Rev Med Devices* 2020;**17**:1231–8. https://doi.org/10.1080/17434440.2020.1841629
1130. Kontopodis N, Papadopoulos G, Galanakis N, Tsetis D, Ioannou CV. Improvement of patient eligibility with the use of new generation endografts for the treatment of abdominal aortic aneurysms. A comparison study among currently used endografts and literature review. *Expert Rev Med Devices* 2017;**14**:245–50. https://doi.org/10.1080/17434440.2017.1281738
1131. Zlatanovic P, Mascia D, Ancetti S, Yeung KK, Graumans MJ, Jongkind V, *et al.* Short term and long term clinical outcomes of endovascular versus open repair for juxtarenal and pararenal abdominal aortic aneurysms using propensity score matching: results from juxta- and pararenal aortic aneurysm multicentre European study (JAMES). *Eur J Vasc Endovasc Surg* 2023;**65**:828–36. https://doi.org/10.1016/j.ejvs.2023.02.070
1132. Hajibandeh S, Hajibandeh S, Antoniou SA, Child E, Torella F, Antoniou GA. Percutaneous access for endovascular aortic aneurysm repair: a systematic review and meta-analysis. *Vascular* 2016;**24**:638–48. https://doi.org/10.1177/1708538116639201
1133. Antoniou GA, Antoniou SA. Editor's choice—percutaneous access does not confer superior clinical outcomes over cutdown access for endovascular aneurysm repair: meta-analysis and trial sequential analysis of randomised controlled trials. *Eur J Vasc Endovasc Surg* 2021;**61**:383–94. https://doi.org/10.1016/j.ejvs.2020.11.008
1134. Cao Z, Wu W, Zhao K, Yang Yu, Jiang C, Zhu R. Safety and efficacy of totally percutaneous access compared with open femoral exposure for endovascular aneurysm repair: a meta-analysis. *J Endovasc Ther* 2017;**24**:246–53. https://doi.org/10.1177/1526602816689679
1135. Wang Q, Wu J, Ma Y, Zhu Y, Song X, Xie S, *et al.* Totally percutaneous versus surgical cut-down femoral artery access for elective bifurcated abdominal endovascular aneurysm repair. *Cochrane Database Syst Rev* 2023;**1**:CD010185. https://doi.org/10.1002/14651858.CD010185.pub4
1136. Antoniou GA, Georgiadis GS, Antoniou SA, Neequaye S, Brennan JA, Torella F, *et al.* Late rupture of abdominal aortic aneurysm after previous endovascular repair: a systematic review and meta-analysis. *J Endovasc Ther* 2015;**22**:734–44. https://doi.org/10.1177/1526602815601405
1137. Fransen GA, Vallabhaneni SR, Sr, van Marrewijk CJ, Laheij RJF, Harris PL, Buth J. Rupture of infra-renal aortic aneurysm after endovascular repair: a series from EUROSTAR registry. *Eur J Vasc Endovasc Surg* 2003;**26**:487–93. https://doi.org/10.1016/s1078-5884(03)00350-2
1138. Marcaccio CL, Patel PB, de Guerre L, Wade JE, Rastogi V, Anjorin A, *et al.* Disparities in 5-year outcomes and imaging surveillance following elective endovascular repair of abdominal aortic aneurysm by sex, race, and ethnicity. *J Vasc Surg* 2022;**76**:1205–15.e4. https://doi.org/10.1016/j.jvs.2022.03.886
1139. Schlösser FJ, Gusberg RJ, Dardik A, Lin PH, Verhagen HJM, Moll FL, *et al.* Aneurysm rupture after EVAR: can the ultimate failure be predicted? *Eur J Vasc Endovasc Surg* 2009;**37**:15–22. https://doi.org/10.1016/j.ejvs.2008.10.011
1140. Stather PW, Sidloff D, Dattani N, Choke E, Bown MJ, Sayers RD. Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm. *Br J Surg* 2013;**100**:863–72. https://doi.org/10.1002/bjs.9101
1141. Swart M, McCarthy R. Shared decision making for elective abdominal aortic aneurysm surgery. *Clin Med (Lond)* 2019;**19**:473–7. https://doi.org/10.7861/clinmed.2019-0352
1142. Stubenrouch FE, Peters LJ, de Mik SML, Klemm PL, Peppelenbosch AG, Schreurs SCWM, *et al.* Improving shared decision making in vascular surgery: a stepped wedge cluster randomised trial. *Eur J Vasc Endovasc Surg* 2022;**64**:73–81. https://doi.org/10.1016/j.ejvs.2022.04.016
1143. Machin M, Van Herzeele I, Ubbink D, Powell JT. Shared decision making in and management of intact abdominal aortic aneurysm: a scoping review of the literature. *Eur J Vasc Endovasc Surg* 2023;**65**:839–49. https://doi.org/10.1016/j.ejvs.2023.01.036
1144. Karthaus EG, Tong TML, Vahl A, Hamming JF. Saccular abdominal aortic aneurysms: patient characteristics, clinical presentation, treatment, and outcomes in the Netherlands. *Ann Surg* 2019;**270**:852–8. https://doi.org/10.1097/sla.0000000000003529

1145. O'Donnell TF, McElroy IE, Mohebali J, Boitano LT, Lamuraglia GM, Kwolek CJ, *et al.* Late type 1A endoleaks: associated factors, prognosis and management strategies. *Ann Vasc Surg* 2022;**80**:273–82. https://doi.org/10.1016/j.avsg.2021.08.057
1146. De Rango P, Verzini F, Parlani G, Cieri E, Simonte G, Farchioni L, *et al.* Safety of chronic anticoagulation therapy after endovascular abdominal aneurysm repair (EVAR). *Eur J Vasc Endovasc Surg* 2014;**47**:296–303. https://doi.org/10.1016/j.ejvs.2013.12.009
1147. Rokosh RS, Wu WW, Dalman RL, Chaikof EL. Society for Vascular Surgery implementation of clinical practice guidelines for patients with an abdominal aortic aneurysm. Endoleak management. *J Vasc Surg* 2021;**74**:1792–4. https://doi.org/10.1016/j.jvs.2021.04.042
1148. Jordan WD, Jr, Mehta M, Varnagy D, Moore WM, Arko FR, Joye J, *et al.* Results of the ANCHOR prospective, multicenter registry of EndoAnchors for type Ia endoleaks and endograft migration in patients with challenging anatomy. *J Vasc Surg* 2014;**60**:885–92.e2. https://doi.org/10.1016/j.jvs.2014.04.063
1149. Sidloff DA, Stather PW, Choke E, Bown MJ, Sayers RD. Type II endoleak after endovascular aneurysm repair. *Br J Surg* 2013;**100**:1262–70. https://doi.org/10.1002/bjs.9181
1150. Daye D, Walker TG. Complications of endovascular aneurysm repair of the thoracic and abdominal aorta: evaluation and management. *Cardiovasc Diagn Ther* 2018;**8**:S138–56. https://doi.org/10.21037/cdt.2017.09.17
1151. Latson LA, Jr, DeAnda A, Jr, Ko JP. Imaging of the postsurgical thoracic aorta: a state-of-the-art review. *J Thorac Imaging* 2017;**32**:1–25. https://doi.org/10.1097/rti.0000000000000246
1152. Prescott-Focht JA, Martinez-Jimenez S, Hurwitz LM, Hoang JK, Christensen JD, Ghoshhajra BB, *et al.* Ascending thoracic aorta: postoperative imaging evaluation. *Radiographics* 2013;**33**:73–85. https://doi.org/10.1148/rg.331125090
1153. Riambau V, Böckler D, Brunkwall J, Cao P, Chiesa R, Coppi G, *et al.* Editor's choice—management of descending thoracic aorta diseases: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2017;**53**:4–52. https://doi.org/10.1016/j.ejvs.2016.06.005
1154. Quevedo HC, Santiago-Trinidad R, Castellanos J, Atianzar K, Anwar A, Abi Rafeh N. Systematic review of interventions to repair ascending aortic pseudoaneurysms. *Ochsner J* 2014;**14**:576–85.
1155. Mesana TG, Caus T, Gaubert J, Collart F, Ayari R, Bartoli J-M, *et al.* Late complications after prosthetic replacement of the ascending aorta: what did we learn from routine magnetic resonance imaging follow-up? *Eur J Cardiothorac Surg* 2000;**18**:313–20. https://doi.org/10.1016/s1010-7940(00)00512-1
1156. Bianco V, Kilic A, Gleason TG, Arnaoutakis GJ, Sultan I. Management of thoracic aortic graft infections. *J Card Surg* 2018;**33**:658–65. https://doi.org/10.1111/jocs.13792
1157. Liisberg M, Baudier F, Akgül C, Lindholt JS. Long-term thoracic endovascular repair follow-up from 1999 to 2019: a single-center experience. *Ann Vasc Surg* 2022;**86**:399–407. https://doi.org/10.1016/j.avsg.2022.04.013
1158. Nakhaei P, Bashir M, Jubouri M, Banar S, Ilkhani S, Borzeshi EZ, *et al.* Aortic remodeling, distal stent-graft induced new entry and endoleak following frozen elephant trunk: a systematic review and meta-analysis. *J Card Surg* 2022;**37**:3848–62. https://doi.org/10.1111/jocs.16918
1159. Iribarne A, Keenan J, Benrashid E, Wang H, Meza JM, Ganapathi A, *et al.* Imaging surveillance after proximal aortic operations: is it necessary? *Ann Thorac Surg* 2017;**103**:734–41. https://doi.org/10.1016/j.athoracsur.2016.06.085
1160. Hensley SE, Upchurch GR, Jr. Repair of abdominal aortic aneurysms: JACC focus seminar, part 1. *J Am Coll Cardiol* 2022;**80**:821–31. https://doi.org/10.1016/j.jacc.2022.04.066
1161. Bastos Gonçalves F, Baderkhan H, Verhagen HJ, Wanhainen A, Björck M, Stolker RJ, *et al.* Early sac shrinkage predicts a low risk of late complications after endovascular aortic aneurysm repair. *Br J Surg* 2014;**101**:802–10. https://doi.org/10.1002/bjs.9516
1162. Troutman DA, Chaudry M, Dougherty MJ, Calligaro KD. Endovascular aortic aneurysm repair surveillance may not be necessary for the first 3 years after an initially normal duplex postoperative study. *J Vasc Surg* 2014;**60**:558–62. https://doi.org/10.1016/j.jvs.2014.03.278
1163. Jean-Baptiste E, Feugier P, Cruzel C, Sarlon-Bartoli G, Reix T, Steinmetz E, *et al.* Computed tomography-aortography versus color-duplex ultrasound for surveillance of endovascular abdominal aortic aneurysm repair: a prospective multicenter diagnostic-accuracy study (the ESSEA trial). *Circ Cardiovasc Imaging* 2020;**13**:e009886. https://doi.org/10.1161/circimaging.119.009886
1164. Johnsen L, Hisdal J, Jonung T, Braaten A, Pedersen G. Contrast-enhanced ultrasound detects type II endoleaks during follow-up for endovascular aneurysm repair. *J Vasc Surg* 2020;**72**:1952–9. https://doi.org/10.1016/j.jvs.2020.02.020
1165. George J, Tadros RO, Rao A, Png CYM, Han DK, Ilonzo N, *et al.* Duplex ultrasound can successfully identify endoleaks and renovisceral stent patency in patients undergoing complex endovascular aneurysm repair. *Vasc Endovascular Surg* 2021;**55**:234–8. https://doi.org/10.1177/1538574420980605
1166. Smith L, Thomas N, Arnold A, Bell R, Zayed H, Tyrrell M, *et al.* Editor's choice—a comparison of computed tomography angiography and colour duplex ultrasound surveillance post infrarenal endovascular aortic aneurysm repair: financial implications and impact of different international surveillance guidelines. *Eur J Vasc Endovasc Surg* 2021;**62**:193–201. https://doi.org/10.1016/j.ejvs.2021.04.005
1167. Iscan HZ, Unal EU, Akkaya B, Daglı M, Karahan M, Civelek I, *et al.* Color Doppler ultrasound for surveillance following EVAR as the primary tool. *J Card Surg* 2021;**36**:111–7. https://doi.org/10.1111/jocs.15194
1168. Antoniou GA, Kontopodis N, Rogers SK, Golledge J, Forbes TL, Torella F, *et al.* Editor's choice—meta-analysis of compliance with endovascular aneurysm repair surveillance: the EVAR surveillance paradox. *Eur J Vasc Endovasc Surg* 2023;**65**:244–54. https://doi.org/10.1016/j.ejvs.2022.10.033
1169. Baderkhan H, Haller O, Wanhainen A, Björck M, Mani K. Follow-up after endovascular aortic aneurysm repair can be stratified based on first postoperative imaging. *Br J Surg* 2018;**105**:709–18. https://doi.org/10.1002/bjs.10766
1170. Png CY, Tadros RO, Faries PL, Torres MR, Kim SY, Lookstein R, *et al.* The effect of age on post-EVAR outcomes. *Ann Vasc Surg* 2016;**35**:156–62. https://doi.org/10.1016/j.avsg.2016.01.022
1171. Xiong X, Wu Z, Qin X, Huang Q, Wang X, Qin J, *et al.* Meta-analysis suggests statins reduce mortality after abdominal aortic aneurysm repair. *J Vasc Surg* 2022;**75**:356–62.e4. https://doi.org/10.1016/j.jvs.2021.06.033
1172. Schrimpf C, Teebken OE, Wilhelmi M. Thoracic endovascular aortic repair after iatrogenic aortic dissection and false lumen stent grafting. *Ann Thorac Surg* 2015;**99**:1447–9. https://doi.org/10.1016/j.athoracsur.2014.05.101
1173. Sampson UK, Norman PE, Fowkes FG, Aboyans V, Song Y, Harrell FE, Jr, *et al.* Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. *Glob Heart* 2014;**9**:171–80.e110. https://doi.org/10.1016/j.gheart.2013.12.010
1174. Clough RE, Nienaber CA. Management of acute aortic syndrome. *Nat Rev Cardiol* 2015;**12**:103–14. https://doi.org/10.1038/nrcardio.2014.203
1175. Evangelista A, Isselbacher EM, Bossone E, Gleason TG, Eusanio MD, Sechtem U, *et al.* Insights from the international registry of acute aortic dissection: a 20-year experience of collaborative clinical research. *Circulation* 2018;**137**:1846–60. https://doi.org/10.1161/circulationaha.117.031264
1176. Booher AM, Isselbacher EM, Nienaber CA, Trimarchi S, Evangelista A, Montgomery DG, *et al.* The IRAD classification system for characterizing survival after aortic dissection. *Am J Med* 2013;**126**:730.e19–24. https://doi.org/10.1016/j.amjmed.2013.01.020
1177. Howard C, Ponnapalli A, Shaikh S, Idhrees M, Bashir M. Non-A non-B aortic dissection: a literature review. *J Card Surg* 2021;**36**:1806–13. https://doi.org/10.1111/jocs.15349
1178. Urbanski PP, Wagner M. Acute non-A-non-B aortic dissection: surgical or conservative approach? *Eur J Cardiothorac Surg* 2016;**49**:1249–54. https://doi.org/10.1093/ejcts/ezv301
1179. Carino D, Singh M, Molardi A, Agostinelli A, Goldoni M, Pacini D, *et al.* Non-A non-B aortic dissection: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2019;**55**:653–9. https://doi.org/10.1093/ejcts/ezy337
1180. Sievers HH, Rylski B, Czerny M, Baier ALM, Kreibich M, Siepe M, *et al.* Aortic dissection reconsidered: type, entry site, malperfusion classification adding clarity and enabling outcome prediction. *Interact Cardiovasc Thorac Surg* 2020;**30**:451–7. https://doi.org/10.1093/icvts/ivz281
1181. Aboyans V, Boukhris M. Dissecting the epidemiology of aortic dissection. *Eur Heart J Acute Cardiovasc Care* 2021;**10**:710–1. https://doi.org/10.1093/ehjacc/zuab065
1182. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, *et al.* Presentation, diagnosis, and outcomes of acute aortic dissection: 17-year trends from the international registry of acute aortic dissection. *J Am Coll Cardiol* 2015;**66**:350–8. https://doi.org/10.1016/j.jacc.2015.05.029
1183. Januzzi JL, Isselbacher EM, Fattori R, Cooper JV, Smith DE, Fang J, *et al.* Characterizing the young patient with aortic dissection: results from the international registry of aortic dissection (IRAD). *J Am Coll Cardiol* 2004;**43**:665–9. https://doi.org/10.1016/j.jacc.2003.08.054
1184. Dalen JE, Alpert JS, Goldberg RJ, Weinstein RS. The epidemic of the 20(th) century: coronary heart disease. *Am J Med* 2014;**127**:807–12. https://doi.org/10.1016/j.amjmed.2014.04.015
1185. Bossone E, Pyeritz RE, O'Gara P, Harris KM, Braverman AC, Pape L, *et al.* Acute aortic dissection in blacks: insights from the international registry of acute aortic dissection. *Am J Med* 2013;**126**:909–15. https://doi.org/10.1016/j.amjmed.2013.04.020
1186. Rylski B, Hoffmann I, Beyersdorf F, Suedkamp M, Siepe M, Nitsch B, *et al.* Iatrogenic acute aortic dissection type A: insight from the German registry for acute aortic dissection type A (GERAADA). *Eur J Cardiothorac Surg* 2013;**44**:353–9; discussion 359. https://doi.org/10.1093/ejcts/ezt055
1187. Núñez-Gil IJ, Bautista D, Cerrato E, Salinas P, Varbella F, Omedè P, *et al.* Incidence, management, and immediate- and long-term outcomes after iatrogenic aortic dissection during diagnostic or interventional coronary procedures. *Circulation* 2015;**131**:2114–9. https://doi.org/10.1161/circulationaha.115.015334
1188. Carbone A, Ranieri B, Castaldo R, Franzese M, Rega S, Cittadini A, *et al.* Sex differences in type A acute aortic dissection: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2023;**30**:1074–89. https://doi.org/10.1093/eurjpc/zwad009
1189. Nienaber CA, Fattori R, Mehta RH, Richartz BM, Evangelista A, Petzsch M, *et al.* Gender-related differences in acute aortic dissection. *Circulation* 2004;**109**:3014–21. https://doi.org/10.1161/01.Cir.0000130644.78677.2c

1190. Manalo-Estrella P, Barker AE. Histopathologic findings in human aortic media associated with pregnancy. *Arch Pathol* 1967;**83**:336–41.
