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ESC GUIDELINES

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC)

Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC)

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Patient Forum

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All experts involved in the development of these guidelines have submitted declarations of interest. These have been compiled in a report and published in a supplementary document simultaneously to the guidelines. The report is also available on the ESC website www.escardio.org/Guidelines

See the *European Heart Journal* online for supplementary data that includes background information and detailed discussion of the data that have provided the basis of the guidelines.

Click here to access the corresponding ESC CardioMed chapters.

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Abbreviations and acronyms

AAD	Anti-arrhythmic drug
ACE-I	Angiotensin-converting enzyme inhibitor
ACS	Acute coronary syndrome
AED	Automated external defibrillator
AF	Atrial fibrillation
AH	Atrial–His interval
ALS	Advanced life support
ARB	Angiotensin receptor blocker
ARNI	Angiotensin receptor neprilysin inhibitor
ARVC	Arrhythmogenic right ventricular cardiomyopathy
ATP	Anti-tachycardia pacing
AV	Atrioventricular
AVRT	AV re-entry tachycardia
BBR-VT	Bundle branch re-entrant ventricular tachycardia
BrS	Brugada syndrome
CA	Cardiac arrest
cAMP	Cyclic adenosine monophosphate
CAD	Coronary artery disease
CAG	Coronary angiogram
CCB	Calcium channel blocker
CHD	Congenital heart disease
CIED	Cardiac implantable electronic devices
CMR	Cardiac magnetic resonance
CPR	Cardiopulmonary resuscitation
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CRT	Cardiac resynchronization therapy
CT/CTA	Computed tomography/Computed tomography angiography
DCM	Dilated cardiomyopathy
DNA	Deoxyribonucleic acid
ECG	Electrocardiogram
EF	Ejection fraction
ERP	Early repolarization pattern
ERS	Early repolarization syndrome
FBI	Fast, broad, irregular
HCM	Hypertrophic cardiomyopathy
HFrEF	Heart failure with reduced ejection fraction
HNDCM	Hypokinetic non-dilated cardiomyopathy
HTX	Heart transplantation
HV	His–ventricular interval
ICD	Implantable cardioverter defibrillator
ILR	Implantable loop recorder
IVF	Idiopathic ventricular fibrillation
LBBB	Left bundle branch block
LCSD	Left cardiac sympathetic denervation
LGE	Late gadolinium enhancement
LMNA	Lamin A/C
LQTS	Long QT syndrome
LV	Left ventricular
LVAD	Left ventricular assist device
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVNC	Left ventricular non-compaction
LVOT	Left ventricle outflow tract
MI	Myocardial infarction
MRA	Mineralocorticoid receptor antagonist
MVP	Mitral valve prolapse
MVT	Monomorphic ventricular tachycardia
NSVT	Non-sustained ventricular tachycardia
NYHA	New York Heart Association
OHCA	Out-of-hospital cardiac arrest
OMT	Optimal medical treatment
PCI	Percutaneous coronary intervention
PCR	Polymerase chain reaction
PES	Programmed electrical stimulation
PET-CT	Positron emission tomography computed tomography
PPCM	Peri-partum cardiomyopathy
PVC	Premature ventricular complex
PVT	Polymorphic ventricular tachycardia
QI	Quality indicators
RBBB	Right bundle branch block

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RCM	Restrictive cardiomyopathy
RCT	Randomized control trial
RV	Right ventricular
RVOT	Right ventricle outflow tract
SADS	Sudden arrhythmic death syndrome
SaECG	Signal-averaged ECG
SCA	Sudden cardiac arrest
SCD	Sudden cardiac death
SD	Sudden death
SGLT2	Sodium–glucose co-transporter 2
SHD	Structural heart disease
S-ICD	Subcutaneous implantable cardioverter defibrillator
SMVT	Sustained monomorphic ventricular tachycardia
SPTV	Sustained polymorphic ventricular tachycardia
SQTS	Short QT syndrome
STEMI	ST elevation myocardial infarction
SVT	Supraventricular tachycardia
TAVI	Transcatheter aortic valve implantation
TdP	Torsades de pointes
TOF	Tetralogy of Fallot
VA	Ventricular arrhythmia
VF	Ventricular fibrillation
VT	Ventricular tachycardia
WCD	Wearable cardioverter defibrillator
WPW	Wolff–Parkinson–White

1. Preamble

Guidelines summarize and evaluate available evidence with the aim of assisting health professionals in proposing the best management strategies for an individual patient with a given condition. Guidelines and their recommendations should facilitate decision making of health professionals in their daily practice. However, guidelines are not a substitute for the patient's relationship with their practitioner. The final decisions concerning an individual patient must be made by the responsible health professional(s), based on what they consider to be the most appropriate in the circumstances. These decisions are made in consultation with the patient and caregiver as appropriate.

Guidelines are intended for use by health professionals. To ensure that all users have access to the most recent recommendations, the ESC makes its guidelines freely available. The ESC warns readers that the technical language may be misinterpreted and declines any responsibility in this respect.

A great number of guidelines have been issued in recent years by the ESC. Because of their impact on clinical practice, quality criteria for the development of guidelines have been established to make all decisions transparent to the user. The recommendations for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines). The ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated.

In addition to the publication of Clinical Practice Guidelines, the ESC carries out the EURObservational Research Programme of international registries of cardiovascular diseases and interventions that are essential to assess diagnostic/therapeutic processes, use of resources, and adherence to guidelines. These registries aim at providing a better understanding of medical practice in Europe and around the world, based on high-quality data collected during routine clinical practice.

Furthermore, the ESC develops sets of quality indicators (QIs), which are tools to evaluate the level of implementation of the guidelines and may be used by the ESC, hospitals, healthcare providers, and professionals to measure clinical practice, and in educational

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/effcacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/effcacy.	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

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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.

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programmes, alongside the key messages from the guidelines, to improve quality of care and clinical outcomes.

The Members of this task force were selected by the ESC to represent professionals involved with the medical care of patients with this pathology. The selection procedure aimed to ensure that there is a representative mix of members predominantly 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. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk–benefit ratio. The level of evidence and the strength of the recommendation of particular management options were weighed and scored according to predefined scales, as outlined below. The task force followed the ESC voting procedures. All recommendations subject to a vote achieved at least 75% among voting members.

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 and can be found on the ESC website (http://www.escardio.org/Guidelines) and have been compiled in a report and published in a supplementary document simultaneously to the guidelines.

This process ensures transparency and prevents potential biases in the development and review processes. Any changes in declarations of interest that arise during the writing period were notified to the ESC and updated. The task force received its entire financial support from the ESC without any involvement from the healthcare industry.

The ESC CPG Committee supervises and coordinates the preparation of new guidelines. The Committee is also responsible for the approval process of these guidelines. The ESC Guidelines undergo extensive review by the CPG Committee and external experts, including a mix of members from across the whole of the ESC region and from relevant ESC Subspecialty Communities and National Cardiac Societies. After appropriate revisions, the guidelines are signed off by all the experts involved in the task force. The finalized document is signed off by the CPG Committee for publication in the *European Heart Journal*. The guidelines were developed after careful consideration of the scientific and medical knowledge and the evidence available at the time of their writing.

The task of developing ESC Guidelines also includes the creation of educational tools and implementation programmes for the recommendations, including condensed pocket guideline versions, summary slides, summary cards for non-specialists, and an electronic version for digital applications (smartphones, etc.). These versions are abridged and thus, for more detailed information, the user should always access the full-text version of the guidelines, which is freely available via the ESC website and the *European Heart Journal*. The National Cardiac Societies of the ESC are encouraged to endorse, adopt, translate, and implement all ESC Guidelines. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.

Health professionals are encouraged to take the ESC Guidelines fully into account when exercising their clinical judgement, as well as in the determination and the implementation of preventive, diagnostic, or therapeutic medical strategies. However, the ESC Guidelines do not override in any way whatsoever 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, where appropriate, to respect the ethical rules of their profession.

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

(1) the specific situation of the patient. In this respect, it is specified that, unless otherwise provided for by national regulations, off-

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label use of medication should be limited to situations where it is in the patient's interest to do so, with regard to the quality, safety, and efficacy of care, and only after the patient has been informed and has provided consent;

(2) country-specific health regulations, indications by governmental drug regulatory agencies, and the ethical rules to which health professionals are subject, where applicable.

2. Introduction

This document presents an update of the 2015 ESC Guidelines for the management of patients with ventricular arrhythmias (VA) and the prevention of sudden cardiac death (SCD). New insights into the epidemiology of SCD, new evidence on genetics, imaging, and clinical findings for risk stratification for VA and SCD, and advances in diagnostic evaluation and therapeutic strategies made this revision necessary. The committee was composed of 25 members including 23 expert physicians, one methodologist, and one patient representative. Experts were selected to cover all areas of VA and SCD as well as subspecialties of cardiology with the assistance of related ESC working groups.

All 25 members of the task force committee approved the guideline recommendations after an anonymous voting process. Ninety-nine peer reviewers reviewed the document. A systematic literature survey was conducted, after instructions by the methodologist in the group, that led to the incorporation of 1155 references, of which 485 were selected to support the recommendations and further specified in the table of evidence (Supplementary data).

2.1. What is new

The diagnostic and management parts of the guidelines have been adapted to facilitate their use in everyday clinical decision-making.

The first general part has new sections on diagnostic evaluation, including pharmacologic provocative tests, genetic testing, and a systematic work-up of probands and relatives with primary electrical diseases. Comprehensive flowcharts and recommendations for the diagnostic evaluation at first presentation with a VA of patients without a previously known cardiac disease are provided for five frequently encountered clinical scenarios. Practical recommendations for optimization of implantable cardioverter defibrillator (ICD) programming and algorithms for management of patients experiencing regular wide complex tachycardia and electrical storm are presented (*Table 3*).

Table 3 New sections and concepts

New sections and concepts	Section
Provocative diagnostic tests	5.1.3.5
Genetic testing	5.1.4
Diagnostic evaluation at first presentation with VA in patients without known cardiac disease	5.2
Management of patients with electrical storm	6.1.3
Special aspects of device therapy	6.2.3

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Table 4 New recommendations in 2022

Recommendations	Class
Public basic life support and access to AEDs	
It is recommended that public-access defibrillation be available at sites where cardiac arrest is more likely to occur.[a]	I
Prompt CPR by bystanders is recommended at OHCA.	I
It is recommended to promote community training in basic life support to increase bystander CPR rate and AED use.	I
Mobile phone-based alerting of basic life support-trained bystander volunteers to assist nearby OHCA victims should be considered.	IIa
Treatment of VA. General aspects	
DC cardioversion is recommended as the first-line treatment for patients presenting with tolerated SMVT provided that the anaesthetic/sedation risk is low.	I
Optimal medical treatment including ACE-I/ARB/ARNIs, MRAs, beta-blockers, and SGLT2 inhibitors is indicated in all heart failure patients with reduced EF.	I
Implantation of a cardioverter defibrillator is only recommended in patients who have an expectation of good-quality survival >1 year.	I
In patients presenting with a haemodynamically tolerated SMVT and known or suspected SHD, intravenous procainamide should be considered.	IIa
In patients presenting with a haemodynamically tolerated SMVT in the absence of an established diagnosis, intravenous amiodarone may be considered.	IIb
In patients with SMVT or SPVT/VF triggered by a PVC with similar morphology and an indication for ICD, catheter ablation may be considered when an ICD is not available, contraindicated for concurrent medical reasons, or declined by the patient.	IIb
The WCD may be considered in the early phase after MI in selected patients.	IIb
Coronary artery disease	
In patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy.	I
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test after surgery in patients with anomalous aortic origin of a coronary artery with a history of aborted CA.	I
In SCA survivors with coronary artery spasm, implantation of an ICD should be considered.	IIa
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.	IIa
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT and NSVT, if they are inducible for SMVT by PES.	IIa

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In patients with CAD and haemodynamically well-tolerated SMVT and LVEF ≥40%, catheter ablation in experienced centres should be considered as an alternative to ICD therapy, provided that established endpoints have been reached.[b]	IIa
Catheter ablation should be considered in patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite beta-blocker or sotalol treatment.	IIa
Idiopathic PVC/VT and PVC-induced cardiomyopathy	
Catheter ablation as first-line treatment is recommended for symptomatic idiopathic VT/PVCs from the RVOT or the left fascicles.	I
Beta-blockers or non-dihydropyridine CCBs are indicated in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.	I
In patients with PVCs/VT and a presentation not typical for an idiopathic origin,[c] CMR should be considered, despite a normal echocardiogram.	IIa
Beta-blockers, non-dihydropyridine CCBs or flecainide should be considered when catheter ablation is not available, not desired, or is particularly risky in symptomatic patients with idiopathic VT/PVCs from the RVOT or the left fascicles.	IIa
Catheter ablation or flecainide should be considered in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.	IIa
In patients with an unexplained reduced EF and a PVC burden of at least 10%, PVC-induced cardiomyopathy should be considered.	IIa
In patients with suspected PVC-induced cardiomyopathy, CMR should be considered.	IIa
In non-responders to CRT with frequent, predominately monomorphic PVCs limiting optimal biventricular pacing despite pharmacological therapy, catheter ablation or AADs should be considered.	IIa
Catheter ablation may be considered for idiopathic VT/PVCs in asymptomatic patients with repeatedly more than 20% of PVCs per day at follow-up.	IIb
Amiodarone as a first-line treatment is not recommended in patients with idiopathic VTs/PVCs.	III
DCM/HNDCM	
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) is recommended in patients with DCM/HNDCM and AV conduction delay at <50 years, or who have a family history of DCM/HNDCM or SCD in a first-degree relative (at age <50 years).	I
In a first-degree relative of a DCM/HNDCM patient, an ECG, and an echocardiogram are recommended if: • the index patient was diagnosed <50 years of age or has clinical features suggestive of an inherited cause, or • there is a family history of DCM/HNDCM, or premature unexpected SD.	I
CMR with LGE should be considered in DCM/HNDCM patients for assessing the aetiology and the risk of VA/SCD.	IIa
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) should be considered for risk stratification in patients with apparently sporadic DCM/HNDCM, who present at young age or with signs suspicious for an inherited aetiology.	IIa
ICD implantation should be considered in DCM/HNDCM patients with an LVEF <50% and ≥2 risk factors (syncope, LGE on CMR, inducible SMVT at PES, pathogenic mutations in LMNA, *PLN*, *FLNC*, and *RBM20* genes).	IIa
ICD implantation should be considered in patients with DCM/HNDCM and haemodynamically tolerated SMVT.	IIa
In a first-degree relative of a patient with apparently sporadic DCM/HNDCM, an ECG, and an echocardiogram may be considered.	IIb
Participation in high-intensity exercise including competitive sports is not recommended for individuals with DCM/HNDCM and a *LMNA* mutation.	III
ARVC	
In patients with suspected ARVC, CMR is recommended.	I
In patients with a suspected or definite diagnosis of ARVC, genetic counselling and testing are recommended.	I
ICD implantation should be considered in symptomatic[d] patients with definite ARVC, moderate right or left ventricular dysfunction, and either NSVT or inducibility of SMVT at PES.	IIa
In ARVC patients with indication for ICDs, a device with the capability of ATP programming for SMVT up to high rates should be considered.	IIa
Avoidance of high-intensity[e] exercise may be considered in carriers of ARVC-related pathogenic mutations and no phenotype.	IIb
Beta-blocker therapy may be considered in all patients with a definite diagnosis of ARVC.	IIb
In patients with ARVC and symptoms highly suspicious for VA, PES may be considered for risk stratification.	IIb
HCM	
CMR with LGE is recommended in HCM patients for diagnostic work-up.	I
Genetic counselling and testing are recommended in HCM patients.	I
In a first-degree relative of a patient with HCM, ECG, and echocardiogram are recommended.	I
ICD implantation should be considered in HCM patients aged 16 years or more with an intermediate 5-year risk of SCD (≥4 to <6%)[f], and with (a) significant LGE at CMR (usually ≥15% of LV mass); or (b) LVEF <50%; or (c) abnormal blood pressure response during exercise test[g]; or (d) LV apical aneurysm; or (e) presence of sarcomeric pathogenic mutation.	IIa
In children <16 years of age with HCM and an estimated 5-year risk of SD ≥6% (based on HCM Risk-Kids score[h]), ICD implantation should be considered.	IIa
In patients with HCM presenting with haemodynamically tolerated SMVT, ICD implantation should be considered.	IIa

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In patients with HCM and recurrent, symptomatic VA, or recurrent symptomatic ICD therapy, AAD treatment should be considered.	IIa
Participation in high-intensity exercise may be considered for asymptomatic adult HCM patients without risk markers.	IIb
ICD implantation may be considered in HCM patients aged 16 years or more with a low estimated 5-year risk of SCD (<4%),[f] and with (a) significant LGE at CMR (usually ≥15% of LV mass); or (b) LVEF < 50%; or (c) LV apical aneurysm.	IIb
Catheter ablation in specialized centres may be considered in selected patients with HCM and recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb
LVNC and RCM	
In patients with an LVNC cardiomyopathy phenotype based on CMR or echocardiography, implantation of an ICD for primary prevention of SCD should be considered to follow DCM/HNDCM recommendations.	IIa
An ICD should be considered in patients with light-chain amyloidosis or transthyretin-associated cardiac amyloidosis and haemodynamically not-tolerated VT.	IIa
Neuromuscular diseases	
Invasive electrophysiological evaluation is recommended in patients with myotonic dystrophy and palpitations or syncope suggestive of VA or surviving a CA.	I
ICD implantation is recommended in patients with myotonic dystrophy and SMVT or aborted CA not caused by BBR-VT.	I
Invasive electrophysiological evaluation should be considered in patients with myotonic dystrophy and a sudden increase in the PR interval or QRS duration.	IIa
Invasive electrophysiological evaluation should be considered in patients with myotonic dystrophy and a PR interval ≥240 ms or QRS duration ≥120 ms or who are older than 40 years and have supraventricular arrhythmias, or who are older than 40 years and have significant LGE on CMR	IIa
In myotonic dystrophy patients without AV conduction delay and a syncope highly suspicious for VA, ICD implantation should be considered.	IIa
In myotonic dystrophy patients with palpitations highly suspicious for VA and induction of a non-BBR-VT, ICD implantation should be considered.	IIa
In patients with limb-girdle type 1B or Emery–Dreifuss muscular dystrophies and indication for pacing, ICD implantation should be considered.	IIa
Implantation of an ICD may be considered in patients with Duchenne/Becker muscular dystrophy and significant LGE at CMR.	IIb
Implantation of an ICD over a permanent pacemaker may be considered in myotonic dystrophy patients with additional risk factors[i] for VA and SCD.	IIb
In patients with myotonic dystrophy, serial electrophysiological evaluation of AV conduction and arrhythmia induction is not recommended without arrhythmia suspicion or progression of ECG conduction disorders.	III

Continued

Inflammatory diseases	
In patients with haemodynamically not-tolerated sustained VT or VF during the acute phase of myocarditis, ICD implantation before hospital discharge should be considered.	IIa
In post-myocarditis patients with recurrent, symptomatic VT, AAD treatment should be considered.	IIa
Catheter ablation, performed in specialized centres, should be considered in post-myocarditis patients with recurrent, symptomatic SMVT, or ICD shocks for SMVT in whom AADs are ineffective, not tolerated, or not desired.	IIa
In patients with haemodynamically tolerated SMVT occurring in the chronic phase of myocarditis, ICD implantation should be considered.	IIa
In patients with cardiac sarcoidosis who have an LVEF >35% but significant LGE at CMR after resolution of acute inflammation, ICD implantation should be considered.	IIa
In patients with cardiac sarcoidosis who have an LVEF 35–50% and minor LGE at CMR, after resolution of acute inflammation, PES for risk stratification should be considered.	IIa
In patients with cardiac sarcoidosis, LVEF 35–50%, and inducible SMVT at PES, ICD implantation should be considered.	IIa
In patients with cardiac sarcoidosis and recurrent, symptomatic VA, AAD treatment should be considered.	IIa
Amiodarone should be considered to reduce arrhythmia burden in patients with Chagas' cardiomyopathy who present with symptomatic PVCs or VT.	IIa
In patients with Chagas' cardiomyopathy and recurrent, symptomatic SMVT, or ICD shocks for SMVT in whom AADs are ineffective, contraindicated, or not tolerated, catheter ablation in specialized centres should be considered.	IIa
In patients with haemodynamically well-tolerated SMVT occurring in the chronic phase of myocarditis, preserved LV function and a limited scar amenable to ablation, catheter ablation may be considered as an alternative to ICD therapy, after discussion with the patient and provided that established endpoints have been reached.[b]	IIb
Catheter ablation, in specialized centres, may be considered in cardiac sarcoidosis ICD recipients with recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb
Congenital heart disease	
In patients with CHD presenting with sustained VAs, evaluation for residual lesions or new structural abnormalities is recommended.	I
In selected patients with CHD (including atrial baffle repair for transposition of the great arteries, Fontan operation, and Ebstein anomaly) presenting with CA, evaluation and treatment of SVT with rapid ventricular conduction should be considered.	IIa
In patients with repaired TOF undergoing surgical or transcutaneous pulmonary valve replacement, pre-operative catheter mapping and transection of VT-related anatomical isthmuses before or during the intervention may be considered.	IIb

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In patients with repaired TOF with a preserved biventricular function and symptomatic SMVT, catheter ablation or concomitant surgical ablation performed in specialized centres may be considered as an alternative to ICD therapy.	IIb
Idiopathic VF	
It is recommended that idiopathic VF is diagnosed in a SCA survivor, preferably with documentation of VF, after exclusion of an underlying structural, channelopathic, metabolic, or toxicological aetiology.	I
Isoproterenol infusion, verapamil, or quinidine for acute treatment of an electrical storm or recurrent ICD discharges should be considered in idiopathic VF.	IIa
Quinidine should be considered for chronic therapy to suppress an electrical storm or recurrent ICD discharges in idiopathic VF.	IIa
Clinical testing (history, ECG, and high precordial lead ECG, exercise test, echocardiogram) of first-degree family members of idiopathic VF patients may be considered.	IIb
In idiopathic VF patients, genetic testing of genes related to channelopathy and cardiomyopathy may be considered.	IIb
Long QT syndrome	
In patients with clinically diagnosed LQTS, genetic testing, and genetic counselling are recommended.	I
Beta-blockers, ideally non-selective beta-blockers (nadolol or propranolol), are recommended in LQTS patients with documented QT interval prolongation, to reduce risk of arrhythmic events.	I
Mexiletine is indicated in LQT3 patients with a prolonged QT interval.	I
In LQTS, it should be considered to calculate the arrhythmic risk before initiation of therapy based on the genotype and the duration of QTc interval.	IIa
ICD implantation may be considered in asymptomatic LQTS patients with high-risk profile (according to the 1-2-3 LQTS Risk calculator) in addition to genotype-specific medical therapies (mexiletine in LQT3 patients).	IIb
Routine diagnostic testing with epinephrine challenge is not recommended in LQTS.	III
Andersen–Tawil syndrome	
Genetic testing is recommended in patients with suspected Andersen–Tawil syndrome.	I
ICD implantation is recommended in patients with Andersen–Tawil syndrome after aborted CA or not-tolerated sustained VT.	I
Andersen–Tawil syndrome should be considered in patients without SHD who present with at least two of the following: • Prominent U waves with or without prolongation of the QT interval • Bidirectional and/or polymorphic PVCs/VT • Dysmorphic features • Periodic paralysis • KCNJ2 pathogenic loss of function mutation.	IIa
Beta-blockers and/or flecainide with or without acetazolamide should be considered in patients with Andersen–Tawil syndrome to treat VA.	IIa
An ILR should be considered in patients with Andersen–Tawil syndrome and unexplained syncope.	IIa
ICD implantation may be considered in patients with Andersen–Tawil syndrome who have a history of unexplained syncope or suffer from tolerated sustained VT.	IIb
Brugada syndrome	
Genetic testing for *SCN5A* gene is recommended for probands with BrS.	I
BrS should be considered in patients with no other heart disease and induced type 1 Brugada pattern who have at least one of the following: • Arrhythmic syncope or nocturnal agonal respiration • A family history of BrS • A family history of SD (<45 years old) with a negative autopsy and circumstance suspicious for BrS.	IIa
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope.	IIa
BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an induced type 1 Brugada ECG.	IIb
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG.	IIb
Sodium channel blocker test is not recommended in patients with a prior type I Brugada pattern.	III
Catheter ablation in asymptomatic BrS patients is not recommended.	III
Early repolarization syndrome	
It is recommended that the ERP is diagnosed as J-point elevation of ≥1 mm in two adjacent inferior and/or lateral ECG leads.	I
It is recommended that the ERS is diagnosed in a patient resuscitated from unexplained VF/PVT in the presence of ERP.	I
ICD implantation is recommended in patients with a diagnosis of ERS who have survived a CA.	I
In a SCD victim with a negative autopsy and medical chart review, and an ante-mortem ECG demonstrating the ERP, the diagnosis of ERS should be considered.	IIa
First-degree relatives of ERS patients should be considered for clinical evaluation for ERP with additional high-risk features.[j]	IIa
ILR should be considered in individuals with ERP and at least one risk feature[k] or arrhythmic syncope.	IIa
Isoproterenol infusion should be considered for ERS patients with electrical storm.	IIa
Quinidine in addition to an ICD should be considered for recurrent VF in ERS patients.	IIa
PVC ablation should be considered in ERS patients with recurrent VF episodes triggered by a similar PVC non-responsive to medical treatment.	IIa
Genetic testing in ERS patients may be considered.	IIb
ICD implantation or quinidine may be considered in individuals with ERP and arrhythmic syncope and additional risk features.[k]	IIb

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ICD implantation or quinidine may be considered in asymptomatic individuals who demonstrate a high-risk ERP[j] in the presence of a family history of unexplained juvenile SD.	IIb
Clinical evaluation is not recommended routinely in asymptomatic subjects with ERP.	III
ICD implantation is not recommended in asymptomatic patients with an isolated ERP.	III
CPVT	
Genetic testing and genetic counselling are indicated in patients with clinical suspicion or clinical diagnosis of CPVT.	I
Beta-blockers, ideally non-selective (nadolol or propranolol) are recommended in all patients with a clinical diagnosis of CPVT.	I
Epinephrine or isoproterenol challenge may be considered for the diagnosis of CPVT when an exercise test is not possible.	IIb
Short QT syndrome	
Genetic testing is indicated in patients diagnosed with SQTS.	I
SQTS should be considered in the presence of a QTc ≤320 ms.	IIa
SQTS should be considered in the presence of a QTc ≥320 ms and ≤360 ms and arrhythmic syncope.	IIa
ILR should be considered in young SQTS patients.	IIa
ICD implantation should be considered in SQTS patients with arrhythmic syncope.	IIa
SQTS may be considered in the presence of a QTc ≥320 ms and ≤360 ms and a family history of SD at age <40 years.	IIb
Quinidine may be considered in (a) SQTS patients who qualify for an ICD but present a contraindication to the ICD or refuse it, and (b) asymptomatic SQTS patients and a family history of SCD.	IIb
Isoproterenol may be considered in SQTS patients with an electrical storm.	IIb
Selected populations	
It is recommended that athletes diagnosed with a cardiovascular disease associated with SCD are managed according to current guidelines for sports eligibility.	I
Continuation of beta-blockers should be considered during pregnancy in women with ARVC.	IIa
Oral metoprolol, propranolol, or verapamil should be considered for long-term management of idiopathic sustained VT during pregnancy.	IIa
Catheter ablation using non-fluoroscopic mapping systems should be considered, preferably after the first trimester, in women with highly symptomatic recurrent SMVT refractory or who are intolerant to AADs.	IIa
In selected transplanted patients with cardiac allograft vasculopathy or treated rejection, ICD implantation may be considered.	IIb
In elderly patients in whom a benefit from the defibrillator is not expected due to the patient's age and comorbidities, omission of ICD implantation for primary prevention may be considered.	IIb

Continued

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AAD, anti-arrhythmic drug; ACE-Is, angiotensin-converting enzyme inhibitors; AED, automated external defibrillator; ARBs, angiotensin receptor blockers; ARNIs, angiotensin receptor neprilysin inhibitors; ARVC, arrhythmogenic right ventricular cardiomyopathy; ATP, anti-tachycardia pacing; AV, atrioventricular; BBR-VT, bundle branch re-entry; BrS, Brugada syndrome; CA, cardiac arrest; CAD, coronary artery disease; CCB, calcium channel blocker; CHD, congenital heart disease; CMR, cardiac magnetic resonance; CPR, cardiopulmonary resuscitation; CPVT, catecholaminergic polymorphic ventricular tachycardia; CRT, cardiac resynchronization therapy; DC, direct current; DCM, dilated cardiomyopathy; ECG, electrocardiogram; EF, ejection fraction; ERP, early repolarization pattern; ERS, early repolarization syndrome; HCM, hypertrophic cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; LGE, late gadolinium enhancement; LMNA, lamin A/C; LQTS, long QT syndrome; LV, left ventricular; LVEF, left ventricular ejection fraction; LVNC, left ventricular non-compaction; MI, myocardial infarction; MRAs, mineralocorticoid receptor antagonists; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; OHCA, out-of-hospital cardiac arrest; OMT, optimal medical therapy; PES, programmed electrical stimulation; PVC, premature ventricular complex; RCM, restrictive cardiomyopathy; RVOT, right ventricular outflow tract; SCA, sudden cardiac arrest; SCD, sudden cardiac death; SD, sudden death; SGLT2, sodium–glucose co-transporter 2; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; SPVT, sustained polymorphic ventricular tachycardia; SQTS, short QT syndrome; SVT, supraventricular tachycardia; TOF, tetralogy of Fallot; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia; WCD, wearable cardioverter defibrillator.

[a]Shopping malls, stadiums, public transport stations, casinos.

[b]VT non-inducibility and elimination of electrograms consistent with conduction delay.

[c]Including but not limited to older age, right bundle branch block (RBBB) morphology, SMVT consistent with re-entry.

[d]Presyncope or palpitations suggestive of VA.

[e]The 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease.[4]

[f]Based on the HCM Risk SCD: https://doc2do.com/hcm/webHCM.html

[g]Defined as a failure to increase systolic pressure by at least 20 mmHg from rest to peak exercise, or a fall of >20 mmHg from peak pressure.

[h]Based on the HCM Kid Risk score: https://hcmriskkids.org

[i]Factors favouring ICD implantation: Age,[5,6,11] CTG expansion,[6–9,13,16] SD or family history of SD,[5] ECG conduction abnormalities,[16] PR prolongation,[13] LBBB,[5] atrial arrhythmias,[6,16] non-sustained VT,[5] LV dysfunction,[17] structural abnormalities in CMR.[14,15,18]

[j]ERP high risk features: J waves > 2 mm, dynamic changes in J point and ST morphology.

[k]High-risk ERP: family history of unexplained SD <40 years, family history of ERS.

The second part of the guidelines is structured according to disease-specific management, providing a link to the updated ESC CardioMed chapter for additional content. Risk stratification, SCD prevention, treatment of VA, and management of family members are addressed in a systematic fashion. Indications for cardiac magnetic resonance (CMR) imaging, genetic testing, and updated indications for catheter ablation of ventricular arrhythmias are presented. Flowcharts summarizing the workflow for diagnostic and treatment are provided for the disease entities. The colour-coding of the flowcharts reflects the class of recommendation according to this guideline and other ESC Guidelines.[1–3]

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Table 5 Changes in recommendations since 2015

	Class	
	2015	2022
Coronary artery disease		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.	IIa	I
Intravenous amiodarone treatment should be considered for patients with recurrent PVT/VF during the acute phase of ACS.	I	IIa
In patients with CAD eligible for ICD implantation, catheter ablation may be considered just before (or immediately after) ICD implantation to decrease subsequent VT burden and ICD shocks.	IIa	IIb
PVC-induced cardiomyopathy		
In patients with a cardiomyopathy suspected to be caused by frequent and predominately monomorphic PVCs, catheter ablation is recommended.	IIa	I
DCM/HNDCM		
ICD implantation should be considered in patients with DCM/HNDCM, symptomatic heart failure (NYHA class II–III) and LVEF ≤35% after ≥3 months of OMT.	I	IIa
Catheter ablation in specialized centres should be considered in patients with DCM/HNDCM and recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb	IIa
ARVC		
ICD implantation should be considered in patients with definite ARVC and an arrhythmic syncope.	IIb	IIa
ICD implantation should be considered in patients with definite ARVC and severe RV or LV systolic dysfunction.	IIb	IIa
Inflammatory diseases		
In patients with haemodynamically not-tolerated SMVT occurring in the chronic phase of myocarditis, ICD implantation is recommended.	IIa	I
ICD implantation is recommended in patients with cardiac sarcoidosis who have an LVEF ≤35%.	IIb	I
ICD implantation is recommended in patients with cardiac sarcoidosis who (1) have documented sustained VT, or (2) aborted CA.	IIb	I
In patients with cardiac sarcoidosis who have an indication for permanent cardiac pacing related to high-degree AV block, ICD implantation should be considered, regardless of LVEF.	IIb	IIa
In patients with Chagas' cardiomyopathy and symptomatic VT in whom AADs (amiodarone and beta-blockers) are ineffective or not tolerated, ICD implantation may be considered.	IIa	IIb
CHD		
In patients after repair of TOF without arrhythmia symptoms, but with a combination of other risk factors,[a] electrophysiologic evaluation, including PES, may be considered.	IIa	IIb
In patients with CHD and recurrent, symptomatic SMVT, or ICD shocks for SMVT not manageable by medical therapy or ICD reprogramming, catheter ablation performed in specialized centres should be considered.	I	IIa
Primary electrical disease and selected populations		
ICD implantation is recommended in patients with LQTS who are symptomatic[b] while receiving beta-blockers and genotype-specific therapies.	IIa	I
ICD implantation should be considered in patients with CPVT who experience arrhythmic syncope and/or documented bidirectional/PVT while on the highest tolerated beta-blocker dose and on flecainide.	I	IIa
Pre-participation cardiovascular evaluation of competitive athletes should be considered.	I	IIa
Catheter ablation of triggering PVCs and/or RVOT epicardial substrate should be considered in BrS patients with recurrent appropriate ICD shocks refractory to drug therapy.	IIb	IIa
LCSD should be considered in patients with diagnosis of CPVT when the combination of beta-blockers and flecainide at therapeutic dosage are either not effective, not tolerated, or contraindicated.	IIb	IIa

Continued

AAD, anti-arrhythmic drug; ACS, acute coronary syndrome; ARVC, arrhythmogenic right ventricular cardiomyopathy; AV, atrioventricular; BrS, Brugada syndrome; CA, cardiac arrest; CAD, coronary artery disease; CHD, congenital heart disease; CPVT, catecholaminergic polymorphic ventricular tachycardia; DCM, dilated cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; LCSD, left cardiac sympathetic denervation; LQTS, long QT syndrome; LV, left ventricle; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OMT, optimal medical treatment; PES, programmed electrical stimulation; PVC, premature ventricular complex; PVT, polymorphic ventricular tachycardia; RV, right ventricle; RVOT, right ventricular outflow tract; SMVT, sustained monomorphic ventricular tachycardia; STEMI, ST elevation myocardial infarction; TdP, torsade de pointes; TOF, tetralogy of Fallot; VF, ventricular fibrillation; VT, ventricular tachycardia.

[a]Other risk factors include moderate RV or LV dysfunction, extensive RV scarring on CMR, QRS duration ≥180 ms, and severe QRS fragmentation.

[b]Arrhythmic syncope or haemodynamically not-tolerated VA.

Another novel concept of this document is the table of evidence (see Supplementary data). The trials and studies that have been selected to support a recommendation are systematically described in the table of evidence after careful review of the available data and the applied methodology, prioritizing papers published after 2015. Recommendations with level of evidence C that are not accompanied by a reference are supported by this panel of experts. To assist physicians in their daily clinical practice, diagnostic and therapeutic procedures with promising usefulness, typically classified as class IIb, but for which evidence is limited and difficult to collect in the near future, the related recommendations are not only described in the narratives but are listed in the table of recommendation.

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3. Definitions

3.1. Ventricular arrhythmia subtypes

Premature ventricular complex (PVC): Premature occurrence of an abnormal QRS complex (duration typically ≥120 ms, corresponding T-wave typically broad and in the opposite direction of the major QRS deflection, no preceding P-wave).

Unifocal or monomorphic PVCs: PVCs with a single QRS morphology.

Multifocal, multiform, or polymorphic PVCs: PVCs with different QRS morphologies.

Short-coupled PVC: A PVC that interrupts the T-wave of the preceding conducted beat.

Ventricular tachycardia (VT): ≥3 consecutive beats with a rate >100 b.p.m. originating from the ventricles, independent from atrial and atrioventricular (AV) nodal conduction.

Non-sustained ventricular tachycardia (NSVT): Run of consecutive ventricular beats persisting for 3 beats to 30 s.

Monomorphic ventricular tachycardia (MVT): Same QRS morphology from beat to beat.

Polymorphic ventricular tachycardia (PVT): Continually changing QRS morphology.

Sustained monomorphic/polymorphic ventricular tachycardia (SMVT/SPVT): Continuous VT for at least 30 s, or which requires an intervention for termination.

Bidirectional ventricular tachycardia: Beat to beat alternation of the frontal QRS axis (e.g. in catecholaminergic polymorphic ventricular tachycardia [CPVT], Andersen–Tawil, digoxin toxicity, acute myocarditis).

Torsades de pointes ventricular tachycardia (TdP): Subtype of a polymorphic VT in the context of QT prolongation with continually changing QRS complexes that appear to spiral around the baseline of the electrocardiogram (ECG) lead in a sinusoidal pattern.

Ventricular fibrillation (VF): A chaotic rhythm with undulations that are irregular in timing and morphology, without discrete QRS complexes on the surface ECG.

Electrical storm: VA that occurs 3 or more times within 24 h (separated by at least 5 min), each requiring termination by an intervention.

Incessant VT: Continuous sustained VT that recurs promptly despite repeated intervention for termination over several hours.

3.2. Sudden cardiac death

Sudden cardiac arrest (SCA): Sudden cessation of normal cardiac activity with haemodynamic collapse.