1191. Lempel JK, Frazier AA, Jeudy J, Kligerman SJ, Schultz R, Ninalowo HA, *et al.* Aortic arch dissection: a controversy of classification. *Radiology* 2014;**271**:848–55. https://doi.org/10.1148/radiol.14131457
1192. Mussa FF, Horton JD, Moridzadeh R, Nicholson J, Trimarchi S, Eagle KA. Acute aortic dissection and intramural hematoma: a systematic review. *JAMA* 2016;**316**:754–63. https://doi.org/10.1001/jama.2016.10026
1193. Tsai TT, Trimarchi S, Nienaber CA. Acute aortic dissection: perspectives from the international registry of acute aortic dissection (IRAD). *Eur J Vasc Endovasc Surg* 2009;**37**:149–59. https://doi.org/10.1016/j.ejvs.2008.11.032
1194. Neri E, Toscano T, Papalia U, Frati G, Massetti M, Capannini G, *et al.* Proximal aortic dissection with coronary malperfusion: presentation, management, and outcome. *J Thorac Cardiovasc Surg* 2001;**121**:552–60. https://doi.org/10.1067/mtc.2001.112534
1195. Trimarchi S, Tsai T, Eagle KA, Isselbacher EM, Froehlich J, *et al.* Acute abdominal aortic dissection: insight from the International Registry of Acute Aortic Dissection (IRAD). *J Vasc Surg* 2007;**46**:913–9. https://doi.org/10.1016/j.jvs.2007.07.030
1196. Gorla R, Erbel R, Kahlert P, Tsagakis K, Jakob H, Mahabadi A-A, *et al.* Accuracy of a diagnostic strategy combining aortic dissection detection risk score and D-dimer levels in patients with suspected acute aortic syndrome. *Eur Heart J Acute Cardiovasc Care* 2017;**6**:371–8. https://doi.org/10.1177/2048872615594497
1197. Strayer RJ, Shearer PL, Hermann LK. Screening, evaluation, and early management of acute aortic dissection in the ED. *Curr Cardiol Rev* 2012;**8**:152–7. https://doi.org/10.2174/157340312801784970
1198. Nazerian P, Mueller C, Soeiro AM, Leidel BA, Salvadeo SAT, Giachino F, *et al.* Diagnostic accuracy of the aortic dissection detection risk score plus D-dimer for acute aortic syndromes: the ADvISED prospective multicenter study. *Circulation* 2018;**137**:250–8. https://doi.org/10.1161/circulationaha.117.029457
1199. Bima P, Pivetta E, Nazerian P, Toyofuku M, Gorla R, Bossone E, *et al.* Systematic review of aortic dissection detection risk score plus d-dimer for diagnostic rule-out of suspected acute aortic syndromes. *Acad Emerg Med* 2020;**27**:1013–27. https://doi.org/10.1111/acem.13969
1200. Rogers AM, Hermann LK, Booher AM, Nienaber CA, Williams DM, Kazerooni EA, *et al.* Sensitivity of the aortic dissection detection risk score, a novel guideline-based tool for identification of acute aortic dissection at initial presentation: results from the international registry of acute aortic dissection. *Circulation* 2011;**123**:2213–8. https://doi.org/10.1161/CIRCULATIONAHA.110.988568
1201. Suzuki T, Distante A, Zizza A, Trimarchi S, Villani M, Salerno Uriarte JA, *et al.* Diagnosis of acute aortic dissection by D-dimer: the international registry of acute aortic dissection substudy on biomarkers (IRAD-bio) experience. *Circulation* 2009;**119**:2702–7. https://doi.org/10.1161/circulationaha.108.833004
1202. Baliga RR, Nienaber CA, Bossone E, Oh JK, Isselbacher EM, Sechtem U, *et al.* The role of imaging in aortic dissection and related syndromes. *JACC Cardiovasc Imaging* 2014;**7**:406–24. https://doi.org/10.1016/j.jcmg.2013.10.015
1203. Nazerian P, Mueller C, Vanni S, Soeiro AM, Leidel BA, Cerini G, *et al.* Integration of transthoracic focused cardiac ultrasound in the diagnostic algorithm for suspected acute aortic syndromes. *Eur Heart J* 2019;**40**:1952–60. https://doi.org/10.1093/eurheartj/ehz207
1204. Shiga T, Wajima Z, Apfel CC, Inoue T, Ohe Y. Diagnostic accuracy of transesophageal echocardiography, helical computed tomography, and magnetic resonance imaging for suspected thoracic aortic dissection: systematic review and meta-analysis. *Arch Intern Med* 2006;**166**:1350–6. https://doi.org/10.1001/archinte.166.13.1350
1205. Nienaber CA, Clough RE. Management of acute aortic dissection. *Lancet* 2015;**385**:800–11. https://doi.org/10.1016/s0140-6736(14)61005-9
1206. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, *et al.* 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023;**44**:3720–826. https://doi.org/10.1093/eurheartj/ehad191
1207. Rogers IS, Banerji D, Siegel EL, Truong QA, Ghoshhajra BB, Irlbeck T, *et al.* Usefulness of comprehensive cardiothoracic computed tomography in the evaluation of acute undifferentiated chest discomfort in the emergency department (CAPTURE). *Am J Cardiol* 2011;**107**:643–50. https://doi.org/10.1016/j.amjcard.2010.10.039
1208. Evangelista A, Maldonado G, Gruosso D, Gutiérrez L, Granato C, Villalva N, *et al.* The current role of echocardiography in acute aortic syndrome. *Echo Res Pract* 2019;**6**:R53–r63. https://doi.org/10.1530/erp-18-0058
1209. Vignon P, Guéret P, Vedrinne JM, Lagrange P, Cornu E, Abrieu O, *et al.* Role of transesophageal echocardiography in the diagnosis and management of traumatic aortic disruption. *Circulation* 1995;**92**:2959–68. https://doi.org/10.1161/01.cir.92.10.2959
1210. Moral S, Avegliano G, Cuéllar H, Ballesteros E, Rodríguez-Palomares J, Teixidó G, *et al.* Usefulness of transesophageal echocardiography in the evaluation of celiac trunk and superior mesenteric artery involvement in acute aortic dissection. *J Am Soc Echocardiogr* 2021;**34**:327–35. https://doi.org/10.1016/j.echo.2020.12.019
1211. Nienaber CA, Clough RE, Sakalihasan N, Suzuki T, Gibbs R, Mussa F, *et al.* Aortic dissection. *Nat Rev Dis Primers* 2016;**2**:16053. https://doi.org/10.1038/nrdp.2016.53
1212. Vilacosta I, San Román JA, di Bartolomeo R, Eagle K, Estrera AL, Ferrera C, *et al.* Acute aortic syndrome revisited: JACC state-of-the-art review. *J Am Coll Cardiol* 2021;**78**:2106–25. https://doi.org/10.1016/j.jacc.2021.09.022
1213. Tadros RO, Tang GHL, Barnes HJ, Mousavi I, Kovacic JC, Faries P, *et al.* Optimal treatment of uncomplicated type B aortic dissection: JACC review topic of the week. *J Am Coll Cardiol* 2019;**74**:1494–504. https://doi.org/10.1016/j.jacc.2019.07.063
1214. Kodama K, Nishigami K, Sakamoto T, Sawamura T, Hirayama T, Misumi H, *et al.* Tight heart rate control reduces secondary adverse events in patients with type B acute aortic dissection. *Circulation* 2008;**118**:S167–70. https://doi.org/10.1161/circulationaha.107.755801
1215. Estrera AL, Miller CC, III, Safi HJ, Goodrick JS, Keyhani A, Porat EE, *et al.* Outcomes of medical management of acute type B aortic dissection. *Circulation* 2006;**114**:I384–389. https://doi.org/10.1161/circulationaha.105.001479
1216. Nejim B, Mathlouthi A, Naazie I, Malas MB. The effect of intravenous and oral beta-blocker use in patients with type B thoracic aortic dissection. *Ann Vasc Surg* 2022;**80**:170–9. https://doi.org/10.1016/j.avsg.2021.07.056
1217. Hameed I, Cifu AS, Vallabhajosyula P. Management of thoracic aortic dissection. *JAMA* 2023;**329**:756–7. https://doi.org/10.1001/jama.2023.0265
1218. Fukui T. Management of acute aortic dissection and thoracic aortic rupture. *J Intensive Care* 2018;**6**:15. https://doi.org/10.1186/s40560-018-0287-7
1219. Suzuki T, Mehta RH, Ince H, Nagai R, Sakomura Y, Weber F, *et al.* Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the international registry of aortic dissection (IRAD). *Circulation* 2003;**108**:II312–7. https://doi.org/10.1161/01.cir.0000087386.07204.09
1220. Mehta RH, Suzuki T, Hagan PG, Bossone E, Gilon D, Llovet A, *et al.* Predicting death in patients with acute type a aortic dissection. *Circulation* 2002;**105**:200–6. https://doi.org/10.1161/hc0202.102246
1221. Mészáros I, Mórocz J, Szlávi J, Schmidt J, Tornóci L, Nagy L, *et al.* Epidemiology and clinicopathology of aortic dissection. *Chest* 2000;**117**:1271–8. https://doi.org/10.1378/chest.117.5.1271
1222. Glower DD, Speier RH, White WD, Smith LR, Rankin JS, Wolfe WG. Management and long-term outcome of aortic dissection. *Ann Surg* 1991;**214**:31–41. https://doi.org/10.1097/00000658-199107000-00006
1223. Nallamothu BK, Mehta RH, Saint S, Llovet A, Bossone E, Cooper JV, *et al.* Syncope in acute aortic dissection: diagnostic, prognostic, and clinical implications. *Am J Med* 2002;**113**:468–71. https://doi.org/10.1016/s0002-9343(02)01254-8
1224. Suzuki T, Isselbacher EM, Nienaber CA, Pyeritz RE, Eagle KA, Tsai TT, *et al.* Type-selective benefits of medications in treatment of acute aortic dissection (from the international registry of acute aortic dissection [IRAD]). *Am J Cardiol* 2012;**109**:122–7. https://doi.org/10.1016/j.amjcard.2011.08.012
1225. Palmer J, Gelmann D, Engelbrecht-Wiggans E, Hollis G, Hart E, Ali A, *et al.* Invasive arterial blood pressure monitoring may aid in the medical management of hypertensive patients with acute aortic disease. *Am J Emerg Med* 2022;**59**:85–93. https://doi.org/10.1016/j.ajem.2022.06.054
1226. Nienaber CA, Kische S, Rousseau H, Eggebrecht H, Rehders TC, Kundt G, *et al.* Endovascular repair of type B aortic dissection: long-term results of the randomized investigation of stent grafts in aortic dissection trial. *Circ Cardiovasc Interv* 2013;**6**:407–16. https://doi.org/10.1161/circinterventions.113.000463
1227. Fattori R, Montgomery D, Lovato L, Kische S, Di Eusanio M, Ince H, *et al.* Survival after endovascular therapy in patients with type B aortic dissection: a report from the international registry of acute aortic dissection (IRAD). *JACC Cardiovasc Interv* 2013;**6**:876–82. https://doi.org/10.1016/j.jcin.2013.05.003
1228. Durham CA, Cambria RP, Wang LJ, Ergul EA, Aranson NJ, Patel VI, *et al.* The natural history of medically managed acute type B aortic dissection. *J Vasc Surg* 2015;**61**:1192–8. https://doi.org/10.1016/j.jvs.2014.12.038
1229. Lou X, Chen EP, Duwayri YM, Veeraswamy RK, Jordan WD, Zehner CA, *et al.* The impact of thoracic endovascular aortic repair on long-term survival in type B aortic dissection. *Ann Thorac Surg* 2018;**105**:31–8. https://doi.org/10.1016/j.athoracsur.2017.06.016
1230. Lou X, Duwayri YM, Chen EP, Jordan WD, Forcillo J, Zehner CA, *et al.* Predictors of failure of medical management in uncomplicated type B aortic dissection. *Ann Thorac Surg* 2019;**107**:493–8. https://doi.org/10.1016/j.athoracsur.2018.08.012
1231. Lou X, Duwayri YM, Jordan WD, Jr, Chen EP, Veeraswamy RK, Leshnower BG. The safety and efficacy of extended TEVAR in acute type B aortic dissection. *Ann Thorac Surg* 2020;**110**:799–806. https://doi.org/10.1016/j.athoracsur.2019.12.036
1232. Hirst AE, Jr, Johns VJ, Jr, Kime SW, Jr. Dissecting aneurysm of the aorta: a review of 505 cases. *Medicine* 1958;**37**:217–79. https://doi.org/10.1097/00005792-195809000-00003
1233. Chiappini B, Schepens M, Tan E, Amore AD, Morshuis W, Dossche K, *et al.* Early and late outcomes of acute type A aortic dissection: analysis of risk factors in 487 consecutive patients. *Eur Heart J* 2005;**26**:180–6. https://doi.org/10.1093/eurheartj/ehi024
1234. Harris KM, Nienaber CA, Peterson MD, Woznicki EM, Braverman AC, Trimarchi S, *et al.* Early mortality in type A acute aortic dissection: insights from the international registry of acute aortic dissection. *JAMA Cardiol* 2022;**7**:1009–15. https://doi.org/10.1001/jamacardio.2022.2718
1235. Zhu Y, Lingala B, Baiocchi M, Tao JJ, Toro Arana V, Khoo JW, *et al.* Type A aortic dissection-experience over 5 decades: JACC historical breakthroughs in perspective. *J Am Coll Cardiol* 2020;**76**:1703–13. https://doi.org/10.1016/j.jacc.2020.07.061

1236. Czerny M, Siepe M, Beyersdorf F, Feisst M, Gabel M, Pilz M, *et al.* Prediction of mortality rate in acute type A dissection: the German registry for acute type A aortic dissection score. *Eur J Cardiothorac Surg* 2020;**58**:700–6. https://doi.org/10.1093/ejcts/ezaa156
1237. Perko MJ, Nørgaard M, Herzog TM, Olsen PS, Schroeder TV, Pettersson G. Unoperated aortic aneurysm: a survey of 170 patients. *Ann Thorac Surg* 1995;**59**:1204–9. https://doi.org/10.1016/0003-4975(95)00132-5
1238. Wolfe SB, Sundt TM, III, Isselbacher EM, Cameron DE, Trimarchi S, Bekeredjian R, *et al.* Survival after operative repair of acute type A aortic dissection varies according to the presence and type of preoperative malperfusion. *J Thorac Cardiovasc Surg* 2024;**168**:37–49.e6. https://doi.org/10.1016/j.jtcvs.2022.09.034
1239. Trimarchi S, Eagle KA, Nienaber CA, Rampoldi V, Jonker FHW, De Vincentiis C, *et al.* Role of age in acute type A aortic dissection outcome: report from the international registry of acute aortic dissection (IRAD). *J Thorac Cardiovasc Surg* 2010;**140**:784–9. https://doi.org/10.1016/j.jtcvs.2009.11.014
1240. Shrestha M, Khaladj N, Haverich A, Hagl C. Is treatment of acute type A aortic dissection in septuagenarians justifiable? *Asian Cardiovasc Thorac Ann* 2008;**16**:33–6. https://doi.org/10.1177/021849230801600109
1241. Bonser RS, Ranasinghe AM, Loubani M, Evans JD, Thalji NMA, Bachet JE, *et al.* Evidence, lack of evidence, controversy, and debate in the provision and performance of the surgery of acute type A aortic dissection. *J Am Coll Cardiol* 2011;**58**:2455–74. https://doi.org/10.1016/j.jacc.2011.06.067
1242. Subramanian S, Leontyev S, Borger MA, Trommer C, Misfeld M, Mohr FW. Valve-sparing root reconstruction does not compromise survival in acute type A aortic dissection. *Ann Thorac Surg* 2012;**94**:1230–4. https://doi.org/10.1016/j.athoracsur.2012.04.094
1243. Urbanski PP, Hijazi H, Dinstak W, Diegeler A. Valve-sparing aortic root repair in acute type A dissection: how many sinuses have to be repaired for curative surgery? *Eur J Cardiothorac Surg* 2013;**44**:439–43; discussion 443–4. https://doi.org/10.1093/ejcts/ezt042
1244. Shrestha M, Baraki H, Maeding I, Fitzner S, Sarikouch S, Khaladj N, *et al.* Long-term results after aortic valve-sparing operation (David I). *Eur J Cardiothorac Surg* 2012;**41**:56–61; discussion 61–2. https://doi.org/10.1016/j.ejcts.2011.04.012
1245. Tsagakis K, Pacini D, Di Bartolomeo R, Gorlitzer M, Weiss G, Grabenwoger M, *et al.* Multicenter early experience with extended aortic repair in acute aortic dissection: is simultaneous descending stent grafting justified? *J Thorac Cardiovasc Surg* 2010;**140**:S116–20; discussion S142–S146. https://doi.org/10.1016/j.jtcvs.2010.07.066
1246. Tsagakis K, Pacini D, Grabenwöger M, Borger MA, Goebel N, Hemmer W, *et al.* Results of frozen elephant trunk from the international E-vita Open registry. *Ann Cardiothorac Surg* 2020;**9**:178–88. https://doi.org/10.21037/acs-2020-fet-25
1247. Beckmann E, Martens A, Kaufeld T, Natanov R, Krueger H, Rudolph L, *et al.* Frozen elephant trunk in acute aortic type a dissection: risk analysis of concomitant root replacement. *Eur J Cardiothorac Surg* 2022;**62**:ezac051. https://doi.org/10.1093/ejcts/ezac051
1248. Cruz I, Stuart B, Caldeira D, Morgado G, Gomes AC, Almeida AR, *et al.* Controlled pericardiocentesis in patients with cardiac tamponade complicating aortic dissection: experience of a centre without cardiothoracic surgery. *Eur Heart J Acute Cardiovasc Care* 2015;**4**:124–8. https://doi.org/10.1177/2048872614549737
1249. Hayashi T, Tsukube T, Yamashita T, Haraguchi T, Matsukawa R, Kozawa S, *et al.* Impact of controlled pericardial drainage on critical cardiac tamponade with acute type A aortic dissection. *Circulation* 2012;**126**:S97–101. https://doi.org/10.1161/CIRCULATIONAHA.111.082685
1250. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, *et al.* The international registry of acute aortic dissection (IRAD): new insights into an old disease. *JAMA* 2000;**283**:897–903. https://doi.org/10.1001/jama.283.7.897
1251. Saczkowski R, Malas T, Mesana T, de Kerchove L, El Khoury G, Boodhwani M. Aortic valve preservation and repair in acute type A aortic dissection. *Eur J Cardiothorac Surg* 2014;**45**:e220–226. https://doi.org/10.1093/ejcts/ezu099
1252. Hysi I, Juthier F, Fabre O, Fouquet O, Rousse N, Banfi C, *et al.* Aortic root surgery improves long-term survival after acute type A aortic dissection. *Int J Cardiol* 2015;**184**:285–90. https://doi.org/10.1016/j.ijcard.2015.02.020
1253. Peterss S, Dumfarth J, Rizzo JA, Bonaros N, Fang H, Tranquilli M, *et al.* Sparing the aortic root in acute aortic dissection type A: risk reduction and restored integrity of the untouched root. *Eur J Cardiothorac Surg* 2016;**50**:232–9. https://doi.org/10.1093/ejcts/ezw012
1254. Chen SK, Qiu ZH, Fang GH, Wu XJ, Chen LW. Reported outcomes after aortic valve resuspension for acute type A aortic dissection: a systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg* 2019;**29**:331–8. https://doi.org/10.1093/icvts/ivz080
1255. Qiu J, Wu J, Xie E, Luo X, Chen JF, Gao W, *et al.* Surgical management and outcomes of the aortic root in acute type A aortic dissection. *Ann Thorac Surg* 2020;**110**:136–43. https://doi.org/10.1016/j.athoracsur.2019.10.014
1256. Umana-Pizano JB, Nissen AP, Sandhu HK, Miller CC, Loghin A, Safi HJ, *et al.* Acute type A dissection repair by high-volume vs low-volume surgeons at a high-volume aortic center. *Ann Thorac Surg* 2019;**108**:1330–6. https://doi.org/10.1016/j.athoracsur.2019.04.040
1257. Goldstone AB, Chiu P, Baiocchi M, Lingala B, Lee J, Rigdon J, *et al.* Interfacility transfer of medicare beneficiaries with acute type A aortic dissection and regionalization of care in the United States. *Circulation* 2019;**140**:1239–50. https://doi.org/10.1161/circulationaha.118.038867
1258. Mosbahi S, Stak D, Gravestock I, Burgstaller JM, Steurer J, Eckstein F, *et al.* A systemic review and meta-analysis: Bentall versus David procedure in acute type A aortic dissection. *Eur J Cardiothorac Surg* 2019;**55**:201–9. https://doi.org/10.1093/ejcts/ezy266
1259. Beckmann E, Martens A, Pertz J, Kaufeld T, Umminger J, Hanke JS, *et al.* Valve-sparing David I procedure in acute aortic type A dissection: a 20-year experience with more than 100 patients. *Eur J Cardiothorac Surg* 2017;**52**:319–24. https://doi.org/10.1093/ejcts/ezx170
1260. Weiss G, Tsagakis K, Jakob H, Di Bartolomeo R, Pacini D, Barberio G, *et al.* The frozen elephant trunk technique for the treatment of complicated type B aortic dissection with involvement of the aortic arch: multicentre early experience. *Eur J Cardiothorac Surg* 2015;**47**:106–14; discussion 114. https://doi.org/10.1093/ejcts/ezu067
1261. Iafrancesco M, Goebel N, Mascaro J, Franke UFW, Pacini D, Di Bartolomeo R, *et al.* Aortic diameter remodelling after the frozen elephant trunk technique in aortic dissection: results from an international multicentre registry. *Eur J Cardiothorac Surg* 2017;**52**:310–8. https://doi.org/10.1093/ejcts/ezx131
1262. Tsagakis K, Wendt D, Dimitriou AM, Thielmann M, Shehada S-D, El Gabry M, *et al.* The frozen elephant trunk treatment is the operation of choice for all kinds of arch disease. *J Cardiovasc Surg (Torino)* 2018;**59**:540–6. https://doi.org/10.23736/s0021-9509.18.10597-0
1263. Widenka KJ, Kosiorowska M, Jakob H, Pacini D, Hemmer W, Grabenwoeger M, *et al.* Early and midterm results of frozen elephant trunk operation with Evita open stent-graft in patients with Marfan syndrome: results of a multicentre study. *BMC Cardiovasc Disord* 2022;**22**:333. https://doi.org/10.1186/s12872-022-02777-5
1264. Jakob H, Shehada SE, Dohle D, Wendt D, El Gabry M, Schlosser T, *et al.* New 3-zone hybrid graft: first-in-man experience in acute type I dissection. *J Thorac Cardiovasc Surg* 2022;**163**:568–74.e1. https://doi.org/10.1016/j.jtcvs.2020.04.113
1265. Tsagakis K, Osswald A, Weymann A, Demircioglu A, Schmack B, Wendt D, *et al.* The frozen elephant trunk technique: impact of proximalization and the four-sites perfusion technique. *Eur J Cardiothorac Surg* 2021;**61**:195–203. https://doi.org/10.1093/ejcts/ezab295
1266. Rampoldi V, Trimarchi S, Eagle KA, Nienaber CA, Oh JK, Bossone E, *et al.* Simple risk models to predict surgical mortality in acute type A aortic dissection: the international registry of acute aortic dissection score. *Ann Thorac Surg* 2007;**83**:55–61. https://doi.org/10.1016/j.athoracsur.2006.08.007
1267. Lawton JS, Liu J, Kulshrestha K, Moon MR, Damiano RJ, Maniar H, *et al.* The impact of surgical strategy on survival after repair of type A aortic dissection. *J Thorac Cardiovasc Surg* 2015;**150**:294–301.e1. https://doi.org/10.1016/j.jtcvs.2015.03.023
1268. Malvindi PG, Modi A, Miskolczi S, Kaarne M, Velissaris T, Barlow C, *et al.* Open and closed distal anastomosis for acute type A aortic dissection repair. *Interact Cardiovasc Thorac Surg* 2016;**22**:776–83. https://doi.org/10.1093/icvts/ivw044
1269. Geirsson A, Shioda K, Olsson C, Ahlsson A, Gunn J, Hansson EC, *et al.* Differential outcomes of open and clamp-on distal anastomosis techniques in acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2019;**157**:1750–8. https://doi.org/10.1016/j.jtcvs.2018.09.020
1270. Yan Y, Xu L, Zhang H, Xu Z-Y, Ding X-Y, Wang S-W, *et al.* Proximal aortic repair versus extensive aortic repair in the treatment of acute type A aortic dissection: a meta-analysis. *Eur J Cardiothorac Surg* 2016;**49**:1392–401. https://doi.org/10.1093/ejcts/ezv351
1271. Poon SS, Theologou T, Harrington D, Kuduvalli M, Oo A, Field M. Hemiarch versus total aortic arch replacement in acute type A dissection: a systematic review and meta-analysis. *Ann Cardiothorac Surg* 2016;**5**:156–73. https://doi.org/10.21037/acs.2016.05.06
1272. Hsieh WC, Kan CD, Yu HC, Aboud A, Lindner J, Henry BM, *et al.* Ascending aorta replacement vs. total aortic arch replacement in the treatment of acute type A dissection: a meta-analysis. *Eur Rev Med Pharmacol Sci* 2019;**23**:9590–611. https://doi.org/10.26355/eurrev_201911_19454
1273. Preventza O, Cervera R, Cooley DA, Bakaeen FG, Mohamed AS, Cheong BYC, *et al.* Acute type I aortic dissection: traditional versus hybrid repair with antegrade stent delivery to the descending thoracic aorta. *J Thorac Cardiovasc Surg* 2014;**148**:119–25. https://doi.org/10.1016/j.jtcvs.2013.07.055
1274. Roselli EE, Idrees JJ, Bakaeen FG, Tong MZ, Soltesz EG, Mick S, *et al.* Evolution of simplified frozen elephant trunk repair for acute DeBakey type I dissection: midterm outcomes. *Ann Thorac Surg* 2018;**105**:749–55. https://doi.org/10.1016/j.athoracsur.2017.08.037
1275. Berretta P, Trimarchi S, Patel HJ, Gleason TG, Eagle KA, Di Eusanio M. Malperfusion syndromes in type A aortic dissection: what we have learned from IRAD. *J Vis Surg* 2018;**4**:65. https://doi.org/10.21037/jovs.2018.03.13
1276. Benedetto U, Mohamed H, Vitulli P, Petrou M. Axillary versus femoral arterial cannulation in type A acute aortic dissection: evidence from a meta-analysis of comparative studies and adjusted risk estimates. *Eur J Cardiothorac Surg* 2015;**48**:953–9. https://doi.org/10.1093/ejcts/ezv035

1277. Geirsson A, Szeto WY, Pochettino A, McGarvey ML, Keane MG, Woo YJ, *et al.* Significance of malperfusion syndromes prior to contemporary surgical repair for acute type A dissection: outcomes and need for additional revascularizations. *Eur J Cardiothorac Surg* 2007;**32**:255–62. https://doi.org/10.1016/j.ejcts.2007.04.012
1278. Yang B, Norton EL, Rosati CM, Wu X, Kim KM, Khaja MS, *et al.* Managing patients with acute type A aortic dissection and mesenteric malperfusion syndrome: a 20-year experience. *J Thorac Cardiovasc Surg* 2019;**158**:675–87.e4. https://doi.org/10.1016/j.jtcvs.2018.11.127
1279. Yang B, Rosati CM, Norton EL, Kim KM, Khaja MS, Dasika N, *et al.* Endovascular fenestration/stenting first followed by delayed open aortic repair for acute type A aortic dissection with malperfusion syndrome. *Circulation* 2018;**138**:2091–103. https://doi.org/10.1161/circulationaha.118.036328
1280. Leshnower BG, Keeling WB, Duwayri YM, Jordan WD, Jr, Chen EP. The "thoracic endovascular aortic repair-first" strategy for acute type A dissection with mesenteric malperfusion: initial results compared with conventional algorithms. *J Thorac Cardiovasc Surg* 2019;**158**:1516–24. https://doi.org/10.1016/j.jtcvs.2019.01.116
1281. Rylski B, Szeto WY, Bavaria JE, Branchetti E, Moser W, Milewski RK. Development of a single endovascular device for aortic valve replacement and ascending aortic repair. *J Card Surg* 2014;**29**:371–6. https://doi.org/10.1111/jocs.12348
1282. Kreibich M, Rylski B, Kondov S, Morlock J, Scheumann J, Kari FA, *et al.* Endovascular treatment of acute type A aortic dissection-the Endo Bentall approach. *J Vis Surg* 2018;**4**:69. https://doi.org/10.21037/jovs.2018.03.14
1283. Brown CR, Chen Z, Khurshan F, Kreibich M, Bavaria J, Groeneveld P, *et al.* Outcomes after thoracic endovascular aortic repair in patients with chronic kidney disease in the Medicare population. *J Thorac Cardiovasc Surg* 2020;**159**:402–13. https://doi.org/10.1016/j.jtcvs.2019.01.118
1284. Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Bossone E, *et al.* Role and results of surgery in acute type B aortic dissection: insights from the international registry of acute aortic dissection (IRAD). *Circulation* 2006;**114**:I357–64. https://doi.org/10.1161/circulationaha.105.000620
1285. Tolenaar JL, Froehlich W, Jonker FH, Upchurch GR, Rampoldi V, Tsai TT, *et al.* Predicting in-hospital mortality in acute type B aortic dissection: evidence from international registry of acute aortic dissection. *Circulation* 2014;**130**:S45–50. https://doi.org/10.1161/circulationaha.113.007117
1286. Martin G, Patel N, Grant Y, Jenkins M, Gibbs R, Bicknell C. Antihypertensive medication adherence in chronic type B aortic dissection is an important consideration in the management debate. *J Vasc Surg* 2018;**68**:693–9.e2. https://doi.org/10.1016/j.jvs.2017.12.063
1287. Brooke BS, Griffin CL, Glotzbach JP, Horns JJ, Patel S, Kraiss LW, *et al.* Predictors of adherence to anti-impulse therapy among patients treated for acute type-B aortic dissections. *Ann Vasc Surg* 2021;**76**:95–103. https://doi.org/10.1016/j.avsg.2021.04.011
1288. Zeeshan A, Woo EY, Bavaria JE, Fairman RM, Desai ND, Pochettino A, *et al.* Thoracic endovascular aortic repair for acute complicated type B aortic dissection: superiority relative to conventional open surgical and medical therapy. *J Thorac Cardiovasc Surg* 2010;**140**:S109–115; discussion S142–S146. https://doi.org/10.1016/j.jtcvs.2010.06.024
1289. Steuer J, Eriksson MO, Nyman R, Björck M, Wanhainen A. Early and long-term outcome after thoracic endovascular aortic repair (TEVAR) for acute complicated type B aortic dissection. *Eur J Vasc Endovasc Surg* 2011;**41**:318–23. https://doi.org/10.1016/j.ejvs.2010.11.024
1290. Zipfel B, Czerny M, Funovics M, Coppi G, Ferro C, Rousseau H, *et al.* Endovascular treatment of patients with types A and B thoracic aortic dissection using Relay thoracic stent-grafts: results from the RESTORE patient registry. *J Endovasc Ther* 2011;**18**:131–43. https://doi.org/10.1583/10-3233mr.1
1291. Hanna JM, Andersen ND, Ganapathi AM, McCann RL, Hughes GC. Five-year results for endovascular repair of acute complicated type B aortic dissection. *J Vasc Surg* 2014;**59**:96–106. https://doi.org/10.1016/j.jvs.2013.07.001
1292. Stelzmueller ME, Nolz R, Mahr S, Beitzke D, Wolf F, Funovics M, *et al.* Thoracic endovascular repair for acute complicated type B aortic dissections. *J Vasc Surg* 2019;**69**:318–26. https://doi.org/10.1016/j.jvs.2018.05.234
1293. Wilson-Smith AR, Muston B, Kamalanathan H, Yung A, Chen C-HJ, Sahai P, *et al.* Endovascular repair of acute complicated type B aortic dissection-systematic review and meta-analysis of long-term survival and reintervention. *Ann Cardiothorac Surg* 2021;**10**:723–30. https://doi.org/10.21037/acs-2021-taes-17
1294. MacGillivray TE, Gleason TG, Patel HJ, Aldea GS, Bavaria JE, Beaver TM, *et al.* The Society of Thoracic Surgeons/American Association for Thoracic Surgery clinical practice guidelines on the management of type B aortic dissection. *J Thorac Cardiovasc Surg* 2022;**163**:1231–49. https://doi.org/10.1016/j.jtcvs.2021.11.091
1295. Brunkwall J, Kasprzak P, Verhoeven E, Heijmen R, Taylor P, Alric P, *et al.* Endovascular repair of acute uncomplicated aortic type B dissection promotes aortic remodelling: 1 year results of the ADSORB trial. *Eur J Vasc Endovasc Surg* 2014;**48**:285–91. https://doi.org/10.1016/j.ejvs.2014.05.012
1296. Hossack M, Patel S, Gambardella I, Neequaye S, Antoniou GA, Torella F. Endovascular vs. medical management for uncomplicated acute and sub-acute type B aortic dissection: a meta-analysis. *Eur J Vasc Endovasc Surg* 2020;**59**:794–807. https://doi.org/10.1016/j.ejvs.2019.08.003
1297. Sa MP, Jacquemyn X, Van den Eynde J, Chu D, Serna-Gallegos D, Singh MJ, *et al.* Midterm outcomes of endovascular vs. medical therapy for uncomplicated type B aortic dissection: meta-analysis of reconstructed time to event data. *Eur J Vasc Endovasc Surg* 2023;**66**:609–19. https://doi.org/10.1016/j.ejvs.2023.07.004
1298. Sa MP, Jacquemyn X, Brown JA, Ahmad D, Serna-Gallegos D, Arnaoutakis GJ, *et al.* Thoracic endovascular aortic repair for hyperacute, acute, subacute and chronic type B aortic dissection: meta-analysis of reconstructed time-to-event data. *Trends Cardiovasc Med* 2023:S1050-1738(23)00113-5. https://doi.org/10.1016/j.tcm.2023.12.005
1299. Jubouri M, Al-Tawil M, Yip HCA, Bashir A, Tan SZCP, Bashir M, *et al.* Mid- and long-term outcomes of thoracic endovascular aortic repair in acute and subacute uncomplicated type B aortic dissection. *J Card Surg* 2022;**37**:1328–39. https://doi.org/10.1111/jocs.16349
1300. Torrent DJ, McFarland GE, Wang G, Malas M, Pearce BJ, Aucoin V, *et al.* Timing of thoracic endovascular aortic repair for uncomplicated acute type B aortic dissection and the association with complications. *J Vasc Surg* 2021;**73**:826–35. https://doi.org/10.1016/j.jvs.2020.05.073
1301. Schwartz SI, Durham C, Clouse WD, Patel VI, Lancaster RT, Cambria RP, *et al.* Predictors of late aortic intervention in patients with medically treated type B aortic dissection. *J Vasc Surg* 2018;**67**:78–84. https://doi.org/10.1016/j.jvs.2017.05.128
1302. Onitsuka S, Akashi H, Tayama K, Okazaki T, Ishihara K, Hiromatsu S, *et al.* Long-term outcome and prognostic predictors of medically treated acute type B aortic dissections. *Ann Thorac Surg* 2004;**78**:1268–73. https://doi.org/10.1016/j.athoracsur.2004.02.031
1303. Hughes GC, Ganapathi AM, Keenan JE, Englum BR, Hanna JM, Schechter MA, *et al.* Thoracic endovascular aortic repair for chronic DeBakey IIIb aortic dissection. *Ann Thorac Surg* 2014;**98**:2092–7; discussion 2098. https://doi.org/10.1016/j.athoracsur.2014.06.066
1304. Jánosi RA, Tsagakis K, Bettin M, Kahlert P, Horacek M, Al-Rashid F, *et al.* Thoracic aortic aneurysm expansion due to late distal stent graft-induced new entry. *Catheter Cardiovasc Interv* 2015;**85**:E43–53. https://doi.org/10.1002/ccd.25614
1305. Cheng L, Xiang D, Zhang S, Zheng C, Wu X. Reintervention after thoracic endovascular aortic repair of uncomplicated type B aortic dissection. *J Clin Med* 2023;**12**:1418. https://doi.org/10.3390/jcm12041418
1306. Akutsu K, Nejima J, Kiuchi K, Sasaki K, Ochi M, Tanaka K, *et al.* Effects of the patent false lumen on the long-term outcome of type B acute aortic dissection. *Eur J Cardiothorac Surg* 2004;**26**:359–66. https://doi.org/10.1016/j.ejcts.2004.03.026
1307. Tsai TT, Evangelista A, Nienaber CA, Myrmel T, Meinhardt G, Cooper JV, *et al.* Partial thrombosis of the false lumen in patients with acute type B aortic dissection. *N Engl J Med* 2007;**357**:349–59. https://doi.org/10.1056/NEJMoa063232
1308. Dake MD, Thompson M, van Sambeek M, Vermassen F, Morales JP. DISSECT: a new mnemonic-based approach to the categorization of aortic dissection. *Eur J Vasc Endovasc Surg* 2013;**46**:175–90. https://doi.org/10.1016/j.ejvs.2013.04.029
1309. Wang J, Jin T, Chen B, Pan Y, Shao C. Systematic review and meta-analysis of current evidence in endograft therapy vs medical treatment for uncomplicated type B aortic dissection. *J Vasc Surg* 2022;**76**:1099–108.e3. https://doi.org/10.1016/j.jvs.2022.03.876
1310. Umaña JP, Lai DT, Mitchell RS, Moore KA, Rodriguez F, Robbins RC, *et al.* Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissections? *J Thorac Cardiovasc Surg* 2002;**124**:896–910. https://doi.org/10.1067/mtc.2002.123131
1311. Umaña JP, Miller DC, Mitchell RS. What is the best treatment for patients with acute type B aortic dissections—medical, surgical, or endovascular stent-grafting? *Ann Thorac Surg* 2002;**74**:S1840–3; discussion S1857–63. https://doi.org/10.1016/s0003-4975(02)04140-1
1312. Morello F, Santoro M, Fargion AT, Grifoni S, Nazerian P. Diagnosis and management of acute aortic syndromes in the emergency department. *Intern Emerg Med* 2021;**16**:171–81. https://doi.org/10.1007/s11739-020-02354-8
1313. Marui A, Mochizuki T, Mitsui N, Koyama T, Kimura F, Horibe M. Toward the best treatment for uncomplicated patients with type B acute aortic dissection: a consideration for sound surgical indication. *Circulation* 1999;**100**:II275–80. https://doi.org/10.1161/01.cir.100.suppl_2.ii-275