Sudden cardiac death (SCD): Sudden natural death presumed to be of cardiac cause that occurs within 1 h of onset of symptoms in witnessed cases, and within 24 h of last being seen alive when it is unwitnessed. SCD in autopsied cases is defined as the natural unexpected death of unknown or cardiac cause.

Sudden unexplained death: Unexplained sudden death occurring in an individual older than 1 year.

Sudden infant death syndrome (SIDS): Unexplained sudden death occurring in an individual younger than 1 year with negative pathological and toxicological assessment and negative forensic examination of the circumstances of death.

Sudden arrhythmic death syndrome (SADS): Unexplained sudden death occurring in an individual older than 1 year with negative pathological and toxicological assessment. Note: Synonymous with 'autopsy-negative sudden unexplained death'.

3.3. Syncope

Unexplained syncope: Transient loss of consciousness due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery, but unexplained after conventional workup. Work-up and differential diagnosis are provided in the 2018 ESC Guidelines for the diagnosis and management of syncope.[1]

Arrhythmic syncope: as above, but highly suspicious for intermittent bradycardia, rapid supraventricular tachycardia (SVT), or VA.

3.4. Specialized centres

Multidisciplinary teams: A multidisciplinary team across specialties is characterized by open communication, positive management and leadership, appropriate resources, and a mix of skills. Decision-making should be shared in the team.

Specialized centre for catheter ablation of VA: Patient and procedural complexity vary widely. Some patients require a more experienced operator and a centre with more capabilities, which is more likely in patients with a non-ischaemic aetiology. A specialized centre has at least one operator with appropriate experience in interventions that may be required for a successful procedure (e.g. percutaneous epicardial access). The centre performs catheter ablation of VT in structural heart disease (SHD) on a regular basis. In addition, the centre has the required resources to manage medical conditions, comorbidities, and potential complications in patients undergoing complex VA ablation; this includes interventional cardiology expertise, acute placement of mechanical circulatory assist devices, and cardiothoracic surgical back-up. Considering the variable availability across European countries, it is preferable to treat complex patients in the most experienced centre within reasonable distance.

3.5. Genetics

Pathogenic variant and likely pathogenic variant: The American College of Medical Genetics has provided a framework for the interpretation of disease causation by genetic variants standardized into classes. The genetic variants most likely to cause an associated disease are termed V, 'pathogenic', and IV, 'likely pathogenic'.

Mutation: This term is used in this document to mean a Class IV or V variant.

Variant of uncertain significance: A change in a gene's deoxyribonucleic acid (DNA) sequence that has an unknown effect on a person's health.

4. Epidemiology of sudden cardiac death, public awareness, and risk stratification

4.1. Incidence of sudden cardiac death

SCD accounts for approximately 50% of all cardiovascular deaths, with up to 50% being the first manifestation of cardiac disease.[19–24] Ideally, cases suspicious of SCD should be identified from multiple

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sources and undergo autopsy, which is required to reliably exclude non-cardiac causes of sudden death (SD).

The incidence of SCD increases markedly with age. With a very low incidence during infancy and childhood (1 per 100 000 person-years),[25–27] the incidence is approximately 50 per 100 000 person-years in middle-aged individuals (in the fifth to sixth decades of life).[28–30] In the eighth decade of life, it reaches an annual incidence of at least 200 per 100 000 person-years.[20] At any age, males have higher SCD rates compared with females, even after adjustment for risk factors of coronary artery disease (CAD).[24,31–33] Ethnic background also seems to have large effects.[34,35] It is estimated that 10–20% of all deaths in Europe are SCD.[36,37] Approximately 300 000 people in Europe have out-of-hospital cardiac arrest (OHCA) treated by emergency medical systems every year.[38,39]

In the Western world, the epidemiology of SCD is closely related to CAD, which is responsible for up to 75–80% of SCD cases.[40] While the prevalence of CAD has not decreased, there has been a significant decline in mortality due to CAD. Reports show that the incidence of SCD is declining,[40–42] but the risk of SCD as a proportion of the overall cardiovascular deaths may have increased.[43,44]

Although regular physical activity benefits cardiovascular health, sport, particularly when practiced vigorously, has been shown to be associated with SCD during or shortly after exercise in selected populations.[45–51] Reports have suggested that the majority of sports-related SCD occurs in a recreational[52,53] rather than competitive setting, especially among middle-aged male participants, suggesting that CAD is the most common underlying cause.[46,54,55]

4.2. Causes of sudden cardiac death in different age groups

Cardiac diseases associated with SCD vary depending on the individual's age. In the young there is a predominance of primary electric diseases and cardiomyopathies, as well as myocarditis, and coronary anomalies.[25,27,56–61] However, half of SCD cases during the fourth decade are related to CAD, especially acute coronary syndrome (ACS).[62,63]

In older populations, chronic structural diseases predominate (CAD either through acute coronary events or chronic coronary stenoses, valvular heart diseases, and heart failure), while potentially inherited electrical diseases or structural non-ischaemic diseases may cause more than 50% of SCD in individuals under the age of 50 years.[27]

Age distribution at presentation with ventricular arrhythmias and sudden cardiac death, dominant arrhythmia subtypes, triggers, genetic factors, and gender associated with increased risk for ventricular arrhythmias in selected primary electrical and structural heart diseases are presented in *Figure 1*.

4.3. Population vs. individual risk prediction

In the general population (individuals without known heart disease), the most effective approach for preventing SCD resides in quantification of the individual risk of developing CAD based on risk score charts.[64,65] Several studies have provided evidence that there is a genetic predisposition to die suddenly during acute ischaemia.[66–70] The goal would be to identify the relatively small, high-risk subgroups from the general population at risk of SCD as their first cardiac event. Models for novel SCD risk stratification in the general population have recently been proposed.[71–73] There are no clear data supporting the benefit of mass screening programs in the general population for preventing SCD.[74–76]

For decades, investigators have envisioned a broad range of 'indicators' for SCD, especially occurring in the setting of CAD. Several non-invasive markers of risk have been proposed (including late potentials, heart rate variability, periodic repolarization dynamics, and baroreflex sensitivity).[77] Despite the promising outcomes of initial studies, however, these 'predictors' have not yet influenced clinical practice. Left ventricular ejection fraction (LVEF) is only used, often in combination with New York Heart Association (NYHA) class, for primary prevention indication of an ICD in the setting of chronic CAD and dilated cardiomyopathy (DCM). Risk stratification schemes and calculators have been developed for inheritable arrhythmogenic diseases, such as hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and lamin A/C (LMNA) cardiomyopathy.[78–82]

What is considered low, intermediate, or high risk will depend on the type of event (e.g. fatal or not) and the risk of an event in the background population. For instance, mortality depends on age, sex, and other risk factors including comorbidities. The situation is further complicated when considering a specific type of death, e.g. SCD. Then non-SCD deaths are competing events (or competing risks) to SCD in the sense that their occurrence prevents the observation of SCD, and may make interventions to prevent SCD, such as an ICD, of limited benefit.

4.4. Risk calculators for sudden cardiac death and review of the methodology

A number of risk calculators for SCD have been proposed for adult and paediatric populations.[80,81,83–85] The field of prediction modelling has evolved over the past decades, establishing standards for the development, validation (internal and external), and reporting of prediction models in SCD.[86,87] In addition to discrimination measures such as the c-index, measures of calibration such as the calibration slope have recently received more attention because it is not only important to distinguish patients with higher risks from those with lower risks but also to obtain a robust quantification of the risk itself from the risk calculators.[88] Typical shortcomings in the development and validation of risk calculators include, but are not limited to, the use of historic samples not representative of contemporary patient cohorts, missing values, composite outcomes with composite events of different clinical importance, lack of external validation, and missing calibration. In this document different cut-off for 5 years risk of SCD/VA is used for indication of ICD. Each cut-off was chosen by the original authors and the task force group considering the competing risk, the outcome measured (SCD vs VA) and the robustness of each risk calculator.

4.5. Awareness and intervention: public basic life support, and access to automated external defibrillators

Survival rate remains strikingly low after OHCA,[89–95] although major regional disparities have been described.[96] Early implementation of

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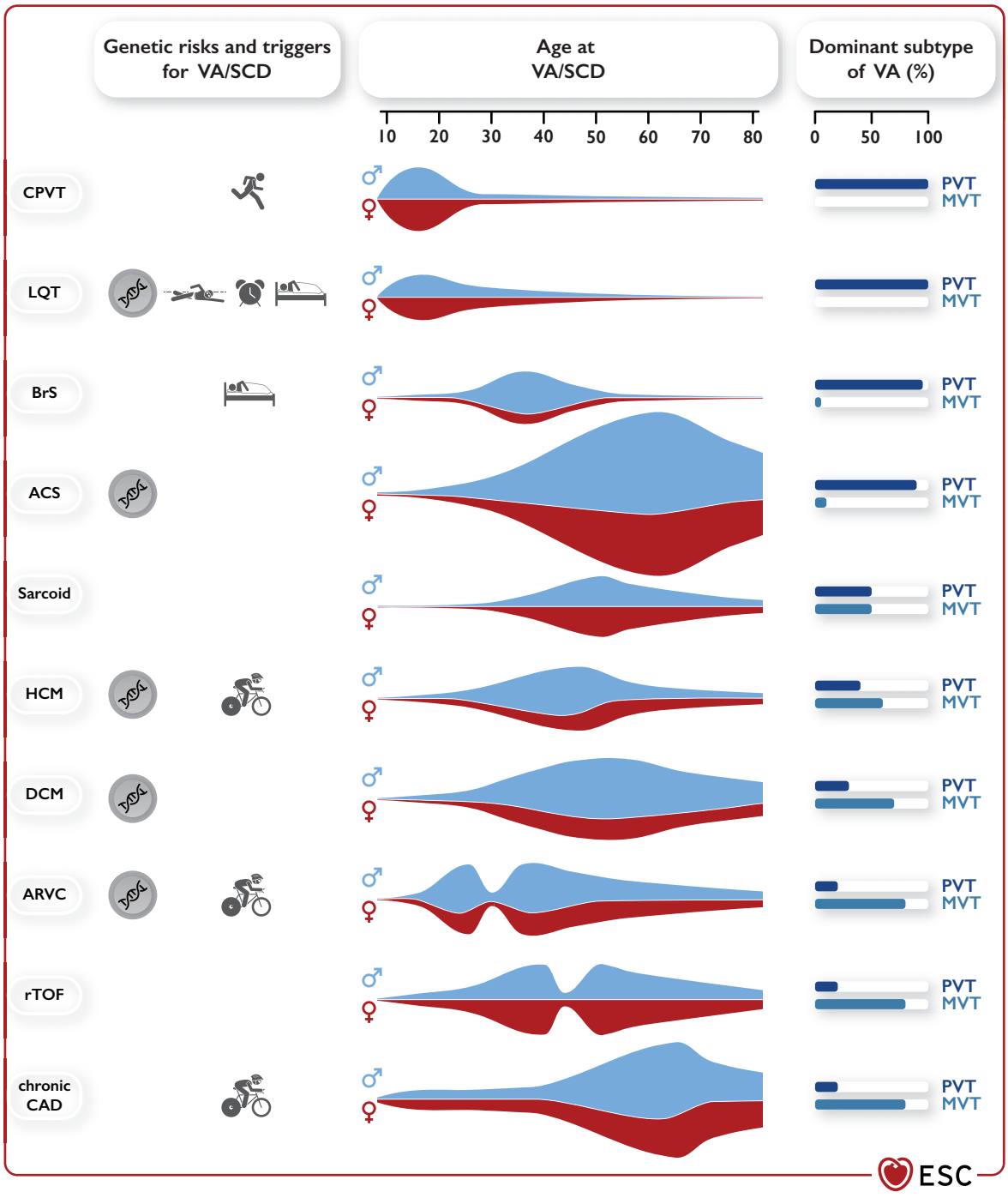

Figure 1 Central figure. Genetic risk for VA/SCD, typical triggers for VA/SCD, age at presentation with VA/SCD, sex predominance, and typical VA (PVT/VF vs. MVT) in different diseases associated with VA/SCD. ACS, acute coronary syndrome; ARVC, arrhythmogenic right ventricular cardiomyopathy; BrS, Brugada syndrome; CAD, coronary artery disease; CPVT, catecholaminergic polymorphic ventricular tachycardia; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LQT, long QT syndrome; MVT, monomorphic ventricular tachycardia; PVT, polymorphic ventricular tachycardia; rTOF, repaired tetralogy of Fallot; SCD, sudden cardiac death; VA, ventricular arrhythmia; VF, ventricular fibrillation.

resuscitative interventions, especially prior to emergency medical system arrival, has been identified as key elements to improve survival.[95,97] Bystander cardiopulmonary resuscitation (CPR) and use of public automated external defibrillators (AEDs) have demonstrated improvement of neurological and functional outcome as well as survival of OHCA patients. Data support the need for increased availability of public access defibrillators and community training in basic life support,[89–95] preferably initiated in childhood and repetitive.[98–100] Finally, dispatch of basic life support-trained volunteers, through specific mobile apps networks, has been shown to increase the rate of bystander-initiated CPR, and as a result, greatly reduces the resuscitation-free interval and improves the outcome of

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OHCA victims.[101–103] Education of public officials and community members regarding the importance of increasing rates of bystander CPR and promoting the use of early defibrillation by lay and professional rescuers is critical to increasing survival rates.

Recommendation Table 1 — Recommendations for public basic life support and access to automated external defibrillators

Recommendations	Class[a]	Level[b]
It is recommended that public access defibrillation be available at sites where cardiac arrest is more likely to occur.[c,90–92]	I	B
Prompt CPR by bystanders is recommended at OHCA.[93–95]	I	B
It is recommended to promote community training in basic life support to increase bystander CPR rate and AED use.[93,97,104]	I	B
Mobile phone-based alerting of basic life support-trained bystander volunteers to assist nearby OHCA victims should be considered.[101–103,105]	IIa	B

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AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest.
[a]Class of recommendation.
[b]Level of evidence.
[c]Shopping centres, stadiums, public transport stations, casinos.

5. Evaluation and treatment. General aspects

5.1. Diagnostic tools

5.1.1. History and physical examination

History should focus on 'red flags', including features of arrhythmic syncope, e.g. absence of vagal prodrome, and family history of premature or SCD including, e.g. drowning or car accident in long QT syndrome (LQTS), and CPVT.[1,106] Subtle features to suggest inherited causes include a family history of epilepsy, sudden infant death syndrome, deafness (LQTS), heart failure, or pacemaker implantation at <50 years old. Features of diseases related to pro-arrhythmic conditions include mid-systolic click in mitral valve prolapse (MVP) and outflow tract murmurs with Valsalva in HCM. Specific skin features may be relevant, e.g. Lupus pernio, erythema nodosum in sarcoidosis, angiokeratoma in Fabry's disease, xanthelasma/xanthoma, and palmoplantar keratosis in ARVC.

5.1.2. Laboratory testing

Natriuretic peptides (b-type-natriuretic peptide, or N-terminal pro-b-type-natriuretic peptide) may have a role in the identification of individuals at increased risk of SCD in the general population[107,108] or in patients with CAD.[109] There is not sufficient evidence to use b-type-natriuretic peptide as a method to select the need for an ICD.[110,111]

5.1.3. Non-invasive and invasive tests

5.1.3.1. Electrocardiogram and ambulatory electrocardiographic monitoring[2]

The 12-lead ECG is an important tool for the diagnosis of underlying disease, for risk stratification in selected populations, and for the diagnosis of the VA subtype, if captured. Documentation of arrhythmias related to symptoms is clinically pivotal but may be challenging with sporadic events. The type of ECG-monitoring device and the recording time should therefore match the frequency of clinical events. Monitoring over a period of 24–48 h (typically 'Holter recording') is appropriate for daily arrhythmias,[112] while intermittent monitoring over a longer period, with patient-activated ECG recorders (or mobile-health/smartphones), should be preferred for infrequent events.[113] Implantable loop recorders (ILR) can be useful in diagnosing arrhythmias in patients with potentially life-threatening symptoms, such as unexplained syncope.[114]

5.1.3.2. Signal-averaged electrocardiogram

Signal-averaged electrocardiogram (SaECG) can detect very low amplitude signals ('late potentials') in the terminal QRS segment[115] using three time-domain measurements: QRS duration, low-amplitude (<40 μV) signal duration and root mean square voltage of terminal 40 ms QRS.[112] Abnormalities in the SaECG can also be assessed by frequency-domain analysis.[112] SaECG can contribute to the diagnosis of ARVC.[116]

5.1.3.3. Exercise testing

Exercise testing is useful for the diagnosis and for evaluating response to therapy in patients with suspected/proven adrenergic-dependent rhythm disturbances, such as exercise-induced idiopathic MVT, PVT, or bidirectional VT in CPVT.[117,118] The 4-minute recovery QTc after exercise testing can contribute to the diagnosis LQTS.[119]

5.1.3.4. Imaging

Imaging is crucial to assess cardiac function and detect cardiomyopathies (📖 ESC CardioMed chapter 10).[120] A negative imaging study supports primary electrical disease in a patient with VA. Echocardiography is a readily available and first-line diagnostic and risk stratification tool for valve diseases, CAD and DCM, HCM, ARVC,[121] and left ventricular non-compaction (LVNC). Echocardiographic strain-rate imaging allows differentiation between active and passive movement of myocardial segments and early detection of myocardial dysfunction. Wall motion abnormalities can indicate previous infarcts, cardiomyopathies, or inflammatory disease. Global longitudinal strain is a robust measure of left ventricular (LV) function and can detect subtle changes in LV function while LVEF is still preserved.[122] Strain imaging can assess mechanical dispersion reflecting inhomogeneous contraction that could be associated with increased risk of VA.[122–125]

CMR currently provides the most accurate and reproducible measurement of atrial, biventricular global and regional systolic function, and can detect myocardial oedema, fibrosis, infiltration, and

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perfusion defects (ESC CardioMed chapter 11.4).[126] CMR is more sensitive than echocardiography to diagnose ARVC,[127] is diagnostic in LVNC, and can detect apical aneurysms in HCM. Fibrosis detection by late gadolinium enhancement (LGE) contributes to VA risk stratification in HCM,[128] DCM,[129] and potentially in mitral valve prolapse arrhythmic syndrome.[130,131] Novel myocardial mapping techniques can detect diffuse fibrosis and can suggest the aetiology of left ventricular hypertrophy (LVH) for specific therapy guiding, e.g. Fabry disease and amyloidosis. The prognostic value remains to be evaluated.

Cardiac imaging by computed tomography (CT) has the advantage of a high spatial resolution (ESC CardioMed chapter 12.1).[132] ECG synchronization, additional breath-hold sequences, and beta-blocker to lower the heart rate improve the quality. Radiation exposure is in the range of an invasive coronary angiogram (CAG). Coronary computed tomography angiography (CTA) is the preferred method to rule out coronary artery stenosis in patients with low probability of CAD.[133,134] The quality of almost all image modalities is influenced by the presence of frequent PVCs.