1314. Crawford ES. The diagnosis and management of aortic dissection. *JAMA* 1990;**264**:2537–41.
1315. Hata M, Shiono M, Inoue T, Sezai A, Niino T, Negishi N, *et al.* Optimal treatment of type B acute aortic dissection: long-term medical follow-up results. *Ann Thorac Surg* 2003;**75**:1781–4. https://doi.org/10.1016/s0003-4975(03)00113-9
1316. Oda T, Minatoya K, Sasaki H, Tanaka H, Seike Y, Itonaga T, *et al.* Surgical indication for chronic aortic dissection in descending thoracic and thoracoabdominal aorta. *Circ Cardiovasc Interv* 2017;**10**:e004292. https://doi.org/10.1161/circinterventions.116.004292
1317. Conrad MF, Chung TK, Cambria MR, Paruchuri V, Brady TJ, Cambria RP. Effect of chronic dissection on early and late outcomes after descending thoracic and

thoracoabdominal aneurysm repair. *J Vasc Surg* 2011;**53**:600–7; discussion 607. https://doi.org/10.1016/j.jvs.2010.09.053
1318. Crawford ES, Crawford JL, Safi HJ, Coselli JS, Hess KR, Brooks B, *et al.* Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg* 1986;**3**:389–404. https://doi.org/10.1067/mva.1986.avs0030389
1319. Zoli S, Etz CD, Roder F, Mueller CS, Brenner RM, Bodian CA, *et al.* Long-term survival after open repair of chronic distal aortic dissection. *Ann Thorac Surg* 2010;**89**:1458–66. https://doi.org/10.1016/j.athoracsur.2010.02.014
1320. Etz CD, Zoli S, Mueller CS, Bodian CA, Di Luozzo G, Lazala R, *et al.* Staged repair significantly reduces paraplegia rate after extensive thoracoabdominal aortic aneurysm repair. *J Thorac Cardiovasc Surg* 2010;**139**:1464–72. https://doi.org/10.1016/j.jtcvs.2010.02.037
1321. Conrad MF, Ergul EA, Patel VI, Paruchuri V, Kwolek CJ, Cambria RP. Management of diseases of the descending thoracic aorta in the endovascular era: a Medicare population study. *Ann Surg* 2010;**252**:603–10. https://doi.org/10.1097/SLA.0b013e3181f4eaef
1322. Sobocinski J, Dias NV, Berger L, Midulla M, Hertault A, Sonesson B, *et al.* Endograft repair of complicated acute type B aortic dissections. *Eur J Vasc Endovasc Surg* 2013;**45**:468–74. https://doi.org/10.1016/j.ejvs.2013.01.031
1323. Conrad MF, Carvalho S, Ergul E, Kwolek CJ, Lancaster RT, Patel VI, *et al.* Late aortic remodeling persists in the stented segment after endovascular repair of acute complicated type B aortic dissection. *J Vasc Surg* 2015;**62**:600–5. https://doi.org/10.1016/j.jvs.2015.03.064
1324. Thrumurthy SG, Karthikesalingam A, Patterson BO, Holt PJE, Hinchliffe RJ, Loftus IM, *et al.* A systematic review of mid-term outcomes of thoracic endovascular repair (TEVAR) of chronic type B aortic dissection. *Eur J Vasc Endovasc Surg* 2011;**42**:632–47. https://doi.org/10.1016/j.ejvs.2011.08.009
1325. Boufi M, Patterson BO, Loundou AD, Boyer L, Grima MJ, Loftus IM, *et al.* Endovascular versus open repair for chronic type B dissection treatment: a meta-analysis. *Ann Thorac Surg* 2019;**107**:1559–70. https://doi.org/10.1016/j.athoracsur.2018.10.045
1326. Conway AM, Qato K, Mondry LR, Stoffels GJ, Giangola G, Carroccio A. Outcomes of thoracic endovascular aortic repair for chronic aortic dissections. *J Vasc Surg* 2018;**67**:1345–52. https://doi.org/10.1016/j.jvs.2017.08.098
1327. Tenorio ER, Oderich GS, Farber MA, Schneider DB, Timaran CH, Schanzer A, *et al.* Outcomes of endovascular repair of chronic postdissection compared with degenerative thoracoabdominal aortic aneurysms using fenestrated-branched stent grafts. *J Vasc Surg* 2020;**72**:822–36.e9. https://doi.org/10.1016/j.jvs.2019.10.091
1328. Marques De Marino P, Ibraheem A, Gafur N, Verhoeven EL, Katsargyris A. Outcomes of fenestrated and branched endovascular aortic repair for chronic postdissection thoracoabdominal aortic aneurysms. *J Cardiovasc Surg* 2020;**61**:427–34. https://doi.org/10.23736/s0021-9509.20.11367-3
1329. Gallitto E, Faggioli G, Melissano G, Fargion A, Isernia G, Bertoglio L, *et al.* Fenestrated and branched endografts for post-dissection thoraco-abdominal aneurysms: results of a national multicentre study and literature review. *Eur J Vasc Endovasc Surg* 2022;**64**:630–8. https://doi.org/10.1016/j.ejvs.2022.06.019
1330. Geisbüsch S, Kuehnl A, Salvermoser M, Reutersberg B, Trenner M, Eckstein H-H. Editor's choice—hospital incidence, treatment, and in hospital mortality following open and endovascular surgery for thoraco-abdominal aortic aneurysms in Germany from 2005 to 2014: secondary data analysis of the Nationwide German DRG microdata. *Eur J Vasc Endovasc Surg* 2019;**57**:488–98. https://doi.org/10.1016/j.ejvs.2018.10.030
1331. Genoni M, Paul M, Jenni R, Graves K, Seifert B, Turina M. Chronic beta-blocker therapy improves outcome and reduces treatment costs in chronic type B aortic dissection. *Eur J Cardiothorac Surg* 2001;**19**:606–10. https://doi.org/10.1016/s1010-7940(01)00662-5
1332. Chen SW, Chan YH, Lin CP, Wu VC-C, Cheng Y-T, Chen D-Y, *et al.* Association of long-term use of antihypertensive medications with late outcomes among patients with aortic dissection. *JAMA Netw Open* 2021;**4**:e210469. https://doi.org/10.1001/jamanetworkopen.2021.0469
1333. Smedberg C, Hultgren R, Leander K, Steuer J. Pharmacological treatment in patients with aortic dissection. *Open Heart* 2022;**9**:e002082. https://doi.org/10.1136/openhrt-2022-002082
1334. Xiong J, Jiang B, Guo W, Wang SM, Tong XY. Endovascular stent graft placement in patients with type B aortic dissection: a meta-analysis in China. *J Thorac Cardiovasc Surg* 2009;**138**:865–72.e1. https://doi.org/10.1016/j.jtcvs.2009.02.005
1335. Zhu JM, Ma WG, Peterss S, Wang L-F, Qiao Z-Y, Ziganshin BA, *et al.* Aortic dissection in pregnancy: management strategy and outcomes. *Ann Thorac Surg* 2017;**103**:1199–206. https://doi.org/10.1016/j.athoracsur.2016.08.089
1336. Yates MT, Soppa G, Smelt J, Fletcher N, van Besouw J-P, Thilaganathan B, *et al.* Perioperative management and outcomes of aortic surgery during pregnancy. *J Thorac Cardiovasc Surg* 2015;**149**:607–10. https://doi.org/10.1016/j.jtcvs.2014.10.038
1337. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, *et al.* 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 2018;**39**:3165–241. https://doi.org/10.1093/eurheartj/ehy340
1338. DeMartino RR, Sen I, Huang Y, Bower TC, Oderich GS, Pochettino A, *et al.* Population-based assessment of the incidence of aortic dissection, intramural hematoma, and penetrating ulcer, and its associated mortality from 1995 to 2015. *Circ Cardiovasc Qual Outcomes* 2018;**11**:e004689. https://doi.org/10.1161/circoutcomes.118.004689
1339. Evangelista A, Dominguez R, Sebastia C, Salas A, Permanyer-Miralda G, Avegliano G, *et al.* Long-term follow-up of aortic intramural hematoma: predictors of outcome. *Circulation* 2003;**108**:583–9. https://doi.org/10.1161/01.Cir.0000081776.49923.5a
1340. Moral S, Ballesteros E, Roque M, Carrato C, Vilardell P, Brugada R, *et al.* Intimal disruption in type B aortic intramural hematoma. Does size matter? A systematic review and meta-analysis. *Int J Cardiol* 2018;**269**:298–303. https://doi.org/10.1016/j.ijcard.2018.07.111
1341. Moral S, Ballesteros E, Evangelista A. Conservative vs surgical treatment in type A intramural hematoma. What is new? *J Card Surg* 2020;**35**:1758–60. https://doi.org/10.1111/jocs.14739
1342. Ishizu K, Kaji S, Nakashima M, Kitai T, Kim K, Ehara N, *et al.* Focal intimal disruption size at multidetector CT and disease progression in type B aortic intramural hematoma. *Radiology* 2021;**301**:311–9. https://doi.org/10.1148/radiol.2021204385
1343. Chou AS, Ziganshin BA, Charilaou P, Tranquilli M, Rizzo JA, Elefteriades JA. Long-term behavior of aortic intramural hematomas and penetrating ulcers. *J Thorac Cardiovasc Surg* 2016;**151**:361–72, 373.e1. https://doi.org/10.1016/j.jtcvs.2015.09.012
1344. Evangelista A, Mukherjee D, Mehta RH, O'Gara PT, Fattori R, Cooper JV, *et al.* Acute intramural hematoma of the aorta: a mystery in evolution. *Circulation* 2005;**111**:1063–70. https://doi.org/10.1161/01.Cir.0000156444.26393.80
1345. Song JK. Update in acute aortic syndrome: intramural hematoma and incomplete dissection as new disease entities. *J Cardiol* 2014;**64**:153–61. https://doi.org/10.1016/j.jjcc.2014.05.005
1346. Song JK, Kim HS, Kang DH, Lim T-H, Song M-G, Park S-W, *et al.* Different clinical features of aortic intramural hematoma versus dissection involving the ascending aorta. *J Am Coll Cardiol* 2001;**37**:1604–10. https://doi.org/10.1016/s0735-1097(01)01184-6
1347. Evangelista A, Maldonado G, Moral S, Teixido-Tura G, Lopez A, Cuellar H, *et al.* Intramural hematoma and penetrating ulcer in the descending aorta: differences and similarities. *Ann Cardiothorac Surg* 2019;**8**:456–70. https://doi.org/10.21037/acs.2019.07.05
1348. Wee I, Varughese RS, Syn N, Choong A. Non-operative management of type A acute aortic syndromes: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2019;**58**:41–51. https://doi.org/10.1016/j.ejvs.2018.10.015
1349. Chow SCY, Wong RHL, Lakhani I, Wong MV, Tse G, Yu PSY, *et al.* Management of acute type A intramural hematoma: upfront surgery or individualized approach? A retrospective analysis and meta-analysis. *J Thorac Dis* 2020;**12**:680–9. https://doi.org/10.21037/jtd.2019.12.109
1350. Evangelista A, Czerny M, Nienaber C, Schepens M, Rousseau H, Cao P, *et al.* Interdisciplinary expert consensus on management of type B intramural haematoma and penetrating aortic ulcer. *Eur J Cardiothorac Surg* 2015;**47**:209–17. https://doi.org/10.1093/ejcts/ezu386
1351. Sa MP, Jacquemyn X, Tasoudis P, Dufendach K, Singh MJ, de la Cruz KI, *et al.* Five year results of endovascular versus medical therapy in acute type B aortic intramural haematoma: meta-analysis of reconstructed time to event data. *Eur J Vasc Endovasc Surg* 2024;**67**:584–92. https://doi.org/10.1016/j.ejvs.2023.12.024
1352. Moral S, Cuéllar H, Avegliano G, Ballesteros E, Salcedo MT, Ferreira-González I, *et al.* Clinical implications of focal intimal disruption in patients with type B intramural hematoma. *J Am Coll Cardiol* 2017;**69**:28–39. https://doi.org/10.1016/j.jacc.2016.10.045
1353. Chakos A, Twindyawardhani T, Evangelista A, Maldonado G, Piffaretti G, Yan TD, *et al.* Endovascular versus medical management of type B intramural hematoma: a meta-analysis. *Ann Cardiothorac Surg* 2019;**8**:447–55. https://doi.org/10.21037/acs.2019.06.11
1354. Song JK, Yim JH, Ahn JM, Kim D-H, Kang JW, Lee TY, *et al.* Outcomes of patients with acute type a aortic intramural hematoma. *Circulation* 2009;**120**:2046–52. https://doi.org/10.1161/circulationaha.109.879783
1355. Ahn JM, Kim H, Kwon O, Om SY, Heo R, Lee S, *et al.* Differential clinical features and long-term prognosis of acute aortic syndrome according to disease entity. *Eur Heart J* 2019;**40**:2727–36. https://doi.org/10.1093/eurheartj/ehz153
1356. Kitamura T, Torii S, Miyamoto T, Mishima T, Ohkubo H, Fujioka S, *et al.* Watch-and-wait strategy for type A intramural haematoma and acute aortic dissection with thrombosed false lumen of the ascending aorta: a Japanese single-centre experience. *Eur J Cardiothorac Surg* 2020;**58**:590–7. https://doi.org/10.1093/ejcts/ezaa080
1357. Jánosi RA, Gorla R, Tsagakis K, Kahlert P, Horacek M, Bruckschen F, *et al.* Thoracic endovascular repair of complicated penetrating aortic ulcer: an 11-year single-center experience. *J Endovasc Ther* 2016;**23**:150–9. https://doi.org/10.1177/1526602815613790

1358. Nguyen VX, Nguyen BD. PET/CT imaging of abdominal aorta with intramural hematomas, penetrating ulcer, and saccular pseudoaneurysm. *Clin Nucl Med* 2014;**39**:467–9. https://doi.org/10.1097/RLU.0b013e318292f152
1359. Gorla R, Erbel R, Kuehl H, Kahlert P, Tsagakis K, Jakob H, *et al.* Prognostic value of (18)F-fluorodeoxyglucose PET-CT imaging in acute aortic syndromes: comparison with serological biomarkers of inflammation. *Int J Cardiovasc Imaging* 2015;**31**:1677–85. https://doi.org/10.1007/s10554-015-0725-8
1360. Eggebrecht H, Plicht B, Kahlert P, Erbel R. Intramural hematoma and penetrating ulcers: indications to endovascular treatment. *Eur J Vasc Endovasc Surg* 2009;**38**:659–65. https://doi.org/10.1016/j.ejvs.2009.09.001
1361. Salim S, Locci R, Martin G, Gibbs R, Jenkins M, Hamady M, *et al.* Short- and long-term outcomes in isolated penetrating aortic ulcer disease. *J Vasc Surg* 2020;**72**:84–91. https://doi.org/10.1016/j.jvs.2019.09.039
1362. Überall MA, Elling C, Eibl C, Müller-Schwefe GHH, Lefeber C, Heine M, *et al.* Tapentadol prolonged release in patients with chronic low back pain: real-world data from the German Pain eRegistry. *Pain Manag* 2022;**12**:211–27. https://doi.org/10.2217/pmt-2021-0058
1363. Ganaha F, Miller DC, Sugimoto K, Do YS, Minamiguchi H, Saito H, *et al.* Prognosis of aortic intramural hematoma with and without penetrating atherosclerotic ulcer: a clinical and radiological analysis. *Circulation* 2002;**106**:342–8. https://doi.org/10.1161/01.cir.0000022164.26075.5a
1364. DeCarlo C, Latz CA, Boitano LT, Waller HD, Kim Y, Sumpio BJ, *et al.* Natural history of penetrating atherosclerotic ulcers in aortic branch vessels. *J Vasc Surg* 2021;**74**:1904–9. https://doi.org/10.1016/j.jvs.2021.06.035
1365. Piazza M, Squizzato F, Porcellato L, Casali E, Grego F, Antonello M. Predictors of intervention in acute type B aortic penetrating ulcer and intramural hematoma. *Semin Thorac Cardiovasc Surg* 2022;**36**:1–10. https://doi.org/10.1053/j.semtcvs.2022.07.009
1366. Kotsis T, Spyropoulos BG, Asaloumidis N, Christoforou P, Katseni K, Papaconstantinou I. Penetrating atherosclerotic ulcers of the abdominal aorta: a case report and review of the literature. *Vasc Specialist Int* 2019;**35**:152–9. https://doi.org/10.5758/vsi.2019.35.3.152
1367. DeCarlo C, Latz CA, Boitano LT, Kim Y, Tanious A, Schwartz SI, *et al.* Prognostication of asymptomatic penetrating aortic ulcers: a modern approach. *Circulation* 2021;**144**:1091–101. https://doi.org/10.1161/circulationaha.121.054710
1368. Demetriades D, Velmahos GC, Scalea TM, Jurkovich GJ, Karmy-Jones R, Teixeira PG, *et al.* Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. *J Trauma* 2008;**64**:561–70; discussion 570–1. https://doi.org/10.1097/TA.0b013e3181641bb3
1369. Katzenschlager R, Ugurluoglu A, Ahmadi A, Hülsmann M, Koppensteiner R, Larch E, *et al.* Incidence of pseudoaneurysm after diagnostic and therapeutic angiography. *Radiology* 1995;**195**:463–6. https://doi.org/10.1148/radiology.195.2.7724767
1370. Mulder EJ, van Bockel JH, Maas J, van den Akker PJ, Hermans J. Morbidity and mortality of reconstructive surgery of noninfected false aneurysms detected long after aortic prosthetic reconstruction. *Arch Surg* 1998;**133**:45–9. https://doi.org/10.1001/archsurg.133.1.45
1371. Chaud GJ, Mohammadi S, Cervetti MR, Guimaron S, Sebestyen A, Dagenais F, *et al.* Aortic pseudoaneurysm after type A aortic dissection: results of conservative management. *Semin Thorac Cardiovasc Surg* 2022;**35**:457–64. https://doi.org/10.1053/j.semtcvs.2022.04.004
1372. Richens D, Kotidis K, Neale M, Oakley C, Fails A. Rupture of the aorta following road traffic accidents in the United Kingdom 1992–1999. The results of the co-operative crash injury study. *Eur J Cardiothorac Surg* 2003;**23**:143–8. https://doi.org/10.1016/s1010-7940(02)00720-0
1373. Harky A, Bleetman D, Chan JSK, Eriksen P, Chaplin G, MacCarthy-Ofosu B, *et al.* A systematic review and meta-analysis of endovascular versus open surgical repair for the traumatic ruptured thoracic aorta. *J Vasc Surg* 2020;**71**:270–82. https://doi.org/10.1016/j.jvs.2019.05.011
1374. Heneghan RE, Aarabi S, Quiroga E, Gunn ML, Singh N, Starnes BW. Call for a new classification system and treatment strategy in blunt aortic injury. *J Vasc Surg* 2016;**64**:171–6. https://doi.org/10.1016/j.jvs.2016.02.047
1375. Januzzi JL, Sabatine MS, Eagle KA, Evangelista A, Bruckman D, Fattori R, *et al.* Iatrogenic aortic dissection. *Am J Cardiol* 2002;**89**:623–6. https://doi.org/10.1016/s0002-9149(01)02312-8
1376. Gómez-Moreno S, Sabaté M, Jiménez-Quevedo P, Vázquez P, Alfonso F, Angiolillo DJ, *et al.* Iatrogenic dissection of the ascending aorta following heart catheterisation: incidence, management and outcome. *EuroIntervention* 2006;**2**:197–202.