5.1.3.5. Provocative diagnostic tests

These are summarized in *Table 6*. Common tests performed are sodium channel blocker testing for Brugada syndrome (BrS) and adenosine test to exclude latent pre-excitation.[135,136] Epinephrine challenge may be useful in CPVT when exercise cannot be performed. Epinephrine test is not recommended for LQTS due to the high false positive rate and utility of exercise testing.[137] Coronary vasospasm as a cause of VF in the absence of obstructive coronary diseases/cardiomyopathy can be tested with incremental intracoronary doses of acetylcholine/ergonovine.

5.1.3.6. Electrophysiological study

Electrophysiological studies including measurement of baseline intervals (e.g. atrial–His interval [AH] and His–ventricular interval [HV]), programmed electrical stimulation (PES), and electroanatomical mapping can be used for diagnostic purposes and to guide therapy.[145–150] The yield of PES varies with the underlying cardiac condition and its severity, the presence or absence of spontaneous VT, concomitant drug therapy, stimulation protocol, and site(s) of stimulation. Typical protocols include stimulation from 2 right ventricular (RV) sites with 2–3 basic drive cycle lengths, introduction of 3 extrastimuli, and isoprenaline administration.[148,151,152]

In the current era, PES is mainly employed to confirm the diagnosis of VT and induce mappable VAs with non-inducibility being an ablation endpoint. Patients with heart failure and LVEF $\leq$35% generally will have an indication for an ICD; therefore, VT/VF induction before implantation is not necessary. In patients with SHD and mildly reduced or preserved LVEF who present with unexplained syncope, induction of SMVT with PES can be helpful to identify the underlying cause and to predict subsequent events.[146,153] PVT/VF induction in SHD is in general considered as a non-specific finding.[154–156]

In primary electrical diseases, PES is not of prognostic value, although there is some evidence to consider its use in BrS.[127] Invasive electrophysiological evaluation can have important clinical implications in patients with myotonic dystrophy.[157]

With advances in high-density mapping, voltage mapping, conduction/repolarisation metrics, and electrogram fractionation can be employed to identify ablation targets, or to diagnose cardiomyopathic disease. Endocardial mapping may be helpful in the differentiation of ARVC from benign outflow tract VT and for targeting biopsy in suspected myocarditis, ARVC, and sarcoidosis cases.[158–162]

5.1.4. Genetic testing

Massive parallel or next-generation sequencing has led to increasing availability of genetic testing at reduced cost. Most diagnostic cardiac genetic testing employs large gene panels determined by associations with disease generated by prior research, i.e. candidate genes.[163] Many previous gene associations have, however, been challenged for their diagnostic utility. Therefore, it is not recommended to include questionable genes in routine diagnostic panels.[164–168] Genome-wide association studies have identified that common genetic variation single nucleotide polymorphisms can cause or modify phenotypes in BrS, LQTS, HCM, and DCM. Polygenic risk scores, measures derived from the cumulative effects of these single nucleotide polymorphisms, may therefore play a role in diagnosis and prognostication in these conditions in the future.[168–173]

Sequencing produces digital data that require subsequent bioinformatic analysis, permitting accurate ascertainment of most DNA alterations affecting the coding frame of each gene.[174] The most common findings are single nucleotide variants causing simple amino acid substitutions (missense), premature terminations, or splicing abnormalities. Insertions and/or deletions are rarer. The clinical importance of most non-coding variants is still to be determined.[174,175]

A framework for the interpretation of disease causation by genetic variants has standardized adjudication into five classes: V 'pathogenic'; IV 'likely pathogenic'; III 'variant of uncertain significance'; II 'likely benign'; and I 'benign'. A combination of evidence is employed: gene–disease association; presence of a variant in healthy and/or diseased populations; *in silico* data; *in vitro* and *in vivo* functional data; and family segregation data.[176]

A mutation (Class IV or V variant) can be used immediately either for confirmation of diagnosis in probands (the first affected family member), or for initial diagnosis of relatives and may help to guide therapy and/or prognosis. Periodic reassessment of all class IV and III variants is indicated.[176]

Pre-implantation genetic testing is an early form of pre-natal genetic diagnosis. Genetic diagnoses of *in vitro* fertilized embryos are identified by biopsies, thereby allowing transfer of genetically normal embryos into the uterus. If the technique is available, it is important to provide information to patients with monogenic heart diseases in child-bearing age. The legislation for pre-implantation genetic testing varies in different countries and strategies differ.

Genetic and clinical testing should be undertaken only by multidisciplinary teams including professionals with skills to counsel on the implications and the uncertainty of results and experienced cardiologists able to direct testing to the correct phenotype.[135,177–179] A negative result does not exclude a diagnosis and should not be used for this purpose. A framework for genetic and other clinical diagnostic tests for primary electrical diseases based on evidence where available has been provided in *Table 7*.

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Table 6 **Intravenous provocative diagnostic tests**

Diagnostic test	Indication	Protocols Dose/infusion rate/duration	Positive test	Contraindications	Criteria to stop test, counselling and management	Observation times	Location	Ref
Ajmaline	Family history of BrS or SADS. Resuscitated CA without SHD.	1 mg/kg over 5–10 min (maximum dose 100 mg) or 1 mg/kg at 10 mg/min. Record in standard and high precordial leads over 30 min.	BrS type 1 ECG.	Type I BrS ECG, HF. Precaution if evidence of conduction disease (consider temporary pacing wire).	VT/VF, Type 1 BrS ECG, PVCs, QRS widening >150%. If VT/VF, administer iv isoprenaline, iv sodium bicarbonate.	30 min if negative test; 4 h if positive test.	Cath lab or outpatient testing location with full resuscitation equipment.	136,138,139
Flecainide	Same as ajmaline.	2 mg/kg over 10 min (maximum dose 150 mg). Record in standard and high precordial leads over 30 min.	Same as ajmaline.	Same as ajmaline.	Same as ajmaline.	4 h if negative test; 24 h if positive test.	Same as ajmaline.	140
Epinephrine	CPVT and resuscitated CA with or without SHD when exercise test not feasible. Family history of SADS.	Rest 10 min. Start at 0.025 μg/ kg/ min for 10 min increase sequentially to 0.05, 0.1 and 0.2 μg/ kg/min in 5 min steps.	≥3 beats of PVT or bidirectional VT.	QTc prolongation ≥480 ms.	Systolic blood pressure ≥ 200 mmHg, non-sustained VT or PVT, >10 PVCs /min, T-wave alternans, or patient intolerance. If symptoms persist after discontinuation, iv metoprolol 2.5–5 mg over 1 min.	30 min.	Same as ajmaline.	141
Acetylcholine	Suspicion of coronary vasospasm.	Intracoronary injection: RCA: 20 and 50 μg. LCA: 20, 50, and 100 μg over 20 s. >3-min intervals between injections. Maximal dose of 50 μg in the RCA and 100 μg in the LCA.	Coronary artery spasm visualized during procedure.	Left main stenosis >50%, 3-vessel disease, 2-vessel disease with total occlusion, NYHA III/IV HF, renal failure, severe bronchial asthma.	Temporary wire for back-up pacing. Risk of cardiogenic shock.	Normal post-procedure observational time.	Cath lab.	142

Continued

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Ergonovine	Same as acetylcholine.	Intracoronary stepwise injection: RCA (20–60 mg) LCA (20–60 mg) over a period of 2–5 min.	Same as acetylcholine	Left main stenosis >50%, 3-vessel disease, 2-vessel disease with total occlusion, NYHA III/V HF, renal failure.	Temporary wire should be placed for back-up pacing. Risk of cardiogenic shock.	Same as acetylcholine.	Cath lab.	[143]
Adenosine	Exclude latent pre-excitation.	6, 12, 18 mg boluses up to maximum dose 24 mg or until AV block or pre-excitation occurs.	Identification of accessory pathway.	Asthma, sinus node disease, allergy to adenosine.	Side effects: Bronchospasm, bradycardia, asystole, AF, seizure. Antagonist: theophylline.	5 min.	Same as ajmaline.	[144]

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AF, atrial fibrillation; AV, atrioventricular; BrS, Brugada syndrome; CA, cardiac arrest; CPVT, catecholaminergic polymorphic ventricular tachycardia; ECG, electrocardiogram; HF, heart failure; LCA, left coronary artery; NYHA, New York Heart Association; PVCs, premature ventricular complexes; PVT, polymorphic ventricular tachycardia; RCA, right coronary artery; SADS, sudden arrhythmic death syndrome; SHD, structural heart disease; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 7 Genetic tests and suggested work-up of probands and relatives with primary electrical diseases

			LQTS	BrS	CPVT	Idiopathic VF	ERS
	Genetic test		Class I[a]	Class I	Class I[a]	Class IIb	Class IIb
Proband	**Initial clinical test**	**Cornerstone for diagnosis**	ECG Exercise test	ECG and high precordial lead ECG Sodium channel blockers provocative test[c]	Exercise test	See *Section 5.2.3*, scenario 3	ECG
		Other tests/processes	Exclude acquired LQTS	Exclude phenocopy[b]	Exclude phenocopy[b]/SHD		Holter Echocardiography
	Follow-up		1–3 years dependent on level of risk				
Relatives	**Clinical screening**		ECG Exercise test (when feasible) From birth	ECG and high precordial lead ECGs: start at 10 years Sodium channel blockers provocative test[c]: start >16 years unless clinically indicated[180,181]	ECG Exercise test From birth	ECG and high precordial lead ECGs Exercise test Echocardiogram[182]	ECG Echocardiogram
	Follow-up	Positive phenotype and/or Class IV/V variant	1–3 years dependent on level of risk				
		Negative phenotype and no Class IV/V variant	Discharge				

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BrS, Brugada syndrome; CPVT, catecholaminergic polymorphic ventricular tachycardia; ECG, electrocardiogram; ERS, early repolarization syndrome; LQTS, long QT syndrome; VF, ventricular fibrillation.
[a]Including neonatal genetic testing.
[b]A phenocopy has characteristics of a genetic disease but is produced environmentally.
[c]Not in case of a documented type 1 Brugada pattern.

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Recommendation Table 2 — Recommendations for genetic testing

Recommendations	Class[a]	Level[b]
Genetic testing is recommended when a condition is diagnosed in a living or deceased individual with a likely genetic basis and a risk of VA and SCD.[56,183]	I	B
When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.[176]	I	C
When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I	C
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.[179]	I	C
It is recommended that Class III (variants of uncertain significance) and Class IV variants should be evaluated for segregation in families where possible, and the variant re-evaluated periodically.	I	C
It is not recommended to undertake genetic testing in index patients with insufficient evidence of a genetic disease.	III	C

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SCD, sudden cardiac death; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.

5.2. Diagnostic evaluation at first presentation with ventricular arrhythmia in patients without known cardiac disease

VA and (aborted) SCD are common first manifestations of a previously not known cardiac condition. A comprehensive diagnostic evaluation is provided for five frequently encountered scenarios.

5.2.1. Scenario 1: Incidental finding of a non-sustained ventricular tachycardia

An algorithm for the evaluation of patients presenting with an incidental finding of NSVT is presented in *Figure 2*.

Incidental NSVT is a common finding during routine cardiological evaluation (e.g. for non-cardiac diseases, pre-initiation of oncological treatments, pre-participation in sports) and monitoring before induction of anaesthesia/sedation for non-cardiac procedures.[184] Patients with incidentally found NSVT require further evaluation. A recent syncope suspicious for cardiac origin is a high-risk symptom and may prompt admission to hospital.[1,185] The morphology of NSVT (polymorphic or monomorphic) is important to assess. Typical MVT morphologies (*Figure 3*) can suggest an idiopathic origin with favourable prognosis. In contrast, short-coupled PVC initiating non-sustained PVT or monomorphic NSVT with short cycle length (usually <300 ms, average 245 ± 28, in one series) may identify patients at higher risk of SCD.[186,187] Resting 12-lead ECG is a first-line evaluation and may show signs of SHD or primary electrical diseases (ESC CardioMed chapter 8.6).[188] Echocardiography is the first-line imaging modality that provides important information about cardiac function and potential SHD (ESC CardioMed 10.3, 10.10, 10.12).[120,189,190] Holter monitoring is useful to assess the frequency of NSVT and related PVCs (ESC CardioMed chapter 8.9).[191] In addition, an at least 3-lead Holter (V1, two inferior leads) may give a first estimate if NSVT/PVC are unifocal or multifocal and of the NSVT site(s) of origin. The latter is important if the NSVT has not been previously documented on a 12-lead ECG.[192]

An exercise test can be helpful to capture the 12-lead ECG of NSVT and to identify exercise-induced arrhythmias. Increasing arrhythmias with exercise, not suggestive of idiopathic origin, should raise suspicion of SHD and may necessitate advice to refrain from physical exercise until diagnosis and initiation of appropriate treatment. Underlying significant CAD should be ruled out according to the patient's pre-test probability.

CMR should be considered when cardiomyopathies or inflammatory diseases are suspected on initial evaluation (ESC CardioMed chapter 10.4).[193] In addition, CMR can identify areas of fibrosis as substrates of NSVT.[129]

Recommendation Table 3 — Recommendations for evaluation of patients presenting with newly documented ventricular arrhythmia

Recommendations	Class[a]	Level[b]
In patients with newly documented VA (frequent PVCs, NSVT, SMVT), a baseline 12-lead ECG, recording of the VA on 12-lead ECG, whenever possible, and an echocardiogram are recommended as first-line evaluation.	I	C
In patients with newly documented VA (frequent PVCs, NSVT, SMVT) and suspicion of SHD other than CAD after initial evaluation, a CMR should be considered.[194,195]	IIa	B
In patients with an incidental finding of a NSVT, a ≥24 h Holter ECG should be considered.	IIa	C

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CAD, coronary artery disease; CMR, cardiac magnetic resonance; ECG, electrocardiogram; NSVT, non-sustained ventricular tachycardia, PVCs, premature ventricular contractions; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.

5.2.2. Scenario 2: First presentation of sustained monomorphic ventricular tachycardia

An algorithm for the evaluation of patients presenting with a first SMVT episode is presented in *Figure 4*.

The majority of patients presenting with SMVT have underlying SHD. SMVT in SHD is mainly due to scar-related re-entry and only occasionally due to re-entry involving a diseased conduction system or due to focal sources.

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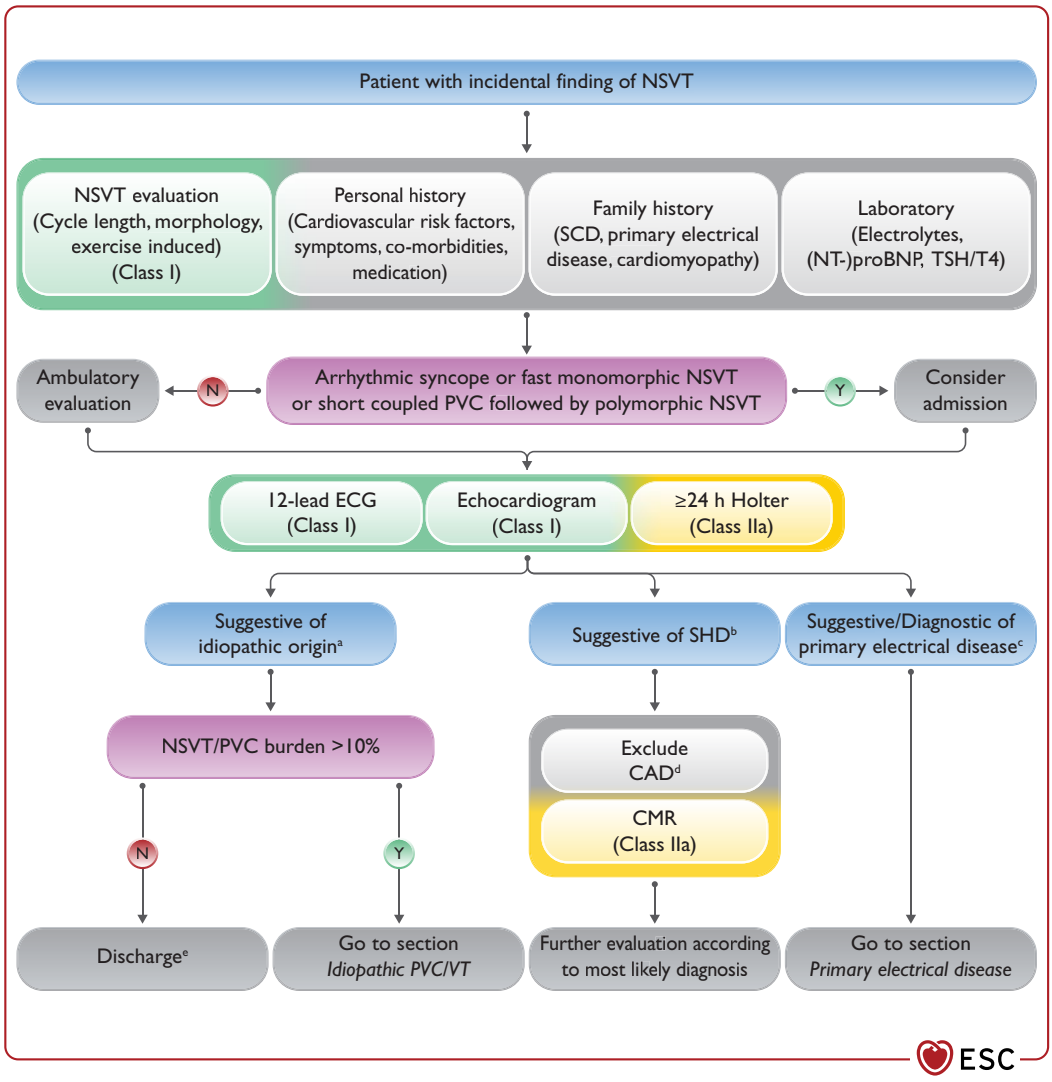

Figure 2 Algorithm for the evaluation of patients presenting with an incidental finding of non-sustained ventricular tachycardia. CAD, coronary artery disease; CMR, cardiac magnetic resonance; ECG, electrocardiogram; N, No; NSVT, non-sustained ventricular tachycardia; PVC, premature ventricular complex; SCD, sudden cardiac death; SHD, structural heart disease; Y, Yes. [a]ECG morphology suggestive of RVOT or fascicular origin, negative family history, normal 12-lead ECG, and echocardiogram. [b]e.g. atrioventricular conduction abnormalities, Q waves, broad QRS complex, ST/T waves deviations, abnormally high or low voltages. Ventricular dysfunction/dilatation/hypertrophy/wall thinning, wall motion abnormalities, multitopic PVCs/NSVTs/increasing ventricular arrhythmia (VA) burden with exercise. [c]e.g. Brugada pattern, long/short QT, polymorphic/bidirectional VA with exercise. [d]Diagnostic test to exclude CAD according to patient profile and symptoms. [e]Consider re-evaluation in case of new symptoms or changes in patient clinical condition.

The diagnosis of the underlying aetiology and identification of patients with idiopathic VT is important. Initial evaluation includes a comprehensive clinical and family history, 12-lead ECG, and echocardiography. Recording of the 12-lead VT ECG is indicated as it provides important information on the VT site of origin. Specific VT morphologies (e.g. right ventricular outflow tract [RVOT] or fascicular origin) (*Figure 3*) in the absence of a family history for cardiomyopathies and without evidence for SHD are suggestive for idiopathic VTs.[196] Atypical ECG morphologies and uncommon clinical presentations should raise suspicions for underlying SHD even if baseline ECG and echocardiogram are normal. In this scenario, additional evaluation with CMR should be considered.[194] Bundle branch reentrant ventricular tachycardia (BBR-VT), resembling bundle branch block configuration on the ECG, is a feature of conduction impairment, e.g. in DCM, myotonic dystrophy, and post-cardiac valve surgery (*Figure 5*).