1377. Dunning DW, Kahn JK, Hawkins ET, O'Neill W. Iatrogenic coronary artery dissections extending into and involving the aortic root. *Catheter Cardiovasc Interv* 2000;**51**:387–93. https://doi.org/10.1002/1522-726x(200012)51:4<387::aid-ccd3>3.0.co;2-b
1378. Bekkers JA, te Riele RJ, Takkenberg JJ, Bol Raap G, Hofland J, Roos-Hesselink JW, *et al.* Thoracic aortic surgery: an overview of 40 years clinical practice. *J Thorac Cardiovasc Surg* 2014;**147**:332–43. https://doi.org/10.1016/j.jtcvs.2012.11.036
1379. Meena RA, Benarroch-Gampel J, Leshnower BG, Escobar GA, Duwayri Y, Jordan WD, *et al.* Surveillance recommendations after thoracic endovascular aortic repair should be based on initial indication for repair. *Ann Vasc Surg* 2019;**57**:51–9. https://doi.org/10.1016/j.avsg.2018.11.001
1380. Giles KA, Beck AW, Lala S, Patterson S, Back M, Fatima J, *et al.* Implications of secondary aortic intervention after thoracic endovascular aortic repair for acute and chronic type B dissection. *J Vasc Surg* 2019;**69**:1367–78. https://doi.org/10.1016/j.jvs.2018.07.080
1381. Kimura N, Itoh S, Yuri K, Adachi K, Matsumoto H, Yamaguchi A, *et al.* Reoperation for enlargement of the distal aorta after initial surgery for acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2015;**149**:S91–8.e1. https://doi.org/10.1016/j.jtcvs.2014.08.008
1382. Ameli-Renani S, Das R, Morgan RA. Thoracic endovascular aortic repair for the treatment of aortic dissection: post-operative imaging, complications and secondary interventions. *Cardiovasc Intervent Radiol* 2015;**38**:1391–404. https://doi.org/10.1007/s00270-015-1072-9
1383. Fleischmann D, Afifi RO, Casanegra AI, Elefteriades JA, Gleason TG, Hanneman K, *et al.* Imaging and surveillance of chronic aortic dissection: a scientific statement from the American Heart Association. *Circ Cardiovasc Imaging* 2022;**15**:e000075. https://doi.org/10.1161/hci.0000000000000075
1384. Colacchio EC, Squizzato F, Piazza M, Menegolo M, Grego F, Antonello M. Clinical and imaging predictors of disease progression in type B aortic intramural hematomas and penetrating aortic ulcers: a systematic review. *Diagnostics (Basel)* 2022;**12**:2727. https://doi.org/10.3390/diagnostics12112727
1385. Vapnik JS, Kim JB, Isselbacher EM, Ghoshhajra BB, Cheng Y, Sundt TM, *et al.* Characteristics and outcomes of ascending versus descending thoracic aortic aneurysms. *Am J Cardiol* 2016;**117**:1683–90. https://doi.org/10.1016/j.amjcard.2016.02.048
1386. Gökalp AL, Takkenberg JJM. Decision-making in thoracic aortic aneurysm surgery-clinician and patient view. *Semin Thorac Cardiovasc Surg* 2019;**31**:638–42. https://doi.org/10.1053/j.semtcvs.2019.05.032
1387. Treasure T, King A, Hidalgo Lemp L, Golesworthy T, Pepper J, Takkenberg JJM. Developing a shared decision support framework for aortic root surgery in Marfan syndrome. *Heart* 2018;**104**:480–6. https://doi.org/10.1136/heartjnl-2017-311598
1388. Jondeau G, Ropers J, Regalado E, Braverman A, Evangelista A, Teixedo G, *et al.* International registry of patients carrying TGFBR1 or TGFBR2 mutations: results of the MAC (Montalcino Aortic Consortium). *Circ Cardiovasc Genet* 2016;**9**:548–58. https://doi.org/10.1161/circgenetics.116.001485
1389. Thakker PD, Braverman AC. Cardiogenetics: genetic testing in the diagnosis and management of patients with aortic disease. *Heart* 2021;**107**:619–26. https://doi.org/10.1136/heartjnl-2020-317036
1390. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, *et al.* Aneurysm syndromes caused by mutations in the TGF-beta receptor. *N Engl J Med* 2006;**355**:788–98. https://doi.org/10.1056/NEJMoa055695
1391. Regalado ES, Morris SA, Braverman AC, Hostetler EM, De Backer J, Li R, *et al.* Comparative risks of initial aortic events associated with genetic thoracic aortic disease. *J Am Coll Cardiol* 2022;**80**:857–69. https://doi.org/10.1016/j.jacc.2022.05.054
1392. Huguenard AL, Johnson GW, Desai RR, Osbun JW, Dacey RG, Braverman AC. Relationship between phenotypic features in Loeys-Dietz syndrome and the presence of intracranial aneurysms. *J Neurosurg* 2022;**138**:1385–92. https://doi.org/10.3171/2022.9.Jns221373
1393. Lopez-Sainz A, Mila L, Rodriguez-Palomares J, Limeres J, Granato C, La Mura L, *et al.* Aortic branch aneurysms and vascular risk in patients with Marfan syndrome. *J Am Coll Cardiol* 2021;**77**:3005–12. https://doi.org/10.1016/j.jacc.2021.04.054
1394. Kaw A, Kaw K, Hostetler EM, Beleza-Meireles A, Smith-Collins A, Armstrong C, *et al.* Expanding ACTA2 genotypes with corresponding phenotypes overlapping with smooth muscle dysfunction syndrome. *Am J Med Genet A* 2022;**188**:2389–96. https://doi.org/10.1002/ajmg.a.62775
1395. Velvin G, Wilhelmsen JE, Johansen H, Bathen T, Geirdal AO. Systematic review of quality of life in persons with hereditary thoracic aortic aneurysm and dissection diagnoses. *Clin Genet* 2019;**95**:661–76. https://doi.org/10.1111/cge.13522
1396. Mariscalco G, Debiec R, Elefteriades JA, Samani NJ, Murphy GJ. Systematic review of studies that have evaluated screening tests in relatives of patients affected by nonsyndromic thoracic aortic disease. *J Am Heart Assoc* 2018;**7**:e009302. https://doi.org/10.1161/jaha.118.009302
1397. Cecchi AC, Boerio ML, Marin I, Pinard A, Milewicz DM. Preventing acute aortic dissections: the power of familial screening and risk assessment. *J Am Heart Assoc* 2022;**11**:e025441. https://doi.org/10.1161/jaha.122.025441
1398. Abbasciano RG, Mariscalco G, Barwell J, Owens G, Zakkar M, Joel-David L, *et al.* Evaluating the feasibility of screening relatives of patients affected by nonsyndromic thoracic aortic diseases: the REST study. *J Am Heart Assoc* 2022;**11**:e023741. https://doi.org/10.1161/jaha.121.023741
1399. Musunuru K, Hershberger RE, Day SM, Klinedinst NJ, Landstrom AP, Parikh VN, *et al.* Genetic testing for inherited cardiovascular diseases: a scientific statement from the American Heart Association. *Circ Genom Precis Med* 2020;**13**:e000067. https://doi.org/10.1161/hcg.0000000000000067

1400. Albornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA, *et al.* Familial thoracic aortic aneurysms and dissections—incidence, modes of inheritance, and phenotypic patterns. *Ann Thorac Surg* 2006;**82**:1400–5. https://doi.org/10.1016/j.athoracsur.2006.04.098
1401. Biddinger A, Rocklin M, Coselli J, Milewicz DM. Familial thoracic aortic dilatations and dissections: a case control study. *J Vasc Surg* 1997;**25**:506–11. https://doi.org/10.1016/s0741-5214(97)70261-1
1402. Robertson EN, van der Linde D, Sherrah AG, Vallely MP, Wilson M, Bannon PG, *et al.* Familial non-syndromal thoracic aortic aneurysms and dissections—incidence and family screening outcomes. *Int J Cardiol* 2016;**220**:43–51. https://doi.org/10.1016/j.ijcard.2016.06.086
1403. De Backer J, Bondue A, Budts W, Evangelista A, Gallego P, Jondeau G, *et al.* Genetic counselling and testing in adults with congenital heart disease: a consensus document of the ESC Working Group of Grown-Up Congenital Heart Disease, the ESC Working Group on Aorta and Peripheral Vascular Disease and the European Society of Human Genetics. *Eur J Prev Cardiol* 2020;**27**:1423–35. https://doi.org/10.1177/2047487319854552
1404. Wolford BN, Hornsby WE, Guo D, Zhou W, Lin M, Farhat L, *et al.* Clinical implications of identifying pathogenic variants in individuals with thoracic aortic dissection. *Circ Genom Precis Med* 2019;**12**:e002476. https://doi.org/10.1161/circgen.118.002476
1405. Renard M, Francis C, Ghosh R, Scott AF, Witmer PD, Adès LC, *et al.* Clinical validity of genes for heritable thoracic aortic aneurysm and dissection. *J Am Coll Cardiol* 2018;**72**:605–15. https://doi.org/10.1016/j.jacc.2018.04.089
1406. De Backer J, Jondeau G, Boileau C. Genetic testing for aortopathies: primer for the nongeneticist. *Curr Opin Cardiol* 2019;**34**:585–93. https://doi.org/10.1097/hco.0000000000000669
1407. Milewicz DM, Guo D, Hostetler E, Marin I, Pinard AC, Cecchi AC, *et al.* Update on the genetic risk for thoracic aortic aneurysms and acute aortic dissections: implications for clinical care. *J Cardiovasc Surg* 2021;**62**:203–10. https://doi.org/10.23736/s0021-9509.21.11816-6
1408. Chou EL, Lindsay ME. The genetics of aortopathies: hereditary thoracic aortic aneurysms and dissections. *Am J Med Genet C Semin Med Genet* 2020;**184**:136–48. https://doi.org/10.1002/ajmg.c.31771
1409. Harris SL, Lindsay ME. Role of clinical genetic testing in the management of aortopathies. *Curr Cardiol Rep* 2021;**23**:10. https://doi.org/10.1007/s11886-020-01435-6
1410. Regalado ES, Guo DC, Prakash S, Bensend TA, Flynn K, Estrera A, *et al.* Aortic disease presentation and outcome associated with ACTA2 mutations. *Circ Cardiovasc Genet* 2015;**8**:457–64. https://doi.org/10.1161/circgenetics.114.000943
1411. Teixidó-Tura G, Franken R, Galuppo V, Gutiérrez García-Moreno L, Borregan M, Mulder BJM, *et al.* Heterogeneity of aortic disease severity in patients with Loeys-Dietz syndrome. *Heart* 2016;**102**:626–32. https://doi.org/10.1136/heartjnl-2015-308535
1412. Baudhuin LM, Kotzer KE, Lagerstedt SA. Increased frequency of FBN1 truncating and splicing variants in Marfan syndrome patients with aortic events. *Genet Med* 2015;**17**:177–87. https://doi.org/10.1038/gim.2014.91
1413. Franken R, Teixido-Tura G, Brion M, Forteza A, Rodriguez-Palomares J, Gutierrez L, *et al.* Relationship between fibrillin-1 genotype and severity of cardiovascular involvement in Marfan syndrome. *Heart* 2017;**103**:1795–9. https://doi.org/10.1136/heartjnl-2016-310631
1414. Wallace SE, Regalado ES, Gong L, Janda AL, Guo D, Russo CF, *et al.* MYLK pathogenic variants aortic disease presentation, pregnancy risk, and characterization of pathogenic missense variants. *Genet Med* 2019;**21**:144–51. https://doi.org/10.1038/s41436-018-0038-0
1415. Seike Y, Matsuda H, Ishibashi-Ueda H, Morisaki H, Morisaki T, Minatoya K, *et al.* Surgical outcome and histological differences between individuals with TGFBR1 and TGFBR2 mutations in Loeys-Dietz syndrome. *Ann Thorac Cardiovasc Surg* 2021;**27**:56–63. https://doi.org/10.5761/atcs.oa.20-00223
1416. Arnaud P, Milleron O, Hanna N, Ropers J, Ould Ouali N, Affoune A, *et al.* Clinical relevance of genotype-phenotype correlations beyond vascular events in a cohort study of 1500 Marfan syndrome patients with FBN1 pathogenic variants. *Genet Med* 2021;**23**:1296–304. https://doi.org/10.1038/s41436-021-01132-x
1417. Silberbach M, Roos-Hesselink JW, Andersen NH, Braverman AC, Brown N, Collins RT, *et al.* Cardiovascular health in Turner syndrome: a scientific statement from the American Heart Association. *Circ Genom Precis Med* 2018;**11**:e000048. https://doi.org/10.1161/hcg.0000000000000048
1418. Gravholt CH, Andersen NH, Conway GS, Dekkers OM, Geffner ME, Klein KO, *et al.* Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. *Eur J Endocrinol* 2017;**177**:G1–70. https://doi.org/10.1530/eje-17-0430
1419. van den Hoven AT, Chelu RG, Duijnhouwer AL, Demulier L, Devos D, Nieman K, *et al.* Partial anomalous pulmonary venous return in Turner syndrome. *Eur J Radiol* 2017;**95**:141–6. https://doi.org/10.1016/j.ejrad.2017.07.024
1420. Carlson M, Airhart N, Lopez L, Silberbach M. Moderate aortic enlargement and bicuspid aortic valve are associated with aortic dissection in Turner syndrome: report of the international Turner syndrome aortic dissection registry. *Circulation* 2012;**126**:2220–6. https://doi.org/10.1161/circulationaha.111.088633
1421. Matura LA, Ho VB, Rosing DR, Bondy CA. Aortic dilatation and dissection in Turner syndrome. *Circulation* 2007;**116**:1663–70. https://doi.org/10.1161/circulationaha.106.685487
1422. Schoemaker MJ, Swerdlow AJ, Higgins CD, Wright AF, Jacobs PA. Mortality in women with Turner syndrome in Great Britain: a national cohort study. *J Clin Endocrinol Metab* 2008;**93**:4735–42. https://doi.org/10.1210/jc.2008-1049
1423. Duijnhouwer AL, Bons LR, Timmers H, van Kimmenade RRL, Snoeren M, Timmermans J, *et al.* Aortic dilatation and outcome in women with Turner syndrome. *Heart* 2019;**105**:693–700. https://doi.org/10.1136/heartjnl-2018-313716
1424. Donadille B, Tuffet S, Cholet C, Nedelcu M, Bourcigaux N, Iserin L, *et al.* Prevalence and progression of aortic dilatation in adult patients with Turner syndrome: a cohort study. *Eur J Endocrinol* 2020;**183**:463–70. https://doi.org/10.1530/eje-20-0284
1425. Meccanici F, Schotte MH, Snoeren M, Bons LR, van den Hoven AT, Kardys I, *et al.* Aortic dilation and growth in women with Turner syndrome. *Heart* 2023;**109**:102–10. https://doi.org/10.1136/heartjnl-2022-320922
1426. Galian-Gay L, Rodriguez-Palomares JF. Turner syndrome and aortic complications: more benign than previously thought. *Heart* 2022;**109**:82–3. https://doi.org/10.1136/heartjnl-2022-321330
1427. Silberbach M, Braverman AC, Prakash SK, Roos-Hesselink JW, Quezada E, Scurlock C. Preventing aortic dissection in Turner syndrome: who faces the risk? *Int J Cardiol* 2023;**377**:44. https://doi.org/10.1016/j.ijcard.2023.01.075
1428. Prakash S, Gen TACRI, Milewicz D. Turner syndrome-specific and general population Z-scores are equivalent for most adults with Turner syndrome. *Am J Med Genet A* 2017;**173**:1094–6. https://doi.org/10.1002/ajmg.a.38100
1429. Corbitt H, Maslen C, Prakash S, Morris SA, Silberbach M. Allometric considerations when assessing aortic aneurysms in Turner syndrome: implications for activity recommendations and medical decision-making. *Am J Med Genet A* 2018;**176**:277–82. https://doi.org/10.1002/ajmg.a.38584
1430. Quigley CA, Fechner PY, Geffner ME, Eugster EA, Ross JL, Habiby RL, *et al.* Prevention of growth failure in Turner syndrome: long-term results of early growth hormone treatment in the "Toddler Turner" Cohort. *Horm Res Paediatr* 2021;**94**:18–35. https://doi.org/10.1159/000513788
1431. Klein KO, Rosenfield RL, Santen RJ, Gawlik AM, Backeljauw PF, Gravholt CH, *et al.* Estrogen replacement in Turner syndrome: literature review and practical considerations. *J Clin Endocrinol Metab* 2018;**103**:1790–803. https://doi.org/10.1210/jc.2017-02183
1432. Quigley CA, Wan X, Garg S, Kowal K, Cutler GB, Ross JL. Effects of low-dose estrogen replacement during childhood on pubertal development and gonadotropin concentrations in patients with Turner syndrome: results of a randomized, double-blind, placebo-controlled clinical trial. *J Clin Endocrinol Metab* 2014;**99**:E1754–1764. https://doi.org/10.1210/jc.2013-4518
1433. Davenport ML, Crowe BJ, Travers SH, Rubin K, Ross JL, Fechner PY, *et al.* Growth hormone treatment of early growth failure in toddlers with Turner syndrome: a randomized, controlled, multicenter trial. *J Clin Endocrinol Metab* 2007;**92**:3406–16. https://doi.org/10.1210/jc.2006-2874
1434. Stephure DK; Canadian Growth Hormone Advisory Committee. Impact of growth hormone supplementation on adult height in Turner syndrome: results of the Canadian randomized controlled trial. *J Clin Endocrinol Metab* 2005;**90**:3360–6. https://doi.org/10.1210/jc.2004-2187
1435. Campens L, Baris L, Scott NS, Broberg CS, Bondue A, Jondeau G, *et al.* Pregnancy outcome in thoracic aortic disease data from the registry of pregnancy and cardiac disease. *Heart* 2021;**107**:1704–9. https://doi.org/10.1136/heartjnl-2020-318183
1436. Grewal J, Valente AM, Egbe AC, Wu FM, Krieger EV, Sybert VP, *et al.* Cardiovascular outcomes of pregnancy in Turner syndrome. *Heart* 2021;**107**:61–6. https://doi.org/10.1136/heartjnl-2020-316719
1437. Thompson T, Zieba B, Howell S, Karakash W, Davis S. A mixed methods study of physical activity and quality of life in adolescents with Turner syndrome. *Am J Med Genet A* 2020;**182**:386–96. https://doi.org/10.1002/ajmg.a.61439
1438. Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. *N Engl J Med* 2000;**342**:673–80. https://doi.org/10.1056/nejm200003093421001
1439. Byers PH, Belmont J, Black J, De Backer J, Frank M, Jeunemaitre X, *et al.* Diagnosis, natural history, and management in vascular Ehlers-Danlos syndrome. *Am J Med Genet C Semin Med Genet* 2017;**175**:40–7. https://doi.org/10.1002/ajmg.c.31553
1440. Oderich GS, Panneton JM, Bower TC, Lindor NM, Cherry KJ, Noel AA, *et al.* The spectrum, management and clinical outcome of Ehlers-Danlos syndrome type IV: a 30-year experience. *J Vasc Surg* 2005;**42**:98–106. https://doi.org/10.1016/j.jvs.2005.03.053
1441. Frank M, Adham S, Seigle S, Legrand A, Mirault T, Henneton P, *et al.* Vascular Ehlers-Danlos syndrome: long-term observational study. *J Am Coll Cardiol* 2019;**73**:1948–57. https://doi.org/10.1016/j.jacc.2019.01.058
1442. Pepin MG, Schwarze U, Rice KM, Liu M, Leistritz D, Byers PH. Survival is affected by mutation type and molecular mechanism in vascular Ehlers-Danlos syndrome (EDS type IV). *Genet Med* 2014;**16**:881–8. https://doi.org/10.1038/gim.2014.72
1443. van de Laar I, Baas AF, De Backer J, Blankenstein JD, Dulfer E, Helderman-van den Enden ATJM, *et al.* Surveillance and monitoring in vascular Ehlers-Danlos syndrome

in European reference network for rare vascular diseases (VASCERN). *Eur J Med Genet* 2022;**65**:104557. https://doi.org/10.1016/j.ejmg.2022.104557
1444. Baderkhan H, Wanhainen A, Stenborg A, Stattin EL, Bjorck M. Celiprolol treatment in patients with vascular Ehlers-Danlos syndrome. *Eur J Vasc Endovasc Surg* 2021;**61**:326–31. https://doi.org/10.1016/j.ejvs.2020.10.020
1445. Ong KT, Perdu J, De Backer J, Bozec E, Collignon P, Emmerich J, *et al.* Effect of celiprolol on prevention of cardiovascular events in vascular Ehlers-Danlos syndrome: a prospective randomised, open, blinded-endpoints trial. *Lancet* 2010;**376**:1476–84. https://doi.org/10.1016/s0140-6736(10)60960-9
1446. Murray ML, Pepin M, Peterson S, Byers PH. Pregnancy-related deaths and complications in women with vascular Ehlers-Danlos syndrome. *Genet Med* 2014;**16**:874–80. https://doi.org/10.1038/gim.2014.53
1447. Loeys BL, Dietz HC, Braverman AC, Callewaert BL, De Backer J, Devereux RB, *et al.* The revised Ghent nosology for the Marfan syndrome. *J Med Genet* 2010;**47**:476–85. https://doi.org/10.1136/jmg.2009.072785
1448. Yildiz M, Nucera M, Jungi S, Heinisch PP, Mosbahi S, Becker D, *et al.* Outcome of Stanford type B dissection in patients with Marfan syndrome. *Eur J Cardiothorac Surg* 2023;**64**:ezad178. https://doi.org/10.1093/ejcts/ezad178
1449. Narula N, Devereux RB, Arbustini E, Ma X, Weinsaft JW, Girardi L, *et al.* Risk of type B dissection in Marfan syndrome: the Cornell aortic aneurysm registry. *J Am Coll Cardiol* 2023;**82**:2009–17. https://doi.org/10.1016/j.jacc.2023.08.055
1450. Senemaud J, Gaudry M, Jouve E, Blanchard A, Milleron O, Dulac Y, *et al.* Primary non-aortic lesions are not rare in Marfan syndrome and are associated with aortic dissection independently of age. *J Clin Med* 2023;**12**:2902. https://doi.org/10.3390/jcm12082902
1451. Judge DP, Rouf R, Habashi J, Dietz HC. Mitral valve disease in Marfan syndrome and related disorders. *J Cardiovasc Transl Res* 2011;**4**:741–7. https://doi.org/10.1007/s12265-011-9314-y
1452. Demolder A, Bianco L, Caruana M, Cervi E, Evangelista A, Jondeau G, *et al.* Arrhythmia and impaired myocardial function in heritable thoracic aortic disease: an international retrospective cohort study. *Eur J Med Genet* 2022;**65**:104503. https://doi.org/10.1016/j.ejmg.2022.104503
1453. Pyeritz RE. Marfan syndrome: improved clinical history results in expanded natural history. *Genet Med* 2019;**21**:1683–90. https://doi.org/10.1038/s41436-018-0399-4
1454. Jondeau G, Detaint D, Tubach F, Arnoult F, Milleron O, Raoux F, *et al.* Aortic event rate in the Marfan population: a cohort study. *Circulation* 2012;**125**:226–32. https://doi.org/10.1161/circulationaha.111.054676
1455. Requejo-Garcia L, Martinez-Lopez R, Plana-Andani E, Medina-Badenes P, Hernándiz-Martínez A, Torres-Blanco A, *et al.* Extrathoracic aneurysms in Marfan syndrome: a systematic review of the literature. *Ann Vasc Surg* 2022;**87**:548–59. https://doi.org/10.1016/j.avsg.2022.08.005
1456. Guala A, Teixidó-Tura G, Rodríguez-Palomares J, Ruiz-Muñoz A, Dux-Santoy L, Villalva N, *et al.* Proximal aorta longitudinal strain predicts aortic root dilation rate and aortic events in Marfan syndrome. *Eur Heart J* 2019;**40**:2047–55. https://doi.org/10.1093/eurheartj/ehz191
1457. Teixido-Tura G, Redheuil A, Rodríguez-Palomares J, Gutiérrez L, Sánchez V, Forteza A, *et al.* Aortic biomechanics by magnetic resonance: early markers of aortic disease in Marfan syndrome regardless of aortic dilatation? *Int J Cardiol* 2014;**171**:56–61. https://doi.org/10.1016/j.ijcard.2013.11.044
1458. Kuijpers JM, Mulder BJ. Aortopathies in adult congenital heart disease and genetic aortopathy syndromes: management strategies and indications for surgery. *Heart* 2017;**103**:952–66. https://doi.org/10.1136/heartjnl-2015-308626
1459. Milewicz DM, Braverman AC, De Backer J, Morris SA, Boileau C, Maumenee IH, *et al.* Marfan syndrome. *Nat Rev Dis Primers* 2021;**7**:64. https://doi.org/10.1038/s41572-021-00298-7
1460. Doyle JJ, Doyle AJ, Wilson NK, Habashi JP, Bedja D, Whitworth RE, *et al.* A deleterious gene-by-environment interaction imposed by calcium channel blockers in Marfan syndrome. *Elife* 2015;**4**:e08648. https://doi.org/10.7554/eLife.08648
1461. Lacro RV, Dietz HC, Sleeper LA, Yetman AT, Bradley TJ, Colan SD, *et al.* Atenolol versus losartan in children and young adults with Marfan's syndrome. *N Engl J Med* 2014;**371**:2061–71. https://doi.org/10.1056/NEJMoa1404731
1462. Teixido-Tura G, Forteza A, Rodríguez-Palomares J, González Mirelis J, Gutiérrez L, Sánchez V, *et al.* Losartan versus atenolol for prevention of aortic dilation in patients with Marfan syndrome. *J Am Coll Cardiol* 2018;**72**:1613–8. https://doi.org/10.1016/j.jacc.2018.07.052
1463. Pitcher A, Spata E, Emberson J, Davies K, Halls H, Holland L, *et al.* Angiotensin receptor blockers and β blockers in Marfan syndrome: an individual patient data meta-analysis of randomised trials. *Lancet* 2022;**400**:822–31. https://doi.org/10.1016/s0140-6736(22)01534-3
1464. Groenink M, den Hartog AW, Franken R, Radonic T, de Waard V, Timmermans J, *et al.* Losartan reduces aortic dilatation rate in adults with Marfan syndrome: a randomized controlled trial. *Eur Heart J* 2013;**34**:3491–500. https://doi.org/10.1093/eurheartj/eht334
1465. Nucera M, Kreibich M, Yildiz M, Berger T, Kolb RK, Kondov S, *et al.* Endovascular aortic repair in patients with Marfan and Loeys-Dietz syndrome is safe and durable when employed by a multi-disciplinary aortic team. *Eur J Cardiothorac Surg* 2024;**65**:ezae069. https://doi.org/10.1093/ejcts/ezae069
1466. Czerny M, Grabenwoger M, Berger T, Aboyans V, Della Corte A, Chen EP, *et al.* EACTS/STS Guidelines for diagnosing and treating acute and chronic syndromes of the aortic organ. *Eur J Cardiothorac Surg* 2024;**65**:ezad426. https://doi.org/10.1093/ejcts/ezad426
1467. Milleron O, Arnoult F, Delorme G, Detaint D, Pellenc Q, Raffoul R, *et al.* Pathogenic FBN1 genetic variation and aortic dissection in patients with Marfan syndrome. *J Am Coll Cardiol* 2020;**75**:843–53. https://doi.org/10.1016/j.jacc.2019.12.043
1468. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller G-P, *et al.* 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J* 2021;**42**:563–645. https://doi.org/10.1093/eurheartj/ehaa554
1469. Martín C, Evangelista A, Serrano-Fiz S, Villar S, Ospina V, Martínez D, *et al.* Aortic complications in Marfan syndrome: should we anticipate preventive aortic root surgery? *Ann Thorac Surg* 2020;**109**:1850–7. https://doi.org/10.1016/j.athoracsur.2019.08.096
1470. Roman MJ, Pugh NL, Hendershot TP, Devereux RB, Dietz H, Holmes K, *et al.* Aortic complications associated with pregnancy in Marfan syndrome: the NHLBI national registry of genetically triggered thoracic aortic aneurysms and cardiovascular conditions (GenTAC). *J Am Heart Assoc* 2016;**5**:e004052. https://doi.org/10.1161/jaha.116.004052
1471. Braverman AC, Mittauer E, Harris KM, Evangelista A, Pyeritz RE, Brinster D, *et al.* Clinical features and outcomes of pregnancy-related acute aortic dissection. *JAMA Cardiol* 2021;**6**:58–66. https://doi.org/10.1001/jamacardio.2020.4876
1472. Narula N, Devereux RB, Malonga GP, Hriljac I, Roman MJ. Pregnancy-related aortic complications in women with Marfan syndrome. *J Am Coll Cardiol* 2021;**78**:870–9. https://doi.org/10.1016/j.jacc.2021.06.034
1473. Davis MB, Arendt K, Bello NA, Brown H, Briller J, Epps K, *et al.* Team-based care of women with cardiovascular disease from pre-conception through pregnancy and postpartum: JACC focus seminar 1/5. *J Am Coll Cardiol* 2021;**77**:1763–77. https://doi.org/10.1016/j.jacc.2021.02.033
1474. Meijboom LJ, Vos FE, Timmermans J, Boers GH, Zwinderman AH, Mulder BJM. Pregnancy and aortic root growth in the Marfan syndrome: a prospective study. *Eur Heart J* 2005;**26**:914–20. https://doi.org/10.1093/eurheartj/ehi103
1475. Kuperstein R, Cahan T, Yoeli-Ullman R, Ben Zekry S, Shinfeld A, Simchen MJ. Risk of aortic dissection in pregnant patients with the Marfan syndrome. *Am J Cardiol* 2017;**119**:132–7. https://doi.org/10.1016/j.amjcard.2016.09.024
1476. Roberts EA, Pistner A, Osobamiro O, Banning S, Shalhub S, Albright C, *et al.* Beta-blocker use during pregnancy correlates with less aortic root dilatation in patients with Marfan's syndrome. *Aorta (Stamford)* 2023;**11**:63–70. https://doi.org/10.1055/a-2072-0469
1477. Roman MJ, Devereux RB. Aortic dissection risk in Marfan syndrome. *J Am Coll Cardiol* 2020;**75**:854–6. https://doi.org/10.1016/j.jacc.2019.12.042
1478. Quan A. Fetopathy associated with exposure to angiotensin converting enzyme inhibitors and angiotensin receptor antagonists. *Early Hum Dev* 2006;**82**:23–8. https://doi.org/10.1016/j.earlhumdev.2005.11.001
1479. Walfisch A, Al-maawali A, Moretti ME, Nickel C, Koren G. Teratogenicity of angiotensin converting enzyme inhibitors or receptor blockers. *J Obstet Gynaecol* 2011;**31**:465–72. https://doi.org/10.3109/01443615.2011.579197
1480. Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer S, Gideon PS, *et al.* Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006;**354**:2443–51. https://doi.org/10.1056/NEJMoa055202
1481. Mas-Stachurska A, Siegert AM, Batlle M, Gorbenko del Blanco D, Meirelles T, Rubies C, *et al.* Cardiovascular benefits of moderate exercise training in Marfan syndrome: insights from an animal model. *J Am Heart Assoc* 2017;**6**:e006438. https://doi.org/10.1161/jaha.117.006438
1482. Gibson C, Nielsen C, Alex R, Cooper K, Farney M, Gaufin D, *et al.* Mild aerobic exercise blocks elastin fiber fragmentation and aortic dilatation in a mouse model of Marfan syndrome associated aortic aneurysm. *J Appl Physiol* 2017;**123**:147–60. https://doi.org/10.1152/japplphysiol.00132.2017
1483. Selamet Tierney ES, Chung S, Stauffer KJ, Brabender J, Collins RT, Folk R, *et al.* Can 10 000 healthy steps a day slow aortic root dilation in pediatric patients with Marfan syndrome? *J Am Heart Assoc* 2022;**11**:e027598. https://doi.org/10.1161/jaha.122.027598
1484. Jouini S, Milleron O, Eliahou L, Jondeau G, Vitiello D. Effects of a personalized home-based training program among patients suffering from Marfan syndrome: a pilot randomized and controlled study. *Intractable Rare Dis Res* 2021;**10**:263–8. https://doi.org/10.5582/irdr.2021.01080