If initial evaluation raises suspicion of underlying CAD, a CAG can exclude significant CAD. If ECG and echocardiography are suggestive for a cardiomyopathy, CMR provides important diagnostic information on scar distribution and tissue characteristics (*Section 5.1.3.4*). When non-invasive evaluation is inconclusive, electroanatomical mapping and PES may be considered for the differential diagnosis between idiopathic VT and early ARVC.[197] Electroanatomical mapping-guided biopsy can be of value to provide a tissue diagnosis for ARVC and inflammatory diseases with a focal distribution (e.g. cardiac sarcoidosis).[198,199] In cases of suspected inflammatory diseases, positron emission tomography CT (PET-CT), autoimmune serology, and biopsies of affected tissue are part of the diagnostic evaluation.[200,201]

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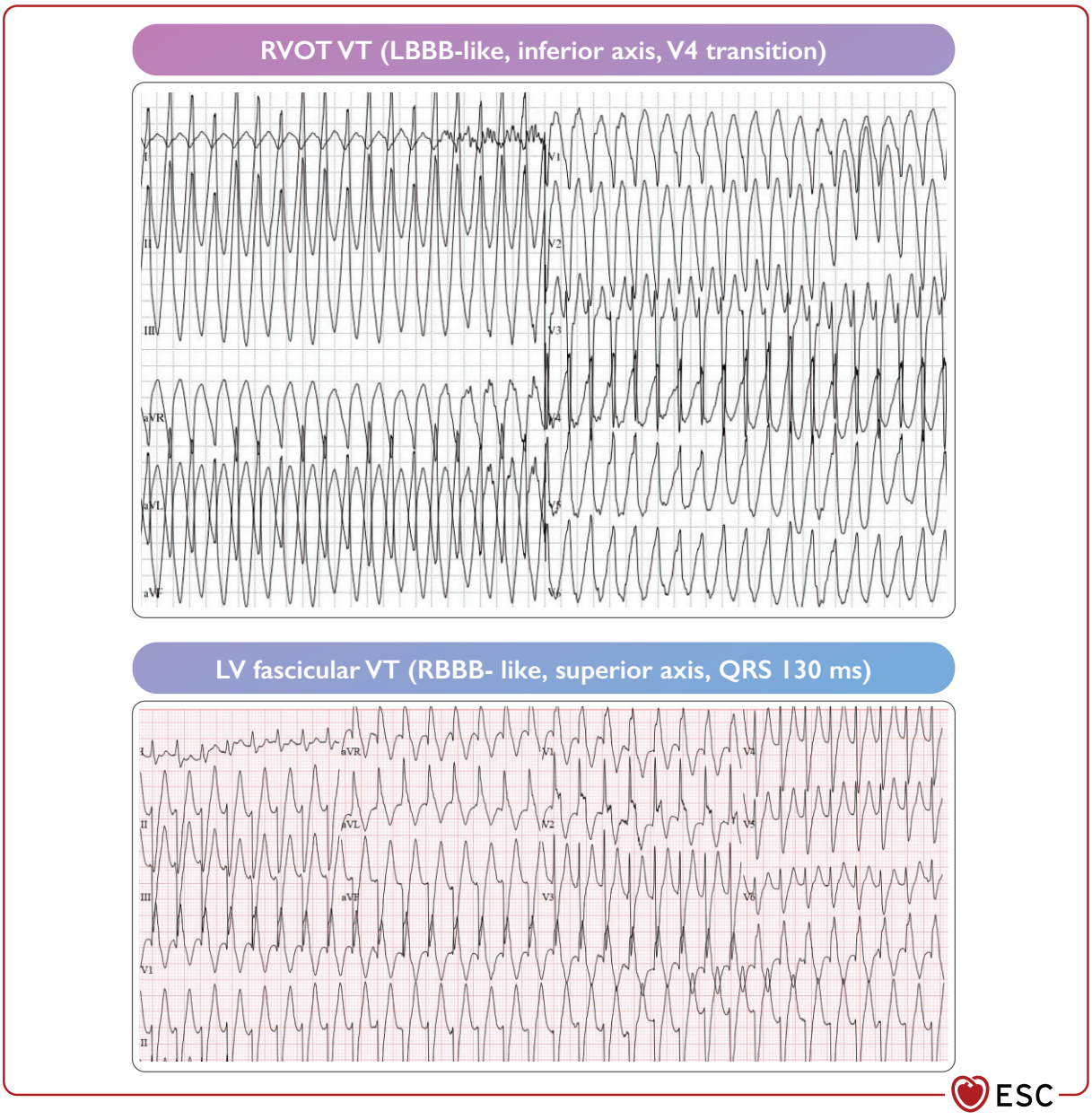

Figure 3 Typical idiopathic ventricular tachycardia morphologies. LBBB, left bundle branch block; LV, left ventricle; RBBB, right bundle branch block; RVOT, right ventricular outflow tract; VT, ventricular tachycardia.

Recommendation Table 4 — Recommendations for evaluation of patients presenting with a first episode of sustained monomorphic ventricular tachycardia

Recommendations	Class[a]	Level[b]
In patients presenting with a first SMVT episode, electrophysiological study, electroanatomical mapping, and mapping-guided biopsies may be considered for aetiological evaluation.[197–199,202]	IIb	C

SMVT, sustained monomorphic ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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5.2.3. Scenario 3: Sudden cardiac arrest survivor

An algorithm for the evaluation of sudden cardiac arrest survivors is presented in *Figure 6*.

Urgent CAG is recommended for patients presenting with ST elevation myocardial infarction (STEMI).[203–206] Despite disparate findings of pooled data analyses,[207–211] three randomized controlled trials (RCTs) have found no significant benefit for early CAG in cardiac arrest (CA) without ST-elevation. In case of electrical instability after CA, suspicious for ongoing ischaemia, this panel found a CAG indicated. Brain and chest CT scan may acutely identify non-cardiac causes of aborted SD,[212] as well as blood test results for pertinent toxicological analysis.[213–215] Retention and storage of suitable blood samples will allow subsequent diagnostic evaluation, including DNA analysis.[213]

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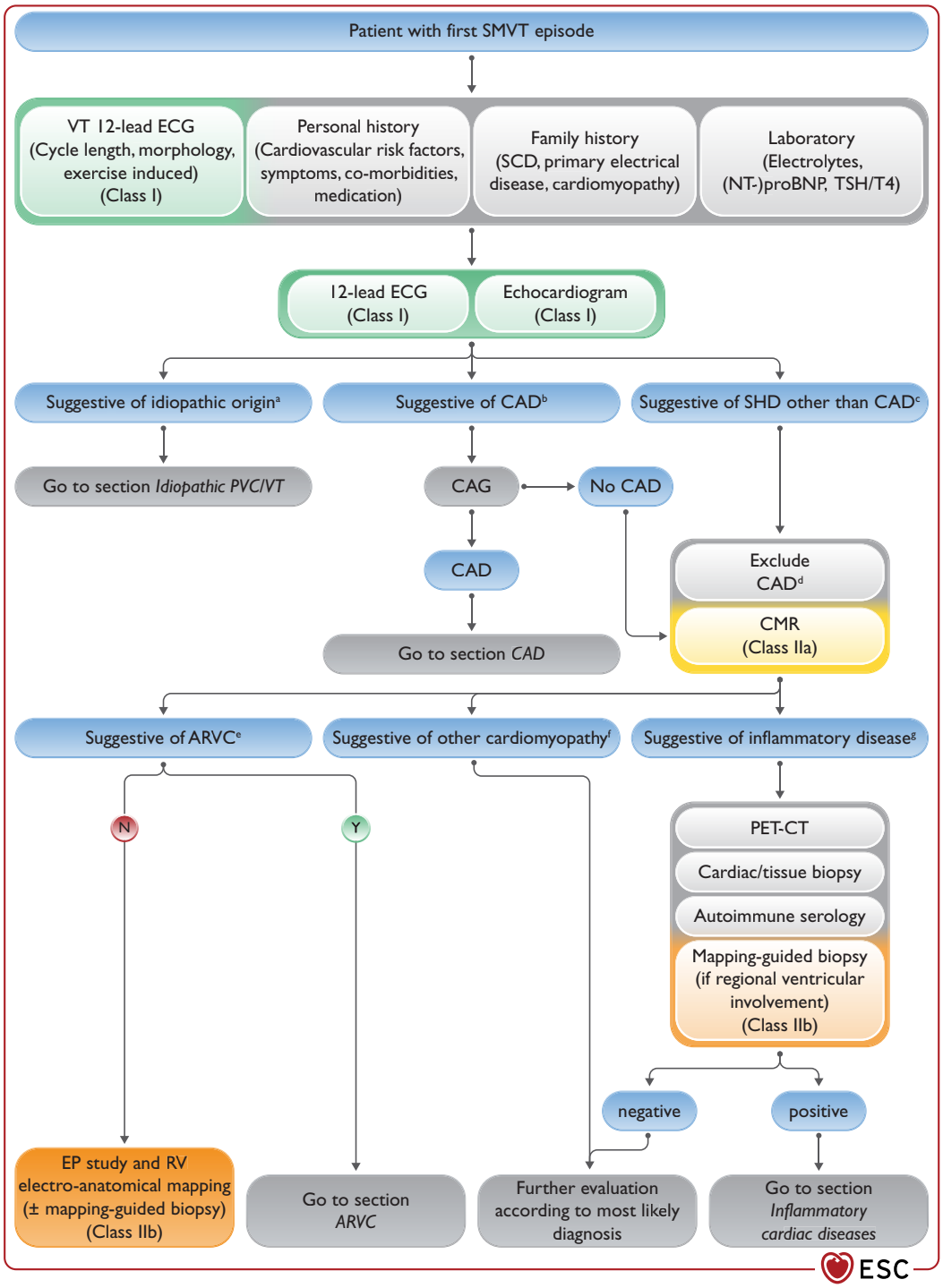

Figure 4 Algorithm for the evaluation of patients presenting with a first sustained monomorphic ventricular tachycardia episode. ARVC, arrhythmogenic RV cardiomyopathy; CAD, coronary artery disease; CAG, coronary angiography; CMR, cardiac magnetic resonance; ECG, electrocardiogram; EP, electrophysiological; LV, left ventricular; N, No; PET-CT, positron emission tomography and computed tomography; PVC, premature ventricular complex; RV, right ventricular; SCD, sudden cardiac death; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; VT, ventricular tachycardia; Y, Yes. [a]ECG morphology suggestive of RV outflow tract or fascicular origin, negative family history, normal 12-lead ECG, and echocardiogram. [b]e.g. Q waves, QRS fragmentation, ST/T abnormalities, wall motion abnormalities in coronary territories. [c]e.g. atrioventricular (AV) conduction abnormalities, Q waves, broad QRS complex, T-wave inversion, abnormally high or low voltages. Ventricular dysfunction/dilatation/hypertrophy/wall thinning/wall motion abnormalities/diffuse hypokinesia. [d]Diagnostic test to exclude CAD according to patient profile and symptoms. [e]According to revised task force criteria.[116] [f]e.g. AV conduction abnormalities, abnormally high or low voltages, broad QRS, ST/T wave deviations, LV dilatation and dysfunction, late gadolinium enhancement with non-ischaemic distribution. [g]e.g. AV conduction abnormalities, broad QRS, ST/T deviations, multifocal PVCs, inflammatory hyperaemia and oedema, fibrosis, LV and RV systolic dysfunction, pericardial effusion.

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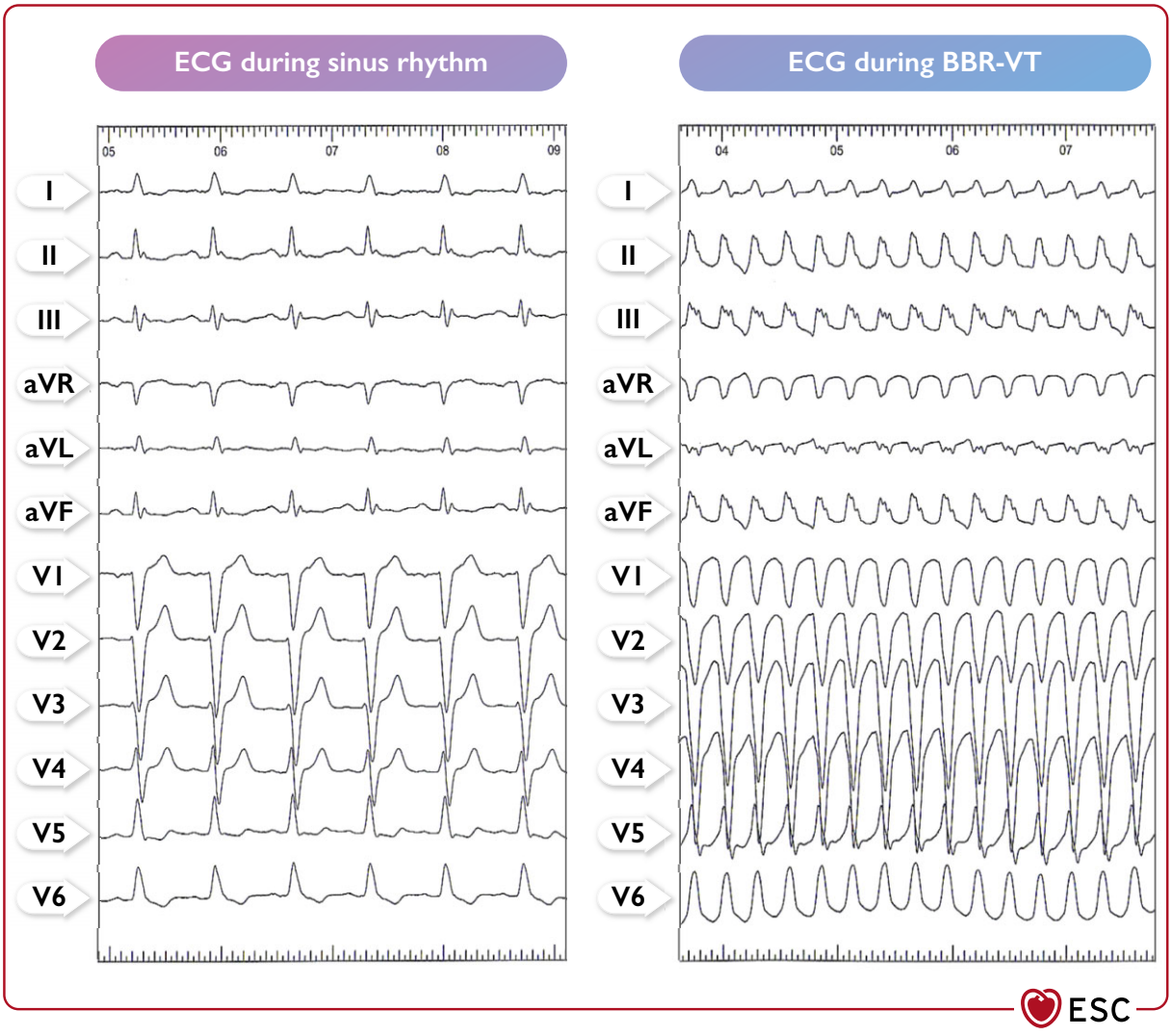

Figure 5 Bundle branch re-entrant ventricular tachycardia. BBR-VT, bundle branch re-entrant ventricular tachycardia; ECG, electrocardiogram.

Any ECG tracing from emergency services, as well as recordings from interrogation of cardiovascular implantable electronic devices (CIEDs) can also contribute to diagnosis.[216–219] The resting 12-lead ECG (including high precordial lead)[220] is fundamental and should be repeated regularly during recovery. Continuous heart rhythm monitoring is recommended until definite treatment.[221,222] Echocardiography may allow early diagnosis to identify any structural abnormality.[222,223] Coronary imaging will be important to exclude CAD, dissection, or anomalies.[62,224] Coronary optical coherence tomography and/or intravascular ultrasound may be helpful to characterize stenosis/plaque stability and underlying mechanism of stenosis.[225] CMR has repeatedly been shown to provide significant incremental diagnostic value, in particular for concealed cardiomyopathy.[131,226–228] Primary electrical diseases may be uncovered by provocative manoeuvres such as sodium channel blocker challenge,[136,229–231] lying to standing ECGs,[232,233] adenosine challenge,[144,234] epinephrine challenge,[141,152,235–239] ergonovine/acetylcholine,[222,240] mental stress,[241,242] and exercise testing.[116,117,119,232,243] Electrophysiological study and electroanatomic mapping may be useful to provide patient-specific insights into the mechanism of CA and to offer therapeutic options in some patients.[244–248] Genetic testing may identify a molecular cause of SCA by identifying pathogenic mutations in genes associated with specific phenotypes.[213,249,250]

Recommendation Table 5 — Recommendations for evaluation of sudden cardiac arrest survivors

Recommendations	Class[a]	Level[b]
Diagnostic evaluation		
The investigation of a SCA survivor without obvious extra-cardiac cause is recommended to be overseen by a multidisciplinary team.[177,251–256]	I	B
In electrically unstable patients after SCA, with suspicion of ongoing myocardial ischaemia, a coronary angiogram is indicated.	I	C

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In SCA survivors, brain/chest CT scan should be considered when patient characteristics, ECG, and echocardiography are not consistent with a cardiac cause.[212,257]	IIa	C
In SCA survivors, collection of blood samples at presentation is recommended for potential toxicology and genetic testing.[56,214]	I	B
Retrieval of recordings from CIEDs and wearable monitors is recommended for all SCA survivors.[217,218]	I	B
In SCA survivors, repeated 12-lead ECGs during stable rhythm (including high precordial lead ECG), as well as continuous cardiac monitoring, are recommended.[220,222]	I	B
Echocardiography is recommended for evaluation of cardiac structure and function in all SCA survivors.	I	C
Coronary imaging and CMR with LGE are recommended for evaluation of cardiac structure and function in all SCA survivors without a clear underlying cause.[62,222,223,226]	I	B
Sodium channel blocker test and exercise testing is recommended in SCA survivors without a clear underlying cause.[117,222,258–260]	I	B
In SCA survivors, ergonovine, acetylcholine, or hyperventilation testing may be considered for the diagnosis of coronary vasospasm.[240,261]	IIb	B

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CIEDs, cardiac insertable electronic devices; CMR, cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiogram; LGE, late gadolinium enhancement; SCA, sudden cardiac arrest.
[a]Class of recommendation.
[b]Level of evidence.

5.2.4. Scenario 4: Sudden death victim

An algorithm for the evaluation of SD victims is presented in *Figure 7*.