1485. Benninghoven D, Hamann D, von Kodolitsch Y, Rybczynski M, Lechinger J, Schroeder F, *et al.* Inpatient rehabilitation for adult patients with Marfan syndrome: an observational pilot study. *Orphanet J Rare Dis* 2017;**12**:127. https://doi.org/10.1186/s13023-017-0679-0
1486. Fuglsang S, Heiberg J, Hjortdal VE, Laustsen S. Exercise-based cardiac rehabilitation in surgically treated type-A aortic dissection patients. *Scand Cardiovasc J* 2017;**51**:99–105. https://doi.org/10.1080/14017431.2016.1257149
1487. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, *et al.* A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused

by mutations in TGFBR1 or TGFBR2. *Nat Genet* 2005;**37**:275–81. https://doi.org/10.1038/ng1511
1488. MacCarrick G, Black JH, III, Bowdin S, El-Hamamsy I, Frischmeyer-Guerrerio PA, Guerrerio AL, *et al.* Loeys-Dietz syndrome: a primer for diagnosis and management. *Genet Med* 2014;**16**:576–87. https://doi.org/10.1038/gim.2014.11
1489. Lindsay ME, Schepers D, Bolar NA, Doyle JJ, Gallo E, Fert-Bober J, *et al.* Loss-of-function mutations in TGFB2 cause a syndromic presentation of thoracic aortic aneurysm. *Nat Genet* 2012;**44**:922–7. https://doi.org/10.1038/ng.2349
1490. Boileau C, Guo DC, Hanna N, Regalado ES, Detaint D, Gong L, *et al.* TGFB2 mutations cause familial thoracic aortic aneurysms and dissections associated with mild systemic features of Marfan syndrome. *Nat Genet* 2012;**44**:916–21. https://doi.org/10.1038/ng.2348
1491. van der Linde D, van de Laar IM, Bertoli-Avella AM, Oldenburg RA, Bekkers JA, Mattace-Raso FUS, *et al.* Aggressive cardiovascular phenotype of aneurysms-osteoarthritis syndrome caused by pathogenic SMAD3 variants. *J Am Coll Cardiol* 2012;**60**:397–403. https://doi.org/10.1016/j.jacc.2011.12.052
1492. Hostetler EM, Regalado ES, Guo DC, Hanna N, Arnaud P, Muiño-Mosquera L, *et al.* SMAD3 pathogenic variants: risk for thoracic aortic disease and associated complications from the Montalcino Aortic Consortium. *J Med Genet* 2019;**56**:252–60. https://doi.org/10.1136/jmedgenet-2018-105583
1493. Renard M, Callewaert B, Malfait F, Campens L, Sharif S, del Campo M, *et al.* Thoracic aortic-aneurysm and dissection in association with significant mitral valve disease caused by mutations in TGFB2. *Int J Cardiol* 2013;**165**:584–7. https://doi.org/10.1016/j.ijcard.2012.09.029
1494. Bertoli-Avella AM, Gillis E, Morisaki H, Verhagen JMA, de Graaf BM, van de Beek G, *et al.* Mutations in a TGF-beta ligand, TGFB3, cause syndromic aortic aneurysms and dissections. *J Am Coll Cardiol* 2015;**65**:1324–36. https://doi.org/10.1016/j.jacc.2015.01.040
1495. Marsili L, Overwater E, Hanna N, Baujat G, Baars MJH, Boileau C, *et al.* Phenotypic spectrum of TGFB3 disease-causing variants in a Dutch-French cohort and first report of a homozygous patient. *Clin Genet* 2020;**97**:723–30. https://doi.org/10.1111/cge.13700
1496. Guo DC, Pannu H, Tran-Fadulu V, Papke CL, Yu RK, Avidan N, *et al.* Mutations in smooth muscle alpha-actin (ACTA2) lead to thoracic aortic aneurysms and dissections. *Nat Genet* 2007;**39**:1488–93. https://doi.org/10.1038/ng.2007.6
1497. Guo DC, Papke CL, Tran-Fadulu V, Regalado ES, Avidan N, Johnson RJ, *et al.* Mutations in smooth muscle alpha-actin (ACTA2) cause coronary artery disease, stroke, and Moyamoya disease, along with thoracic aortic disease. *Am J Hum Genet* 2009;**84**:617–27. https://doi.org/10.1016/j.ajhg.2009.04.007
1498. van de Laar I, Arbustini E, Loeys B, Björck E, Murphy L, Groenink M, *et al.* European reference network for rare vascular diseases (VASCERN) consensus statement for the screening and management of patients with pathogenic ACTA2 variants. *Orphanet J Rare Dis* 2019;**14**:264. https://doi.org/10.1186/s13023-019-1186-2
1499. Brownstein AJ, Ziganshin BA, Kuivaniemi H, Body Simon, Bale A, Elefteriades J. Genes associated with thoracic aortic aneurysm and dissection: an update and clinical implications. *Aorta (Stamford)* 2017;**5**:11–20. https://doi.org/10.12945/j.aorta.2017.17.003
1500. Bray JJH, Freer R, Pitcher A, Kharbanda R. Family screening for bicuspid aortic valve and aortic dilatation: a meta-analysis. *Eur Heart J* 2023;**44**:3152–64. https://doi.org/10.1093/eurheartj/ehad320
1501. Michelena HI, Vallabhajosyula S, Prakash SK. Nosology spectrum of the bicuspid aortic valve condition: complex-presentation valvulo-aortopathy. *Circulation* 2020;**142**:294–9. https://doi.org/10.1161/circulationaha.120.046892
1502. Prakash SK, Bosse Y, Muehlschlegel JD, Michelena HI, Limongelli G, Della Corte A, *et al.* A roadmap to investigate the genetic basis of bicuspid aortic valve and its complications: insights from the International BAVCon (Bicuspid Aortic Valve Consortium). *J Am Coll Cardiol* 2014;**64**:832–9. https://doi.org/10.1016/j.jacc.2014.04.073
1503. Fulmer D, Toomer K, Guo L, Moore K, Glover J, Moore R, *et al.* Defects in the exocyst-cilia machinery cause bicuspid aortic valve disease and aortic stenosis. *Circulation* 2019;**140**:1331–41. https://doi.org/10.1161/circulationaha.119.038376
1504. Luyckx I, Kumar AA, Reyniers E, Dekeyser E, Vanderstraeten K, Vandeweyer G, *et al.* Copy number variation analysis in bicuspid aortic valve-related aortopathy identifies TBX20 as a contributing gene. *Eur J Hum Genet* 2019;**27**:1033–43. https://doi.org/10.1038/s41431-019-0364-y
1505. Xu YJ, Di RM, Qiao Q, Li X-M, Huang R-T, Xue S, *et al.* GATA6 loss-of-function mutation contributes to congenital bicuspid aortic valve. *Gene* 2018;**663**:115–20. https://doi.org/10.1016/j.gene.2018.04.018
1506. Gehlen J, Stundl A, Debiec R, Fontana F, Krane M, Sharipova D, *et al.* Elucidation of the genetic causes of bicuspid aortic valve disease. *Cardiovasc Res* 2023;**119**:857–66. https://doi.org/10.1093/cvr/cvac099
1507. Gago-Díaz M, Brion M, Gallego P, Calvo F, Robledo-Carmona J, Saura D, *et al.* The genetic component of bicuspid aortic valve and aortic dilation. An exome-wide association study. *J Mol Cell Cardiol* 2017;**102**:3–9. https://doi.org/10.1016/j.yjmcc.2016.11.012
1508. Girdauskas E, Geist L, Disha K, Kazakbaev I, Groß T, Schulz S, *et al.* Genetic abnormalities in bicuspid aortic valve root phenotype: preliminary results. *Eur J Cardiothorac Surg* 2017;**52**:156–62. https://doi.org/10.1093/ejcts/ezx065
1509. Mansoorshahi S, Yetman AT, Bissell MM, Kim YY, Michelena H, Hui DS, *et al.* Whole exome sequencing uncovers the genetic complexity of bicuspid aortic valve in families with early onset complications. *medRxiv* 2024. https://doi.org/10.1101/2024.02.07.24302406.
1510. Michelena HI, Della Corte A, Evangelista A, Maleszewski JJ, Edwards WD, Roman MJ, *et al.* International consensus statement on nomenclature and classification of the congenital bicuspid aortic valve and its aortopathy, for clinical, surgical, interventional and research purposes. *Eur J Cardiothorac Surg* 2021;**60**:448–76. https://doi.org/10.1093/ejcts/ezab038
1511. Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med* 2014;**370**:1920–9. https://doi.org/10.1056/NEJMra1207059
1512. Yang LT, Ye Z, Wajih Ullah M, Maleszewski JJ, Scott CG, Padang R, *et al.* Bicuspid aortic valve: long-term morbidity and mortality. *Eur Heart J* 2023;**44**:4549–62. https://doi.org/10.1093/eurheartj/ehad477
1513. Guo MH, Appoo JJ, Saczkowski R, Smith HN, Ouzounian M, Gregory AJ, *et al.* Association of mortality and acute aortic events with ascending aortic aneurysm: a systematic review and meta-analysis. *JAMA Netw Open* 2018;**1**:e181281. https://doi.org/10.1001/jamanetworkopen.2018.1281
1514. Dayan V, Zuasnabar A, Citro R, Bossone E, Michelena HI, Parma G, *et al.* Aortopathy and regurgitation in bicuspid valve patients increase the risk of aortopathy in relatives. *Int J Cardiol* 2019;**286**:117–20. https://doi.org/10.1016/j.ijcard.2019.03.031
1515. Galian-Gay L, Carro Hevia A, Teixido-Turà G, Rodríguez Palomares J, Gutiérrez-Moreno L, Maldonado G, *et al.* Familial clustering of bicuspid aortic valve and its relationship with aortic dilation in first-degree relatives. *Heart* 2019;**105**:603–8. https://doi.org/10.1136/heartjnl-2018-313802
1516. Tessler I, Leshno M, Shmueli A, Shpitzen S, Durst R, Gilon D. Cost-effectiveness analysis of screening for first-degree relatives of patients with bicuspid aortic valve. *Eur Heart J Qual Care Clin Outcomes* 2021;**7**:447–57. https://doi.org/10.1093/ehjqcco/qcab047
1517. Girdauskas E, Rouman M, Disha K, Espinoza A, Misfeld M, Borger MA, *et al.* Aortic dissection after previous aortic valve replacement for bicuspid aortic valve disease. *J Am Coll Cardiol* 2015;**66**:1409–11. https://doi.org/10.1016/j.jacc.2015.07.022
1518. Masri A, Kalahasti V, Svensson LG, Alashi A, Schoenhagen P, Roselli EE, *et al.* Aortic cross-sectional area/height ratio and outcomes in patients with bicuspid aortic valve and a dilated ascending aorta. *Circ Cardiovasc Imaging* 2017;**10**:e006249. https://doi.org/10.1161/circimaging.116.006249
1519. Della Corte A, Michelena HI, Citarella A, Votta E, Piatti F, Lo Presti F, *et al.* Risk stratification in bicuspid aortic valve aortopathy: emerging evidence and future perspectives. *Curr Probl Cardiol* 2021;**46**:100428. https://doi.org/10.1016/j.cpcardiol.2019.06.002
1520. Ye Z, Lane C, Beachey JD. Clinical outcomes in patients with bicuspid aortic valves and ascending aorta ≥50 mm under surveillance. *JACC: Advances* 2023;**2**:100626. https://doi.org/10.1016/j.jacadv.2023.100626.
1521. Michelena HI, Khanna AD, Mahoney D, Margaryan E, Topilsky Y, Suri RM, *et al.* Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011;**306**:1104–12. https://doi.org/10.1001/jama.2011.1286
1522. Michelena HI, Desjardins VA, Avierinos JF, Russo A, Nkomo VT, Sundt TM, *et al.* Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. *Circulation* 2008;**117**:2776–84. https://doi.org/10.1161/CIRCULATIONAHA.107.740878
1523. Girdauskas E, Disha K, Secknus M, Borger M, Kuntze T. Increased risk of late aortic events after isolated aortic valve replacement in patients with bicuspid aortic valve insufficiency versus stenosis. *J Cardiovasc Surg (Torino)* 2013;**54**:653–9.
1524. Cortenbach KRG, Yosofi B, Rodwell L, Meek J, Patel R, Prakash SK, *et al.* Editor's choice—therapeutic options and outcomes in midaortic syndrome: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2023;**65**:120–30. https://doi.org/10.1016/j.ejvs.2022.10.017
1525. Teo LL, Cannell T, Babu-Narayan SV, Hughes M, Mohiaddin RH. Prevalence of associated cardiovascular abnormalities in 500 patients with aortic coarctation referred for cardiovascular magnetic resonance imaging to a tertiary center. *Pediatr Cardiol* 2011;**32**:1120–7. https://doi.org/10.1007/s00246-011-9981-0
1526. Spaziani G, Girolami F, Arcieri L, Calabri GB, Porcedda G, Di Filippo C, *et al.* Bicuspid aortic valve in children and adolescents: a comprehensive review. *Diagnostics (Basel)* 2022;**12**:1751. https://doi.org/10.3390/diagnostics12071751
1527. Raissadati A, Nieminen H, Haukka J, Sairanen H, Jokinen E. Late causes of death after pediatric cardiac surgery: a 60-year population-based study. *J Am Coll Cardiol* 2016;**68**:487–98. https://doi.org/10.1016/j.jacc.2016.05.038
1528. Panzer J, Bové T, Vandekerckhove K, De Wolf D. Hypertension after coarctation repair–a systematic review. *Transl Pediatr* 2022;**11**:270–9. https://doi.org/10.21037/tp-21-418
1529. Batlivala SP, Goldstein BH. Current transcatheter approaches for the treatment of aortic coarctation in children and adults. *Interv Cardiol Clin* 2019;**8**:47–58. https://doi.org/10.1016/j.iccl.2018.08.001

1530. Egbe AC, Miranda WR, Bonnichsen CR, Warnes CA, Connolly HM. Potential benefits of ambulatory blood pressure monitoring in coarctation of aorta. *J Am Coll Cardiol* 2020;**75**:2089–90. https://doi.org/10.1016/j.jacc.2020.02.053
1531. Luitingh TL, Lee MGY, Jones B, Kowalski R, Weskamp Aguero S, Koleff J, *et al.* A cross-sectional study of the prevalence of exercise-induced hypertension in childhood following repair of coarctation of the aorta. *Heart Lung Circ* 2019;**28**:792–9. https://doi.org/10.1016/j.hlc.2018.03.015
1532. Brown ML, Burkhart HM, Connolly HM, Dearani JA, Cetta F, Li Z, *et al.* Coarctation of the aorta: lifelong surveillance is mandatory following surgical repair. *J Am Coll Cardiol* 2013;**62**:1020–5. https://doi.org/10.1016/j.jacc.2013.06.016
1533. Somers T, Nies H, van Kimmenade RRJ, Bosboom DGH, Geuzebroek GSC, Morshuis WJ. Necessity of life-long follow-up after surgery for coarctation of the aorta: a case series of very late false aneurysm formation. *Eur Heart J Case Rep* 2022;**6**:ytac073. https://doi.org/10.1093/ehjcr/ytac073
1534. Padang R, Dennis M, Semsarian C, Bannon PG, Tanous DJ, Celermajer DS, *et al.* Detection of serious complications by MR imaging in asymptomatic young adults with repaired coarctation of the aorta. *Heart Lung Circ* 2014;**23**:332–8. https://doi.org/10.1016/j.hlc.2013.10.055
1535. Bhatt AB, Lantin-Hermoso MR, Daniels CJ, Jaquiss R, Landis BJ, Marino BS, *et al.* Isolated coarctation of the aorta: current concepts and perspectives. *Front Cardiovasc Med* 2022;**9**:817866. https://doi.org/10.3389/fcvm.2022.817866
1536. Erben Y, Oderich GS, Verhagen HJM, Witsenburg M, van den Hoven AT, Debus ES, *et al.* Multicenter experience with endovascular treatment of aortic coarctation in adults. *J Vasc Surg* 2019;**69**:671–9.e1. https://doi.org/10.1016/j.jvs.2018.06.209
1537. Meijs TA, Warmerdam EG, Slieker MG, Krings GJ, Molenschot MMC, Meijboom FJ, *et al.* Medium-term systemic blood pressure after stenting of aortic coarctation: a systematic review and meta-analysis. *Heart* 2019;**105**:1464–70. https://doi.org/10.1136/heartjnl-2019-314965
1538. Layton KF, Kallmes DF, Cloft HJ, Lindell EP, Cox VS. Bovine aortic arch variant in humans: clarification of a common misnomer. *AJNR Am J Neuroradiol* 2006;**27**:1541–2.