Potential genetic cardiac disease can be identified in 25–49% of cases of SCD in the young (<50 years of age). This may also affect relatives of the deceased.[25,56,59] To find the cause of death, it is important to collect all available data on prior symptoms, comorbidities, and family history.[25,56,215,262,263]

The main role of autopsy in SD is to establish the cause of death. An expert cardiac pathologist alters the initial diagnosis in 41% of cases, highlighting the need for expert evaluation.[263–265] Inherited cardiac diseases identified at autopsy include cardiomyopathies (HCM, DCM, ARVC) and premature CAD.[25,27,56,266] A toxicology screen can reveal drug overdose or polypharmacy in 31–56% of young SD cases.[267,268] In autopsy-negative cases with negative toxicology, the term sudden arrhythmic death syndrome (SADS) may be applied and primary electrical diseases are potential causes.[56,183,223,253] Retaining tissue for DNA extraction is important for post-mortem genetic analysis, where the yield can be as high as one out of three.[183,269,270]

Clinical evaluation of first-degree relatives is important if the cause of death after autopsy is unknown (*Section 5.2.5*, scenario 5) or suspected to be inherited, with a reported combined diagnostic yield of genetic and clinical evaluation of 18–53%.[252,266,271] Post-mortem genetic testing on the deceased, targeted to the cause of death, identified mutations in around one-third of cases.[56,266,269]

Recommendation Table 6 — Recommendations for evaluation of sudden death victims

Recommendations	Class[a]	Level[b]
Investigation of unexpected SD, especially in case of suspicion of inherited disease, should be made a public health priority.[20,25,56]	I	B
In cases of SD, it is recommended to collect a detailed description of circumstances of death, symptoms prior to death, the family history, and to review prior medical files.[25,56]	I	B
A comprehensive autopsy is recommended, ideally, in all cases of unexpected SD, and always in those <50 years of age.[183,264,265,267,269,270]	I	B
In cases of SCD, it is recommended to retain samples suitable for DNA extraction and consult a cardiac pathologist when an inherited cause is suspected or the cause of death unexplained.[264,265]	I	B
Toxicology screens are recommended in SD cases with uncertain cause of death.[267,268]	I	B
For SCD where the cause is known or suspected to be heritable, genetic testing targeted to the cause is recommended.[56,266,269]	I	B
Following SADS, post-mortem genetic testing targeted to primary electrical disease is recommended when the decedent is young (<50) and/or the circumstances and/or family history support a primary electrical disease.[56,183,223]	I	B
When an autopsy diagnoses possible heritable cardiac disease, it is recommended to refer first-degree relatives for cardiac assessment in a specialized clinic.[271,272]	I	B
In non-autopsied cases of SD where inherited cardiac disease is suspected, it is recommended to refer first-degree relatives for cardiac assessment in a specialized clinic.[223,253,273]	I	B
Following SADS, post-mortem genetic testing in the decedent for additional genes may be considered.	IIb	C
Following SADS, hypothesis-free post-mortem genetic testing using exome or genome sequencing is not recommended.[274,275]	III	B

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DNA, deoxyribonucleic acid; SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death; SD, sudden death.
[a]Class of recommendation.
[b]Level of evidence.

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5.2.5. Scenario 5: Relatives of sudden arrhythmic death syndrome decedents

An algorithm for the evaluation of relatives of SADS decedents is presented in *Figure 8*.

Studies evaluating families of SADS decedents have identified underlying genetic heart disease in relatives that is presumed to be the cause of death in the absence of other findings. The overall diagnostic yield ranged from 18 to 53%, depending on population and clinical investigative protocols.[276] Aetiologies included LQTS, BrS, CPVT, and other disorders, such as cardiomyopathy.[276] All study protocols relied upon a similar initial approach of evaluating the decedent's pathological reports, medical history, and circumstances of death, and then offering clinical evaluation to relatives with a minimum of personal history, family history, physical examination, ECG and exercise test, and echocardiography.[223,252,253,277–282]

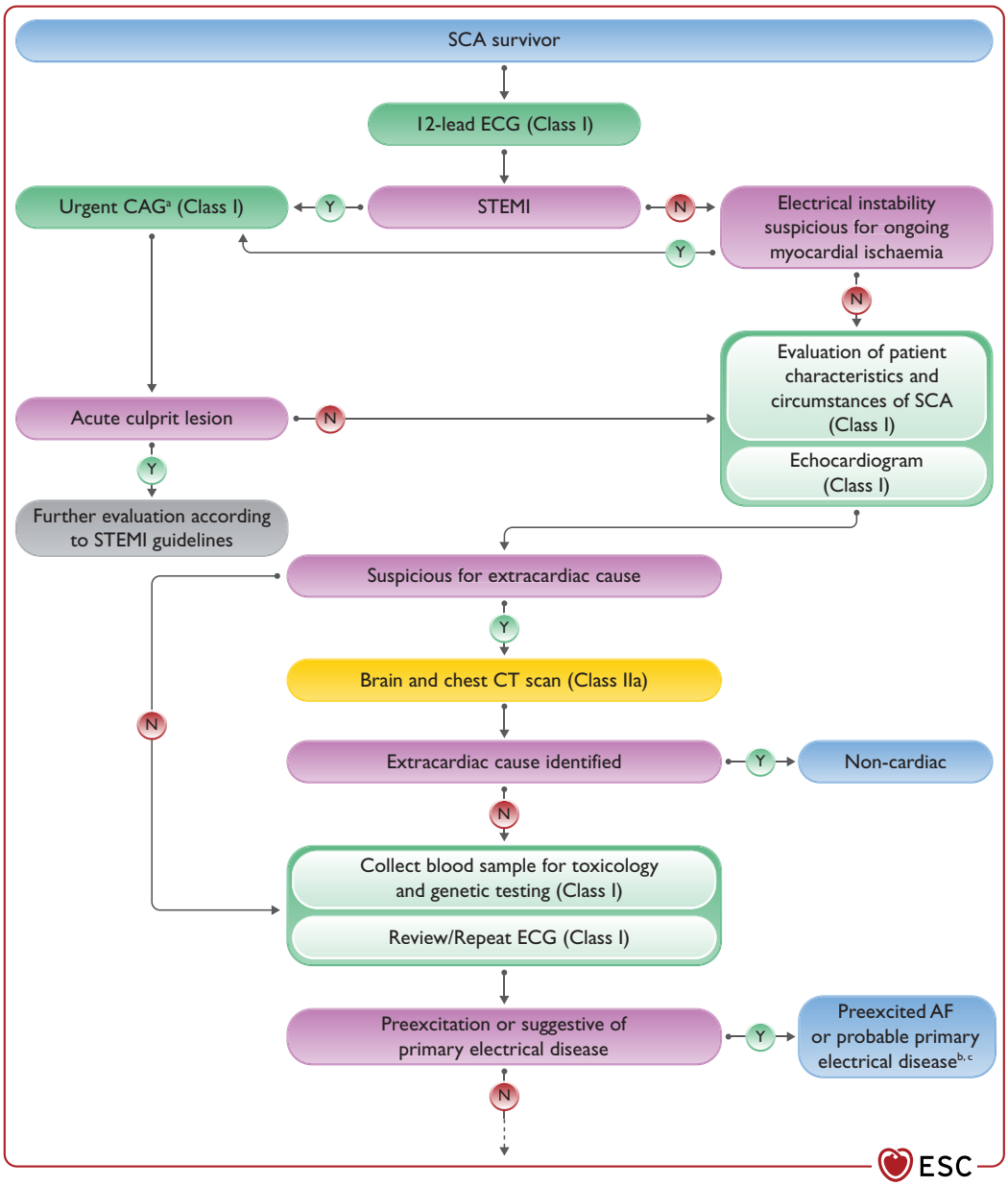

Figure 6 Part One. Algorithm for the evaluation of sudden cardiac arrest survivors.

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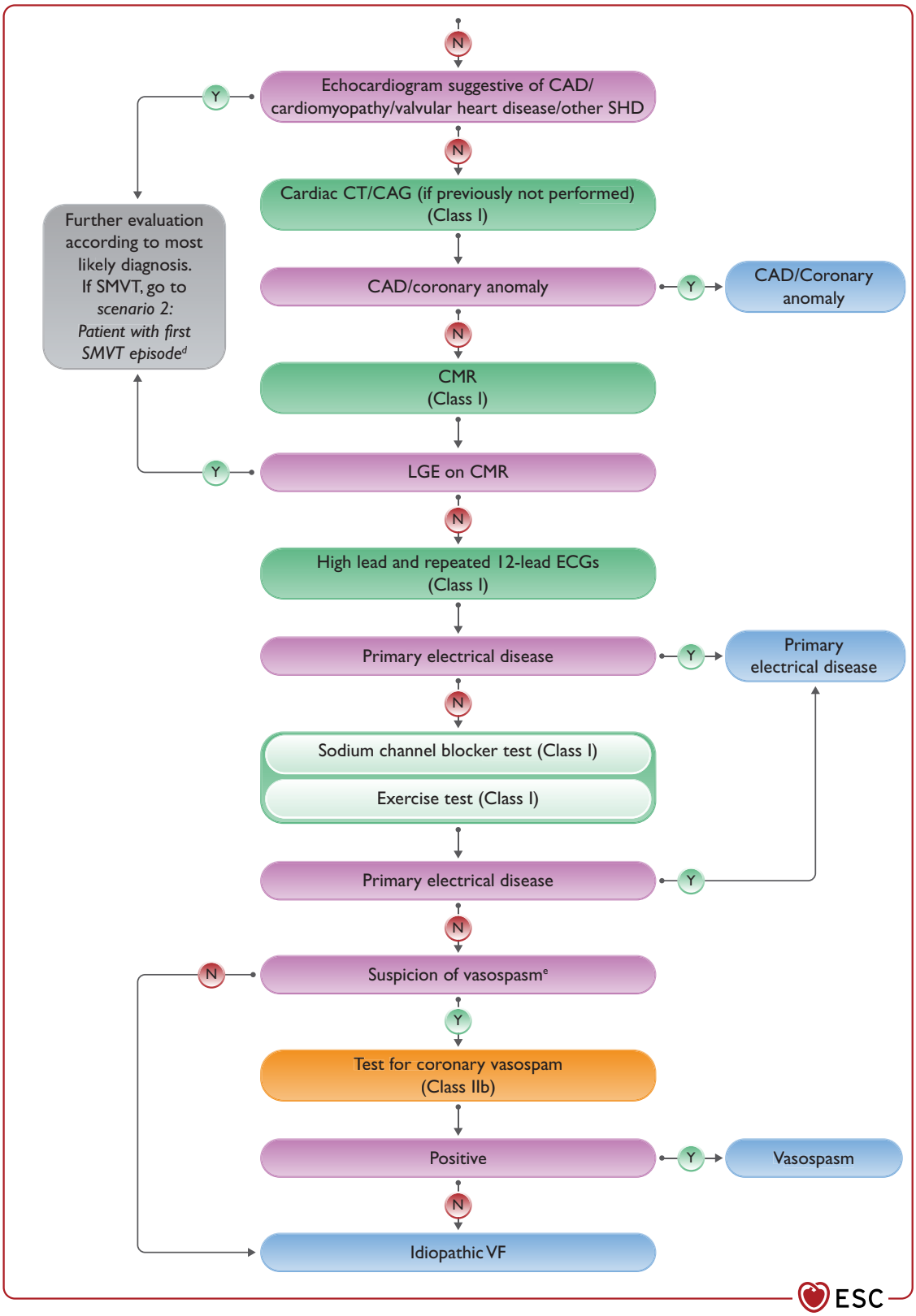

Figure 6 Part Two. Algorithm for the evaluation of sudden cardiac arrest survivors. AF, atrial fibrillation; CAD, coronary artery disease; CAG, coronary angiogram; CMR, cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiogram; LGE, late gadolinium enhancement; N, No; SCA, sudden cardiac arrest; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; STEMI, ST elevation myocardial infarction; VF, ventricular fibrillation; Y, Yes. [a]The 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.[3] [b]Rule out SHD according to patient age and characteristics; QT duration needs to be reassessed several days after arrest. [c]Consider cardiac CT/CAG depending on patient characteristics and clinical context. [d]Left ventricular function on echocardiogram needs to be reassessed several days after arrest to exclude stunning as cause of systolic dysfunction. [e]In case of high clinical suspicion (typical symptoms and transient ST elevation during monitoring), it can be considered to test for coronary vasospasm earlier.

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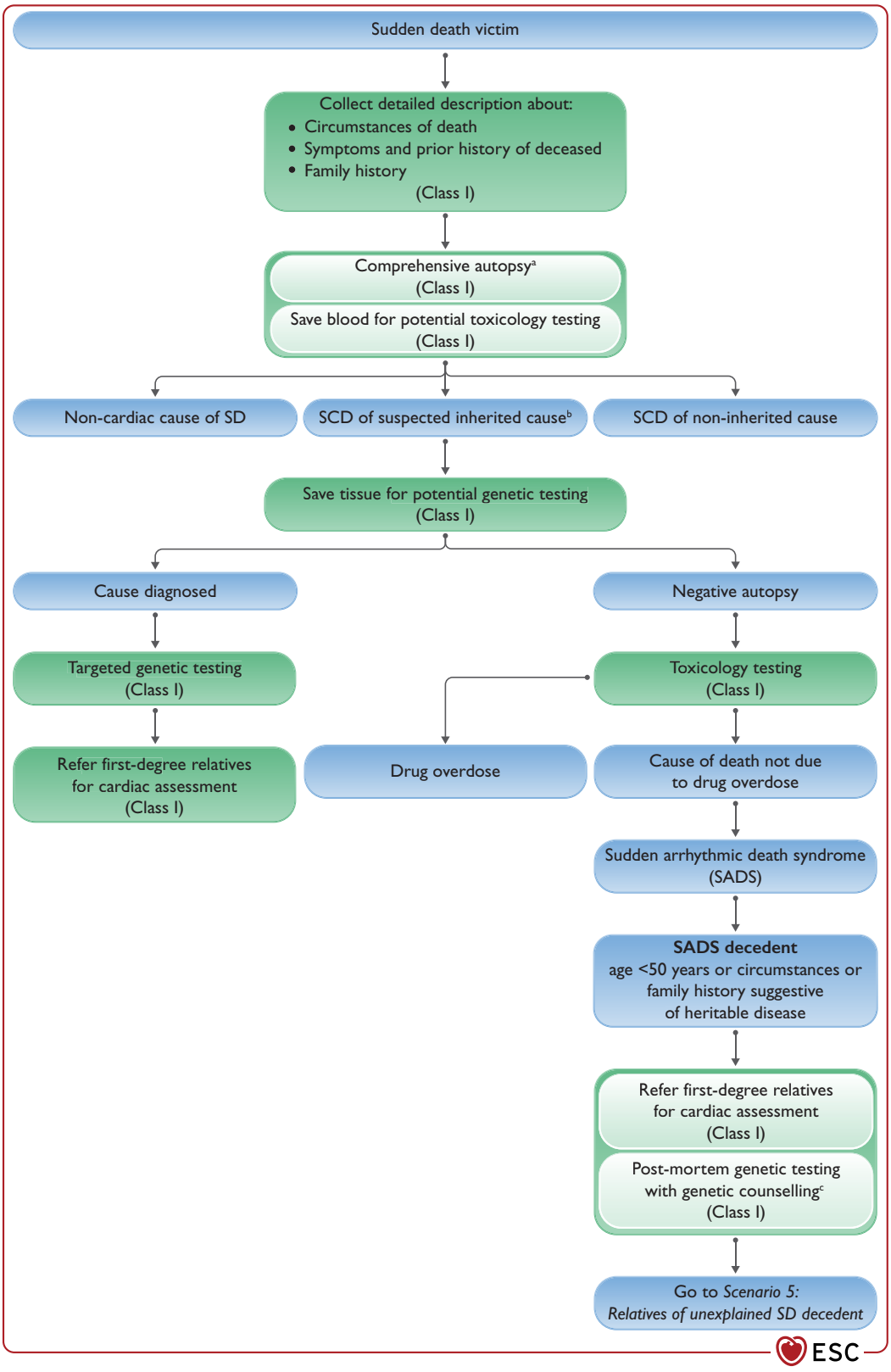

Figure 7 Algorithm for the evaluation of sudden death victims. SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death; SD, sudden death. [a]Autopsy is recommended, ideally in all cases of unexpected SD and always in those under 50 years. Autopsy should include full macroscopic examination and histopathology of all organs. The heart should ideally be examined by an expert cardiac pathologist. Samples suitable for DNA extraction should be retained when inherited causes or unexplained death are suspected. [b]Based on all circumstances, this includes negative autopsies, autopsies with uncertain findings, non-ischaemic cardiomyopathies, coronary artery disease where familial hypercholesterolaemia is suspected and thoracic aortic dissections. [c]After informed consent of relatives.

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Where they diverged was the frequency of usage of additional tests such as high-lead ECGs, Holter monitoring, signal-averaged ECG, CMR, and provocative testing.[135] Sodium channel blocker drug challenge and high-lead ECGs systematically performed in SADS relatives provided a yield of 28% BrS diagnoses in one study[281]; however, there are concerns about false positives.[139] Furthermore, epinephrine challenge has not been studied systematically in SADS families but, in the opinion of this panel, may be of utility in CPVT-suspected patients who are unable to exercise.[137]

Recent data indicated at least a 13% genetic yield in SADS cases.[135,178,183,276,283] Routine follow-up of families without a diagnosis yields little in new diagnoses,[284] although children of decedents may be followed for age-penetrant disease until adulthood.[181]

If an autopsy is ambiguous, or if an autopsy was not undertaken in a young SCD case with family or personal history suspicious for inherited heart disease, then the yield of familial evaluation was similar to that in clear SADS cases.[223,253,271]

Recommendation Table 7 — Recommendations for evaluation of relatives of sudden arrhythmic death syndrome decedents

Recommendations	Class[a]	Level[b]
Familial evaluation of SADS decedents is recommended: • for first-degree relatives • for relatives who must carry a mutation based on analysis of the family history • for relatives with suspicious symptoms • when the decedent's age is <50 years, or if there is other circumstantial data or family history to suggest heritable disease.[223,252,253,277,281]	I	B
Familial evaluation of SADS decedents is recommended to include genetic testing when post-mortem genetic testing in a SADS decedent detects a pathogenic mutation.[183,253,277,281]	I	B
Baseline familial evaluation of SADS decedents is recommended to include taking a medical history and performing physical examination, standard and high precordial lead ECG, echocardiography, and exercise testing.[223,252,253,277,281]	I	B
In SADS families without a diagnosis after clinical evaluation, follow-up is recommended for children of decedents until they reach adulthood.[181,284]	I	C
Pharmacological testing with a sodium channel blocker should be considered in relatives of SADS decedents who are 16 years or older when baseline testing and/or proband findings increase the suspicion of BrS.[277,281]	IIa	B
Ambulatory cardiac rhythm monitoring and CMR may be considered in relatives of SADS decedents.[223,253,277,281]	IIb	C
Pharmacological testing including epinephrine challenge (if exercise testing is impractical) and sodium channel blocker challenge may be considered in first-degree relatives of SADS decedents with normal baseline testing.[223,281]	IIb	B
In SADS families without a diagnosis after clinical evaluation, follow-up is not recommended for asymptomatic adults who can be discharged with advice to return if they develop symptoms or if the family history changes.[181,284]	III	C

BrS, Brugada syndrome; CMR, cardiac magnetic resonance; ECG, electrocardiogram; SADS, sudden arrhythmic death syndrome.
[a]Class of recommendation.
[b]Level of evidence.

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6. Therapies for ventricular arrhythmias. General aspects

6.1. Acute management

6.1.1. Treatment of reversible causes

Reversible causes may account for up to 50% of SCA.[285,286] However, most of the time it is difficult to determine the exact underlying cause of SCA and whether it is reversible. A comprehensive evaluation of patients with SCA is mandatory if the underlying cardiac disease is unknown or disease progression is suspected (*Section 5.2.3*, scenario 3). Electrolyte imbalances, such as hypokalaemia, may trigger VA, and a rapid rise in extracellular potassium may lead to asystole.[287–289] Other factors such as bradycardia, ischaemia, coronary spasm, thrombosis, fever, acute starvation, and dieting may contribute to the occurrence of VA.[290–292] Acute correction of these reversible factors is recommended.

Drug-induced arrhythmias should be suspected in patients being treated with agents known to alter the electrical properties of the heart (e.g. inducing QRS and/or QT prolongation) or causing electrolyte abnormalities (e.g. thiazide and loop diuretics). When drug-induced arrhythmias are presumed, any offending drug needs to be withdrawn and substances that are known to prolong QT (e.g. sotalol) should be avoided.[293,294] Hypomagnesaemia and/or hypokalaemia may be associated with Torsades de pointes (TdP). Intravenous magnesium is an effective therapy for TdP even in the absence of hypomagnesaemia.[295] In refractory cases of recurrent TdP in the setting of acquired long QT, the arrhythmia can be suppressed by increasing the underlying heart rate using isoproterenol (isoprenaline) or transvenous pacing.

Patients who survive SCA in the context of a presumed reversible cause may have a high mortality rate.[286] In a recent large observational study[296] on survivors of SCA attributed to a reversible and correctable cause, subsequent ICD implantation was associated with lower all-cause mortality except for aborted CA occurring in the presence of acute myocardial infarction (MI). Thus, the need for prophylactic ICD implantation should be considered based on the underlying cardiac disease and an individual evaluation of the future risk of life-threatening VA.

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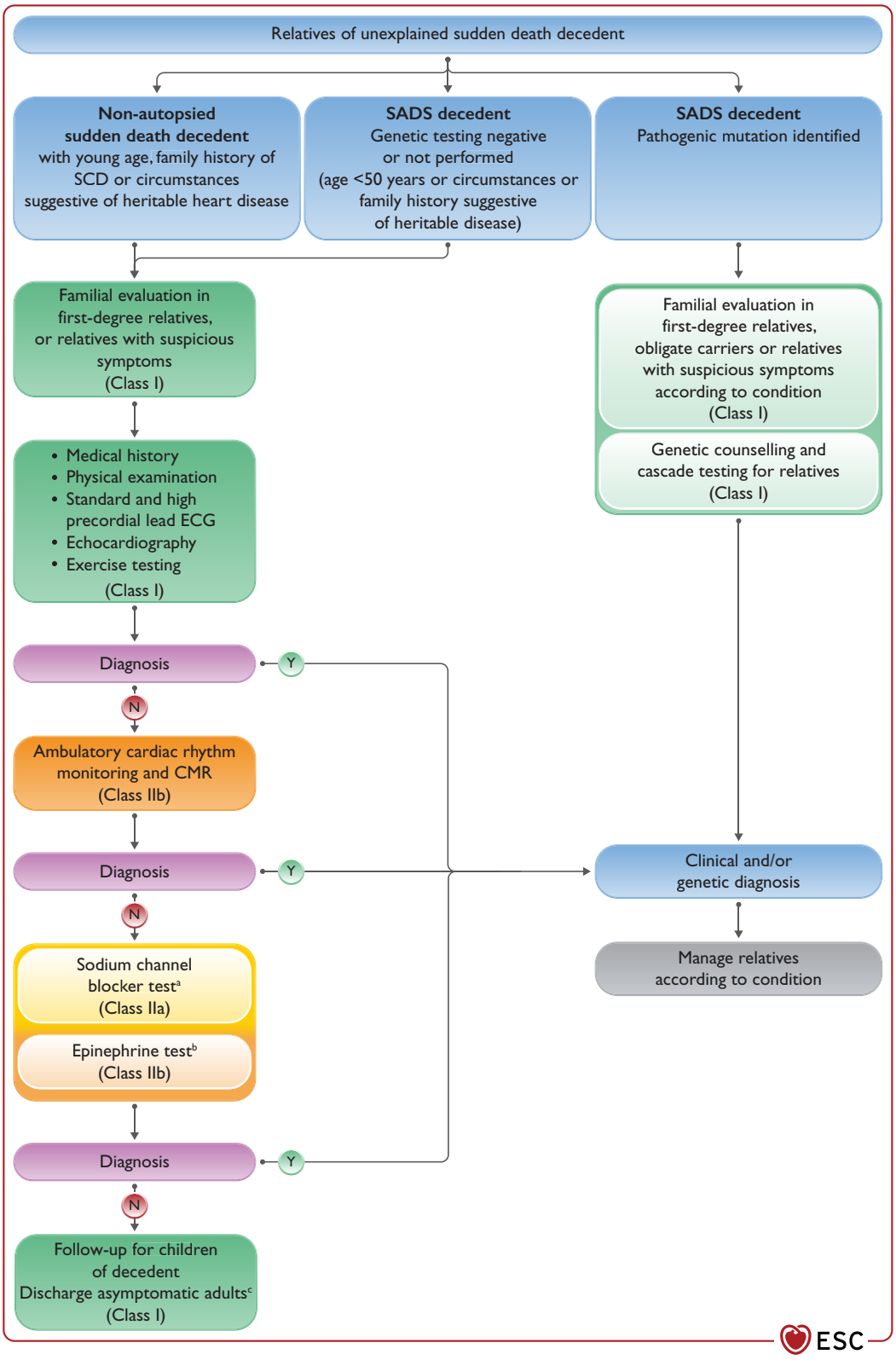

Figure 8 Algorithm for the evaluation of relatives of unexplained sudden death decedents. CMR, cardiac magnetic resonance; ECG, electrocardiogram; N, No; SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death; Y, Yes. [a]Over 16 years old ± any suspicions for Brugada syndrome on tests or decedent circumstances of death. [b]If exercise is not feasible. [c]Re-evaluate if change in family history or new symptoms.

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Recommendation Table 8 — Recommendations for treatment of reversible conditions

Recommendations	Class[a]	Level[b]
Withdrawal of offending agents is recommended whenever drug-induced VAs are suspected.[293,294,297]	I	B
Investigation for reversible causes (e.g. electrolyte imbalances, ischaemia, hypoxaemia, fever)[c] is recommended in patients with VA.[292,298]	I	C
Despite a possible correctable cause for the presenting VA, the need for ICD implantation should be considered based on an individual evaluation of the risk of subsequent VA/SCD.[286,296,299]	IIa	C

ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.
[c]List not exhaustive.

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6.1.2. Acute management of sustained monomorphic ventricular tachycardia

Patients presenting with SMVT should be treated according to symptoms and aetiology (*Figure 9*). Patients presenting with haemodynamic instability require immediate synchronized cardioversion. If synchronization is not possible, an unsynchronized shock should be used. Cardioversion is not indicated in patients with repetitive NSVTs (*Figure 10*). Documentation of any haemodynamically tolerated wide QRS tachycardia on 12-lead ECG is important. Administration of adenosine[300] or vagal manoeuvres with continuous recording of 12-lead ECG should be considered if supraventricular tachycardia (SVT) is likely. Intravenous adenosine may also terminate specific VT subtypes. Such a response supports cyclic adenosine monophosphate (cAMP)-mediated triggered activity as an underlying VT mechanism.[301] Pre-excited atrial fibrillation (AF) can be recognized by the 'FBI' (fast, broad, irregular) ECG pattern. It may mimic VT, and intravenous administration of drugs that slow AV conduction, such as adenosine, beta-blockers, and amiodarone, should be avoided.[302] Prompt termination of SMVT is recommended even for tolerated SMVT, as rapid haemodynamical deterioration may occur.

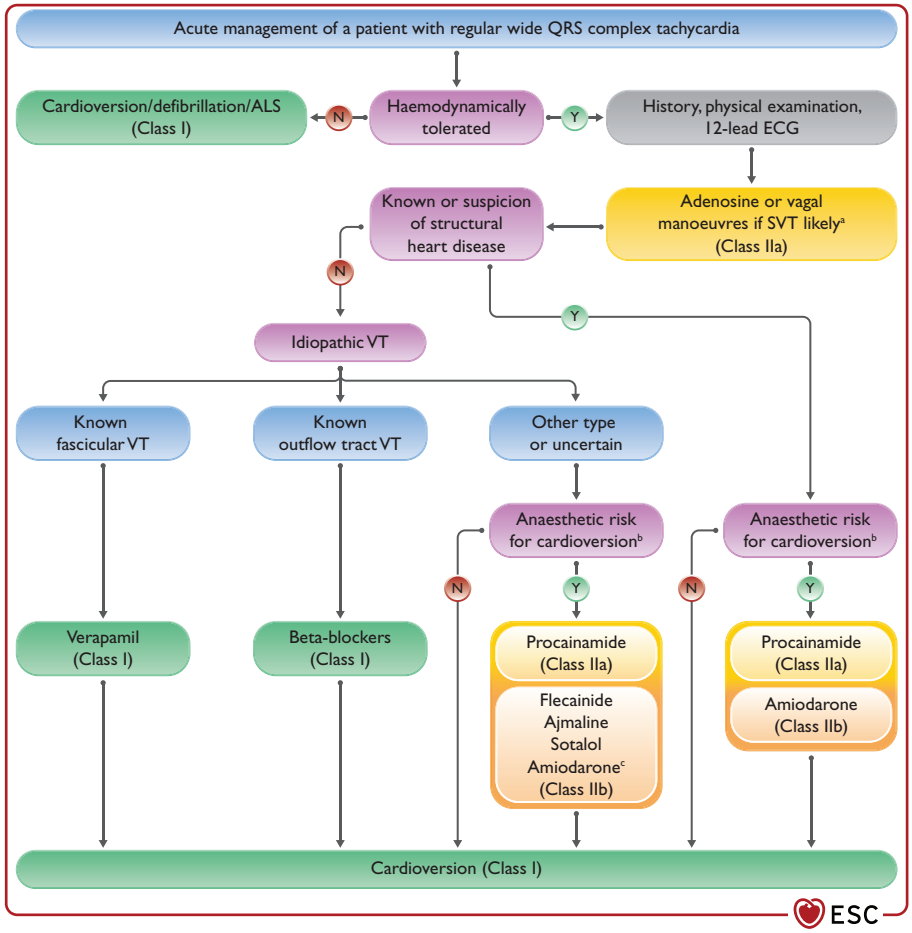

Figure 9 Algorithm for the acute management of regular wide QRS complex tachycardia. ALS, advanced life support; ECG, electrocardiogram; N, No; SVT, supraventricular tachycardia; VT, ventricular tachycardia; Y, Yes. [a]Besides SVT, adenosine may also terminate idiopathic VT, which then indicates triggered activity as the mechanism underlying the arrhythmia. [b]Benefit of cardioversion should be weighed against risks related to anaesthesia/sedation. [c]Considering limited availability of the other anti-arrhythmic drugs.

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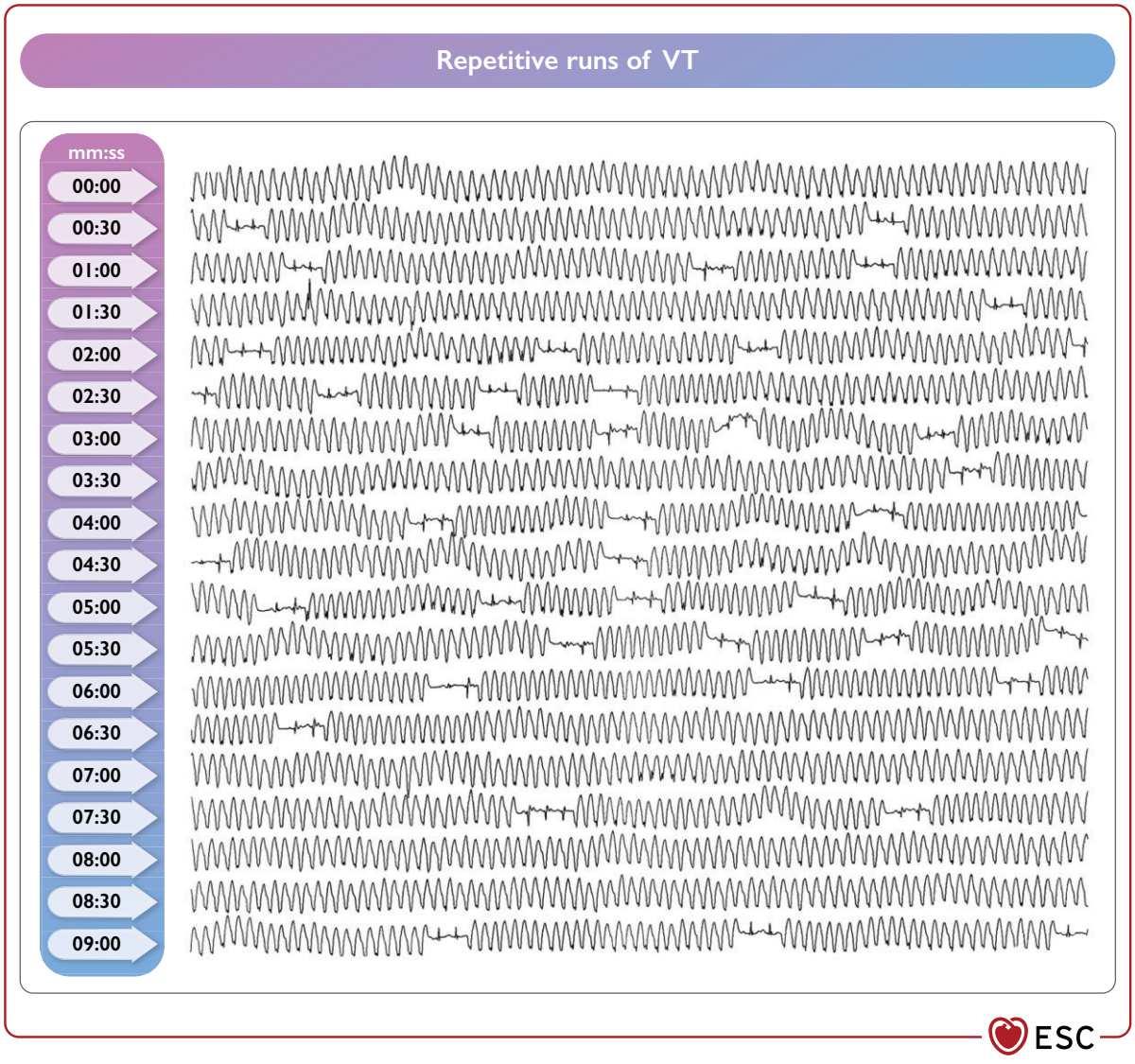

Figure 10 Repetitive runs of ventricular tachycardia interrupted by occasional sinus beats. VT, ventricular tachycardia.

Termination can be achieved with electrical cardioversion, anti-arrhythmic medications, or pacing techniques. All anti-arrhythmic drugs (AADs) may lead to hypotension, but the individual risk of anaesthesia/sedation required for cardioversion also needs to be considered. For pharmacological termination of a haemodynamically tolerated VT of unknown aetiology, intravenous procainamide or amiodarone can be used. In the PROCAMIO trial,[303] procainamide therapy was associated with a higher proportion of tachycardia termination and fewer major cardiac adverse events than amiodarone. Intravenous procainamide should not be used in patients with severe heart failure, acute MI, and end-stage renal disease. Administration of other AADs (ajmaline, sotalol, and flecainide)[304,305] may be considered in patients without significant heart disease, but the risk of adverse events should be carefully weighed. Availability of AADs has to be taken into account, e.g. procainamide is not available in many European countries. In patients with an ICD, manual overdrive pacing may terminate those VTs with a cycle length under the programmed ICD detection rate. In case of a known idiopathic VT (*Figure 4*), treatment with beta-blockers (for RVOT VT)[306] or verapamil (for fascicular VT)[307] is recommended for acute conversion. Although verapamil may terminate other types of idiopathic VT,[307] important adverse effects such as severe hypotension may occur. If the VT aetiology is uncertain, intravenous administration of verapamil is not recommended.[308,309] A comprehensive evaluation of patients presenting with SMVT is mandatory if the underlying cardiac disease is unknown or disease progression is suspected (*Section 5.2.2*, scenario 2).

6.1.3. Management of electrical storm and incessant ventricular tachycardia

An electrical storm is common in ICD patients and has been defined as three or more episodes of sustained VA occurring within 24 h,

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requiring either anti-tachycardia pacing (ATP) or cardioversion/defibrillation, with each event separated by at least 5 min.[310–312] Patients who experience an electrical storm are prone to psychological disorders, heart failure decompensation, and increased mortality.[313,314] The severity of an electrical storm can range from recurrent asymptomatic VT episodes terminated by ATP to a life-threatening electrical instability with VA that recurs frequently after multiple shocks. Frequent ICD shocks can also be inappropriately delivered (*Figure 11*).

In cases of inappropriate ICD shocks (e.g. due to SVTs or lead defects) or unnecessary ICD therapy (e.g. for NSVT or for repetitive VTs that terminate and restart spontaneously), disabling of ICD therapies is recommended. If an electrophysiology specialist or programmer is not available, the ICD can be disabled by placing a magnet over the device.

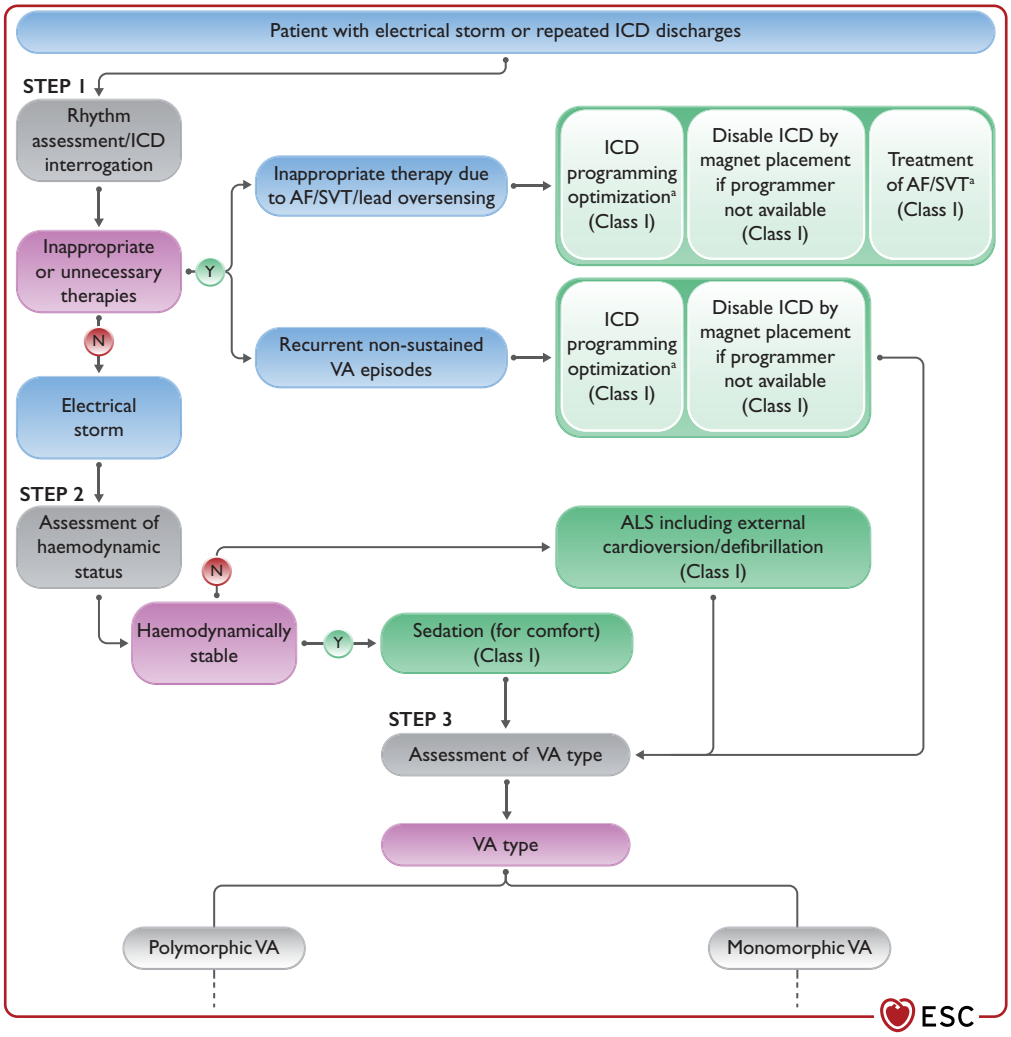

Figure 11 Part One. Management of patients with electrical storm or repeated implantable cardioverter defibrillator discharges.