1539. Berko NS, Jain VR, Godelman A, Stein EG, Ghosh S, Haramati LB. Variants and anomalies of thoracic vasculature on computed tomographic angiography in adults. *J Comput Assist Tomogr* 2009;**33**:523–8. https://doi.org/10.1097/RCT.0b013e3181888343
1540. Dumfarth J, Peterss S, Kofler M, Plaikner M, Ziganshin BA, Schachner T, *et al.* In DeBakey type I aortic dissection, bovine aortic arch is associated with arch tears and stroke. *Ann Thorac Surg* 2017;**104**:2001–8. https://doi.org/10.1016/j.athoracsur.2017.05.026
1541. Hornick M, Moomiaie R, Mojibian H, Ziganshin B, Almuwaqqat Z, Lee ES, *et al.* 'Bovine' aortic arch—a marker for thoracic aortic disease. *Cardiology* 2012;**123**:116–24. https://doi.org/10.1159/000342071
1542. Yousef S, Singh S, Alkukhun A, Alturkmani B, Mori M, Chen J, *et al.* Variants of the aortic arch in adult general population and their association with thoracic aortic aneurysm disease. *J Card Surg* 2021;**36**:2348–54. https://doi.org/10.1111/jocs.15563
1543. Tanaka A, Milner R, Ota T. Kommerell's diverticulum in the current era: a comprehensive review. *Gen Thorac Cardiovasc Surg* 2015;**63**:245–59. https://doi.org/10.1007/s11748-015-0521-3
1544. Upchurch GR, Jr, Escobar GA, Azizzadeh A, Beck AW, Conrad MF, Matsumura JS, *et al.* Society for Vascular Surgery clinical practice guidelines of thoracic endovascular aortic repair for descending thoracic aortic aneurysms. *J Vasc Surg* 2021;**73**:55s–83s. https://doi.org/10.1016/j.jvs.2020.05.076
1545. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, *et al.* Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001;**286**:1317–24. https://doi.org/10.1001/jama.286.11.1317
1546. Suárez C, Zeymer U, Limbourg T, Baumgartner I, Cacoub P, Poldermans D, *et al.* Influence of polyvascular disease on cardiovascular event rates. Insights from the REACH registry. *Vasc Med* 2010;**15**:259–65. https://doi.org/10.1177/1358863x10373299
1547. Alberts MJ, Bhatt DL, Mas JL, Ohman EM, Hirsch AT, Rother J, *et al.* Three-year follow-up and event rates in the international REduction of atherothrombosis for continued health registry. *Eur Heart J* 2009;**30**:2318–26. https://doi.org/10.1093/eurheartj/ehp355
1548. van den Berg MJ, Bhatt DL, Kappelle LJ, de Borst GJ, Cramer MJ, van der Graaf Y, *et al.* Identification of vascular patients at very high risk for recurrent cardiovascular events: validation of the current ACC/AHA very high risk criteria. *Eur Heart J* 2017;**38**:3211–8. https://doi.org/10.1093/eurheartj/ehx102
1549. Subherwal S, Bhatt DL, Li S, Wang TY, Thomas L, Alexander KP, *et al.* Polyvascular disease and long-term cardiovascular outcomes in older patients with non-ST-segment-elevation myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2012;**5**:541–9. https://doi.org/10.1161/circoutcomes.111.964379
1550. van der Meer MG, Cramer MJ, van der Graaf Y, Appelman Y, Doevendans PA, Nathoe HM. The impact of polyvascular disease on long-term outcome in percutaneous coronary intervention patients. *Eur J Clin Invest* 2014;**44**:231–9. https://doi.org/10.1111/eci.12222
1551. Steinvil A, Sadeh B, Arbel Y, Justo D, Belei A, Borenstein N, *et al.* Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. *J Am Coll Cardiol* 2011;**57**:779–83. https://doi.org/10.1016/j.jacc.2010.09.047
1552. Ahmed B, Al-Khaffaf H. Prevalence of significant asymptomatic carotid artery disease in patients with peripheral vascular disease: a meta-analysis. *Eur J Vasc Endovasc Surg* 2009;**37**:262–71. https://doi.org/10.1016/j.ejvs.2008.10.017
1553. Mukherjee D, Eagle KA, Kline-Rogers E, Feldman LJ, Juliard J-M, Agnelli G, *et al.* Impact of prior peripheral arterial disease and stroke on outcomes of acute coronary syndromes and effect of evidence-based therapies (from the global registry of acute coronary events). *Am J Cardiol* 2007;**100**:1–6. https://doi.org/10.1016/j.amjcard.2007.02.046
1554. Fowkes FG, Low LP, Tuta S, Kozak J. Ankle-brachial index and extent of atherothrombosis in 8891 patients with or at risk of vascular disease: results of the international AGATHA study. *Eur Heart J* 2006;**27**:1861–7. https://doi.org/10.1093/eurheartj/ehl114
1555. Durand DJ, Perler BA, Roseborough GS, Grega MA, Borowicz LM, Baumgartner WA, *et al.* Mandatory versus selective preoperative carotid screening: a retrospective analysis. *Ann Thorac Surg* 2004;**78**:159–66; discussion 159–66. https://doi.org/10.1016/j.athoracsur.2004.02.024
1556. Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. *Eur J Vasc Endovasc Surg* 2002;**23**:283–94. https://doi.org/10.1053/ejvs.2002.1609
1557. Jens S, Koelemay MJ, Reekers JA, Bipat S. Diagnostic performance of computed tomography angiography and contrast-enhanced magnetic resonance angiography in patients with critical limb ischaemia and intermittent claudication: systematic review and meta-analysis. *Eur Radiol* 2013;**23**:3104–14. https://doi.org/10.1007/s00330-013-2933-8
1558. Illuminati G, Schneider F, Greco C, Mangieri E, Schiariti M, Tanzilli G, *et al.* Long-term results of a randomized controlled trial analyzing the role of systematic pre-operative coronary angiography before elective carotid endarterectomy in patients with asymptomatic coronary artery disease. *Eur J Vasc Endovasc Surg* 2015;**49**:366–74. https://doi.org/10.1016/j.ejvs.2014.12.030
1559. Eikelboom JW, Bhatt DL, Fox KAA, Bosch J, Connolly SJ, Anand SS, *et al.* Mortality benefit of rivaroxaban plus aspirin in patients with chronic coronary or peripheral artery disease. *J Am Coll Cardiol* 2021;**78**:14–23. https://doi.org/10.1016/j.jacc.2021.04.083
1560. Aboyans V, Lacroix P, Postil A, Guilloux J, Rollé F, Cornu E, *et al.* Subclinical peripheral arterial disease and incompressible ankle arteries are both long-term prognostic factors in patients undergoing coronary artery bypass grafting. *J Am Coll Cardiol* 2005;**46**:815–20. https://doi.org/10.1016/j.jacc.2005.05.066
1561. Rihal CS, Sutton-Tyrrell K, Guo P, Keller NM, Jandova R, Sellers MA, *et al.* Increased incidence of periprocedural complications among patients with peripheral vascular disease undergoing myocardial revascularization in the bypass angioplasty revascularization investigation. *Circulation* 1999;**100**:171–7. https://doi.org/10.1161/01.cir.100.2.171
1562. Aboyans V, Lacroix P. Indications for carotid screening in patients with coronary artery disease. *Presse Med* 2009;**38**:977–86. https://doi.org/10.1016/j.lpm.2009.02.015
1563. Collet JP, Cayla G, Ennezat PV, Leclercq F, Cuisset T, Elhadad S, *et al.* Systematic detection of polyvascular disease combined with aggressive secondary prevention in patients presenting with severe coronary artery disease: the randomized AMERICA study. *Int J Cardiol* 2018;**254**:36–42. https://doi.org/10.1016/j.ijcard.2017.11.081
1564. Neufang A, Dorweiler B, Espinola-Klein C, Savvidis S, Doemland M, Schotten S, *et al.* Outcomes of complex femorodistal sequential autologous vein and biologic prosthesis composite bypass grafts. *J Vasc Surg* 2014;**60**:1543–53. https://doi.org/10.1016/j.jvs.2014.07.103
1565. Calvet D, Touzé E, Varenne O, Sablayrolles J-L, Weber S, Mas J-L. Prevalence of asymptomatic coronary artery disease in ischemic stroke patients: the PRECORIS study. *Circulation* 2010;**121**:1623–9. https://doi.org/10.1161/circulationaha.109.906958
1566. Hofmann R, Kypta A, Steinwender C, Kerschner K, Grund M, Leisch F. Coronary angiography in patients undergoing carotid artery stenting shows a high incidence of significant coronary artery disease. *Heart* 2005;**91**:1438–41. https://doi.org/10.1136/hrt.2004.050906
1567. Masabni K, Raza S, Blackstone EH, Gornik HL, Sabik JF, III. Does preoperative carotid stenosis screening reduce perioperative stroke in patients undergoing coronary artery bypass grafting? *J Thorac Cardiovasc Surg* 2015;**149**:1253–60. https://doi.org/10.1016/j.jtcvs.2015.02.003
1568. Klarin D, Patel VI, Zhang S, Xian Y, Kosinski A, Yerokun B, *et al.* Concomitant carotid endarterectomy and cardiac surgery does not decrease postoperative stroke rates. *J Vasc Surg* 2020;**72**:589–96.e3. https://doi.org/10.1016/j.jvs.2019.10.072
1569. D'Agostino RS, Svensson LG, Neumann DJ, Balkhy HH, Williamson WA, Shahian DM. Screening carotid ultrasonography and risk factors for stroke in coronary artery surgery patients. *Ann Thorac Surg* 1996;**62**:1714–23. https://doi.org/10.1016/s0003-4975(96)00885-5
1570. Weissler EH, Jones WS, Desormais I, Debus S, Mazzolai L, Espinola-Klein C, *et al.* Polyvascular disease: a narrative review of current evidence and a consideration of

the role of antithrombotic therapy. *Atherosclerosis* 2020;**315**:10–7. https://doi.org/10.1016/j.atherosclerosis.2020.11.001
1571. Alkhalil M, Kuzemczak M, Whitehead N, Kavvouras C, Džavík V. Meta-analysis of intensive lipid-lowering therapy in patients with polyvascular disease. *J Am Heart Assoc* 2021;**10**:e017948. https://doi.org/10.1161/jaha.120.017948
1572. Ward RP, Goonewardena SN, Lammertin G, Lang RM. Comparison of the frequency of abnormal cardiac findings by echocardiography in patients with and without peripheral arterial disease. *Am J Cardiol* 2007;**99**:499–503. https://doi.org/10.1016/j.amjcard.2006.09.102
1573. Kelly R, Staines A, MacWalter R, Stonebridge P, Tunstall-Pedoe H, Struthers AD. The prevalence of treatable left ventricular systolic dysfunction in patients who present with noncardiac vascular episodes: a case-control study. *J Am Coll Cardiol* 2002;**39**:219–24. https://doi.org/10.1016/s0735-1097(01)01725-9
1574. Samsky MD, Hellkamp A, Hiatt WR, Fowkes FGR, Baumgartner I, Berger JS, *et al.* Association of heart failure with outcomes among patients with peripheral artery disease: insights from EUCLID. *J Am Heart Assoc* 2021;**10**:e018684. https://doi.org/10.1161/jaha.120.018684
1575. Kahan T. The importance of myocardial fibrosis in hypertensive heart disease. *J Hypertens* 2012;**30**:685–7. https://doi.org/10.1097/HJH.0b013e328350e5db
1576. O'Rourke MF, Safar ME, Dzau V. The Cardiovascular Continuum extended: aging effects on the aorta and microvasculature. *Vasc Med* 2010;**15**:461–8. https://doi.org/10.1177/1358863x10382946
1577. Duscha BD, Annex BH, Green HJ, Pippen AM, Kraus WE. Deconditioning fails to explain peripheral skeletal muscle alterations in men with chronic heart failure. *J Am Coll Cardiol* 2002;**39**:1170–4. https://doi.org/10.1016/s0735-1097(02)01740-0
1578. Mancini DM, Walter G, Reichek N, Lenkinski R, McCully KK, Mullen JL, *et al.* Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. *Circulation* 1992;**85**:1364–73. https://doi.org/10.1161/01.cir.85.4.1364
1579. Hedberg P, Hammar C, Selmeryd J, Viklund J, Leppert J, Hellberg A, *et al.* Left ventricular systolic dysfunction in outpatients with peripheral atherosclerotic vascular disease: prevalence and association with location of arterial disease. *Eur J Heart Fail* 2014;**16**:625–32. https://doi.org/10.1002/ejhf.95
1580. Sandesara PB, Hammadah M, Samman-Tahhan A, Kelli HM, O'Neal WT. Peripheral artery disease and risk of adverse outcomes in heart failure with preserved ejection fraction. *Clin Cardiol* 2017;**40**:692–6. https://doi.org/10.1002/clc.22716
1581. Nakamura Y, Kunii H, Yoshihisa A, Takiguchi M, Shimizu T, Yamauchi H, *et al.* Impact of peripheral artery disease on prognosis in hospitalized heart failure patients. *Circ J* 2015;**79**:785–93. https://doi.org/10.1253/circj.CJ-14-1280
1582. Inglis SC, Bebchuk J, Al-Suhaim SA, Case J, Pfeffer MA, Solomon SD, *et al.* Peripheral artery disease and outcomes after myocardial infarction: an individual-patient meta-analysis of 28,771 patients in CAPRICORN, EPEHESUS, OPTIMAAL and VALIANT. *Int J Cardiol* 2013;**168**:1094–101. https://doi.org/10.1016/j.ijcard.2012.11.033
1583. Jones WS, Clare R, Ellis SJ, Mills JS, Fischman DL, Kraus WE, *et al.* Effect of peripheral arterial disease on functional and clinical outcomes in patients with heart failure (from HF-ACTION). *Am J Cardiol* 2011;**108**:380–4. https://doi.org/10.1016/j.amjcard.2011.03.057
1584. van Straten AH, Firanescu C, Soliman Hamad MA, Tan MESH, ter Woorst JFJ, Martens EJ, *et al.* Peripheral vascular disease as a predictor of survival after coronary artery bypass grafting: comparison with a matched general population. *Ann Thorac Surg* 2010;**89**:414–20. https://doi.org/10.1016/j.athoracsur.2009.11.036
1585. Goto S, Bhatt DL, Rother J, Alberts M, Hill MD, Ikeda Y, *et al.* Prevalence, clinical profile, and cardiovascular outcomes of atrial fibrillation patients with atherothrombosis. *Am Heart J* 2008;**156**:855–63, 863.e2. https://doi.org/10.1016/j.ahj.2008.06.029
1586. Olesen JB, Gislason GH, Torp-Pedersen C, Lip GY. Atrial fibrillation and vascular disease—a bad combination. *Clin Cardiol* 2012;**35**:15–20. https://doi.org/10.1002/clc.20955
1587. Parvar SL, Thiyagarajah A, Nerlekar N, King P, Nicholls SJ. A systematic review and meta-analysis of gender differences in long-term mortality and cardiovascular events in peripheral artery disease. *J Vasc Surg* 2021;**73**:1456–65.e7. https://doi.org/10.1016/j.jvs.2020.09.039
1588. Depta JP, Bhatt DL. Atherothrombosis and atrial fibrillation: important and often overlapping clinical syndromes. *Thromb Haemost* 2010;**104**:657–63. https://doi.org/10.1160/th10-05-0332
1589. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol* 1998;**82**:2n–9n. https://doi.org/10.1016/s0002-9149(98)00583-9
1590. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham heart study. *JAMA* 1994;**271**:840–4.
1591. Zhu J, Tan X, Zhou JZ. Peripheral artery disease and clinical outcomes in patients with atrial fibrillation: a systematic review and meta-analysis. *Clin Cardiol* 2021;**44**:1050–7. https://doi.org/10.1002/clc.23678
1592. Olesen JB, Lip GY, Lane DA, Køber L, Hansen ML, Karasoy D, *et al.* Vascular disease and stroke risk in atrial fibrillation: a nationwide cohort study. *Am J Med* 2012;**125**:826.e13–23. https://doi.org/10.1016/j.amjmed.2011.11.024
1593. Skelding KA, Yakubov SJ, Kleiman NS, Reardon MJ, Adams DH, Huang J, *et al.* Transcatheter aortic valve replacement versus surgery in women at high risk for surgical aortic valve replacement (from the CoreValve US High Risk Pivotal Trial). *Am J Cardiol* 2016;**118**:560–6. https://doi.org/10.1016/j.amjcard.2016.05.051
1594. Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, *et al.* Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med* 2012;**366**:1705–15. https://doi.org/10.1056/NEJMoa1114705
1595. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, *et al.* Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;**363**:1597–607. https://doi.org/10.1056/NEJMoa1008232
1596. Reindl M, Lechner I, Holzknecht M, Tiller C, Fink P, Oberhollenzer F, *et al.* Cardiac magnetic resonance imaging versus computed tomography to guide transcatheter aortic valve replacement (TAVR-CMR): a randomized, open-label, non-inferiority trial. *Circulation* 2023;**148**:1220–30. https://doi.org/10.1161/CIRCULATIONAHA.123.066498
1597. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, *et al.* 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;**42**:373–498. https://doi.org/10.1093/eurheartj/ehaa612
1598. Fanaroff AC, Manandhar P, Holmes DR, Cohen DJ, Harrison JK, Hughes GC, *et al.* Peripheral artery disease and transcatheter aortic valve replacement outcomes: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Therapy Registry. *Circ Cardiovasc Interv* 2017;**10**:e005456. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005456