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In case of haemodynamic instability at initial evaluation, institution of advanced life support (ALS) is recommended.[315] Reversible conditions contributing to initiation and perpetuation of VA need to be corrected (see *Section 6.1.1*). Further management depends on the type of VA and the underlying aetiology.[312,316] A multifaceted approach is often required for management, consisting of ICD reprogramming when appropriate, AAD therapy, sedation, catheter ablation, autonomic modulation, and mechanical circulatory support.

Elevated sympathetic tone needs to be addressed. For patients with recurrent ICD shocks, sedation is indicated to alleviate psychological distress and decrease pro-arrhythmogenic sympathetic tone. Initial treatment with beta-blockers, preferably non-selective beta-blockers like propranolol, which was superior to metoprolol in one study,[317] combined with amiodarone[318] is most commonly used. In patients with recurrent haemodynamically not-tolerated VTs resistant to amiodarone, landiolol (ultra-short-acting β1-selective blocker) was found to be effective for arrhythmia suppression in two smaller studies.[319,320] Administration of other AADs such as procainamide,[321] lidocaine,[322] or quinidine[296,297] depends on the specific situation, type of VA, and underlying aetiology. When electrical storm remains intractable, with multiple shocks in a few hours, despite available anti-arrhythmic therapies, deep sedation/intubation should be considered, along with mechanical ventilation.[325] If beta-blocker treatment is insufficient or not tolerated to decrease sympathetic tone, selected patients may benefit from autonomic modulation, i.e. percutaneous ganglionic stellate blockade,[326] thoracic epidural anaesthesia,[327] or left cardiac sympathetic denervation.[328]

The most common arrhythmia underlying electrical storm is SMVT associated with SHD that is amenable to catheter ablation.[313,329] Successful ablation was associated with a significant reduction in VT and electrical storm recurrence and improved long-term survival in retrospective analyses.[330,331] In patients with incessant slow MVT, catheter ablation is preferred over AAD therapy,

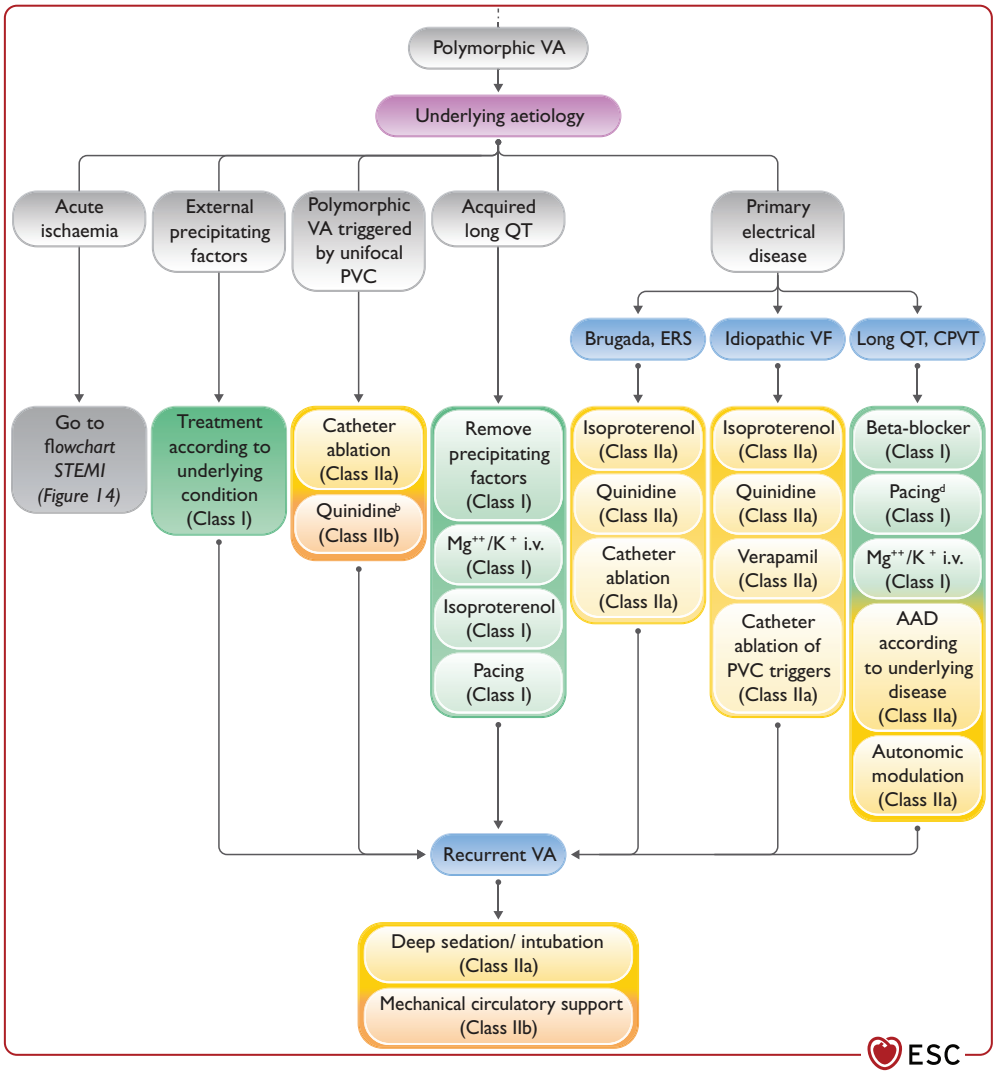

Figure 11 Part Two. Management of patients with electrical storm or repeated implantable cardioverter defibrillator discharges.

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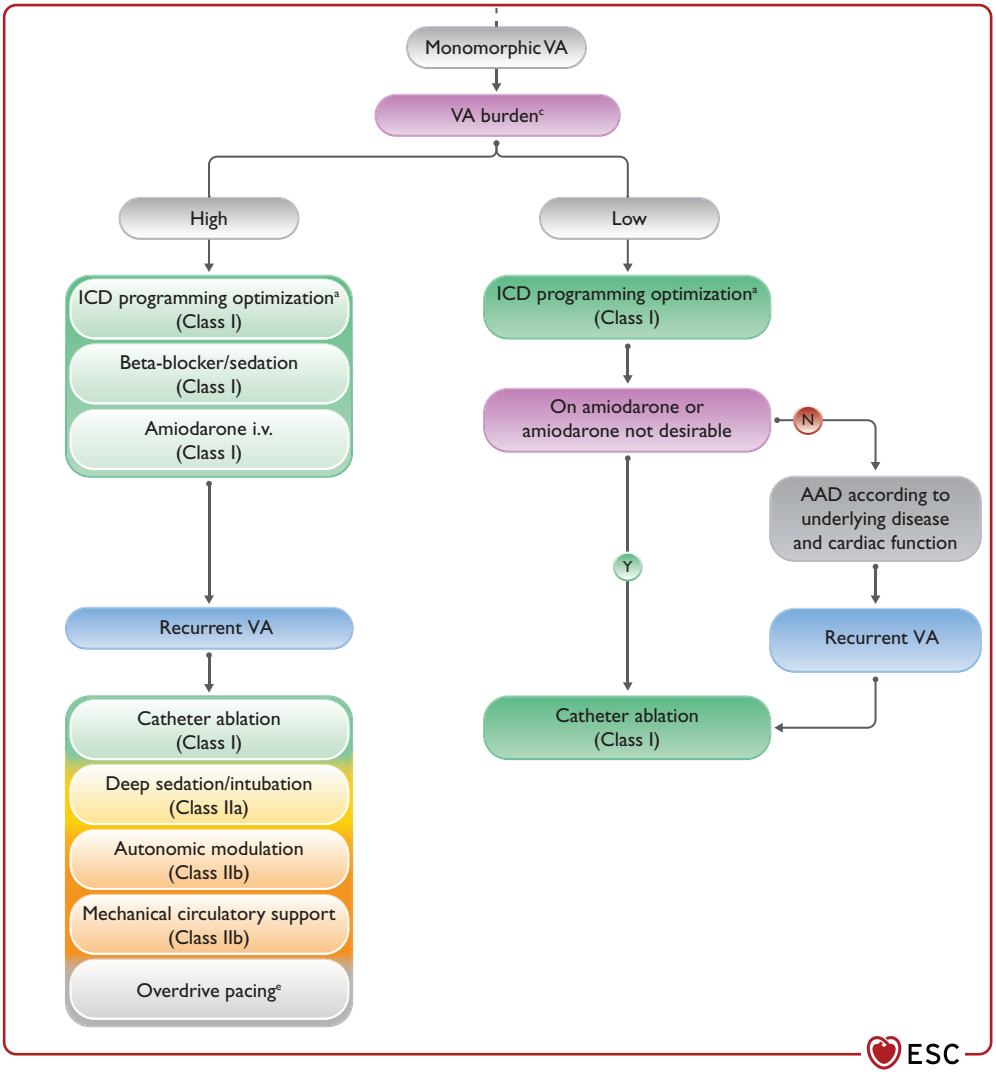

Figure 11 Part Three. Management of patients with electrical storm or repeated implantable cardioverter defibrillator discharges. AAD, antiarrhythmic drug; AF, atrial fibrillation, ALS, Advanced life support; CPVT, catecholaminergic polymorphic ventricular tachycardia; ERS, early repolarization syndrome; ICD, implantable cardioverter defibrillator; N, No; PVC, premature ventricular complex; STEMI, ST-elevation myocardial infarction; SVT, supraventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation; Y, Yes. [a]Special aspects of device therapy section. [b]No data on effect of quinidine on PVC-triggered polymorphic VAs in patients with cardiomyopathies. [c]High VA burden refers to a clinical scenario of very frequent VA episodes requiring ICD shocks, when only short periods of stable rhythm can be achieved. Low VA burden refers to a clinical scenario of repeated ATPs/ICD shocks followed by stable rhythm. [d]If bradycardia or post-extrasystolic pauses facilitate initiation of PVT/VF. [e]Overdrive pacing (by pacing with a slightly higher rate than the baseline rhythm) can be useful to temporarily suppress slow recurrent/incessant VT.

which may only further slow VT. Catheter ablation should also be considered in patients with recurrent symptomatic episodes of PVT or VF triggered by a similar PVC.[221,332–334] Institution of mechanical circulatory support may be considered for haemodynamic stabilization, when conventional therapy fails, and to provide circulatory support during ablation.[335] In a recent meta-analysis[336] including 2465 patients, a substantially lower mortality was observed with prophylactic mechanical circulatory support treatment among patients suffering from electrical storm or high-risk PAINESD score.[337] In contrast, rescue use of mechanical circulatory support during ablation was associated with a high mortality rate.[338] In patients with electrical storm due to recurrent PVT/VF, the underlying aetiology determines further management (*Figure 11*).

Recommendation Table 9 — Recommendations for the acute management of sustained ventricular tachycardia and electrical storm

Recommendations	Class[a]	Level[b]
Acute management of sustained VT		
DC cardioversion is recommended as the first-line treatment for patients with haemodynamically not-tolerated SMVT.[303,339]	I	B
DC cardioversion is recommended as the first-line treatment for patients presenting with tolerated SMVT provided that the anaesthetic/sedation risk is low.	I	C

Continued

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In patients presenting with a haemodynamically tolerated idiopathic VT, treatment with intravenous beta-blocker (RVOT VT) or verapamil (fascicular VT) is recommended.[306,307]	I	C
In patients presenting with a regular haemodynamically tolerated wide QRS complex tachycardia suspected for SVT, administration of adenosine or vagal manoeuvres should be considered.[300]	IIa	C
In patients presenting with a haemodynamically tolerated SMVT and known or suspected SHD, intravenous procainamide should be considered.[303]	IIa	B
In patients presenting with a haemodynamically tolerated SMVT in the absence of an established diagnosis, intravenous amiodarone may be considered.[303]	IIb	B
In patients presenting with a haemodynamically tolerated SMVT in the absence of significant SHD, flecainide, ajmaline, or sotalol may be considered.[304,305]	IIb	C
Intravenous verapamil is not recommended in broad QRS complex tachycardia of unknown mechanism.[308,309]	III	B
Management of electrical storm		
Mild to moderate sedation is recommended in patients with electrical storm to alleviate psychological distress and reduce sympathetic tone.	I	C
Antiarrhythmic therapy with beta-blockers (non-selective preferred) in combination with intravenous amiodarone is recommended in patients with SHD and electrical storm unless contraindicated.[317,318]	I	B
Intravenous magnesium with supplementation of potassium is recommended in patients with TdP.[295]	I	C
Isoproterenol or transvenous pacing to increase heart rate is recommended in patients with acquired LQT syndrome and recurrent TdP despite correction of precipitating conditions and magnesium.	I	C
Catheter ablation is recommended in patients presenting with incessant VT or electrical storm due to SMVT refractory to AADs.[330,331]	I	B
Deep sedation/intubation should be considered in patients with an intractable electrical storm refractory to drug treatment.[325]	IIa	C
Catheter ablation should be considered in patients with recurrent episodes of PVT/VF triggered by a similar PVC, non-responsive to medical treatment or coronary revascularization.[221,332,333]	IIa	C
Quinidine may be considered in patients with CAD and electrical storm due to recurrent PVT when other AAD therapy fails.[323,324]	IIb	C
Autonomic modulation may be considered in patients with electrical storm refractory to drug treatment and in whom catheter ablation is ineffective or not possible.[326,328,340]	IIb	C
Institution of mechanical circulatory support may be considered in the management of drug-refractory electrical storm and cardiogenic shock.[335]	IIb	C

Continued

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AAD, anti-arrhythmic drug; CAD, coronary artery disease; DC, direct current; LQT, long QT; PVC, premature ventricular complex; PVT, polymorphic VT; RVOT, right ventricular outflow tract; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; SVT, supraventricular tachycardia; TdP, Torsades de pointes; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

6.2. Long-term management

6.2.1. Pharmacotherapy

Optimal medical treatment of the underlying cardiac disease, including the maximal tolerated doses of heart failure medication, is mandatory.[341]

In patients with heart failure with reduced ejection fraction (HfrEF), the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure recommend angiotensin-converting enzyme inhibitor (ACE-I)/angiotensin receptor blocker (ARB)/angiotensin receptor neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), beta-blockers, and sodium–glucose co-transporter 2 (SGLT2) inhibitors to reduce mortality due to heart failure and SCD.[342]

Recommendation Table 10 — Recommendations for treatment with heart failure medication

Recommendations	Class[a]	Level[b]
Optimal medical treatment including ACE-I/ARB/ARNIs, MRAs, beta-blockers, and SGLT2 inhibitors is indicated in all heart failure patients with reduced EF.[343–347]	I	A

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ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNIs, angiotensin receptor neprilysin inhibitor; EF, ejection fraction; MRA, mineralocorticoid receptor antagonists; SGLT2, sodium–glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.

AADs have an important role as adjunctive therapy in the management of VA, especially in symptomatic patients (*Table 8*). Until now, no AAD except for beta-blockers has demonstrated reduction in all-cause mortality. Each drug has a significant potential for causing adverse events, including pro-arrhythmia. For example, numerous AADs, as well as a large number of drugs with other therapeutic indications, can prolong the QT interval (http://www.crediblemeds.org) and provoke TdP, have negative chronotropic effects, may deteriorate heart failure, and cause bradycardia. Several drugs increase the risk of VA in patients with BrS (http://www.brugadadrugs.org).

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Table 8 Anti-arrhythmic drugs (acute and chronic treatment)

Anti-arrhythmic drug	Effects on ECG	Indications (specific indication)	Oral dose per day (i.v. dose)	Side effects	Contraindications, precautions, other considerations
Amiodarone	Decreases sinus node frequency, prolongs QT interval[a]	PVC, VT, VF	200–400 mg Loading dose: 600–1200 mg/ 24 h 8–10 days. (Loading dose: 5 mg/kg in 20 min–2 h, 2–3 times in 24 h, then 600–1200 mg/ 24 h 8–10 days)	*Cardiac:* Bradycardia, TdP (infrequent) *Extracardiac:* Photosensitivity, corneal deposits, hypothyroidism, hyperthyroidism, pulmonary toxicity, hepatotoxicity, polyneuropathy, skin discoloration	*Precautions:* Sinus node dysfunction, severe AV conduction disturbances, hyperthyroidism *Other considerations:* Can be used in patients with heart failure. Increases the risk of myopathy when used with statins
Adenosine	Transitory AV block	Regular wide complex tachycardia of unknown origin (outflow tract VT)	No oral use (6–18 mg bolus)	Chest pain, flushing, bronchoconstriction	*Contraindications:* Severe asthma, pre-excited AF *Other considerations:* Antagonist: theophylline
Ajmaline	Prolongs QRS duration and QT interval[a]	VT (unmasking BrS ECG)	No oral use (1 mg/kg over 5–10 min (maximum dose 100 mg) or 1 mg/kg at 10 mg/min)	*Cardiac:* VF (rare in suspected BrS), occasional TdP, negative inotrope *Extracardiac:* Cholestatic jaundice, headache, nausea, thrombocytopenia	*Contraindications:* BrS ECG type I, QT prolongation
Beta-blocker	Decreases sinus node frequency, prolongs PR interval, shortens QT interval	PVC, VT (LQTS, CPVT)	Various (various)	*Cardiac:* Bradycardia, AV block, hypotension, negative inotrope *Extracardiac:* Fatigue, bronchospasm, sexual disturbances, depression, cold extremities	*Contraindications:* Severe sinus node dysfunction, severe AV conduction disturbances, decompensated heart failure, coronary vasospasm, severe asthma, BrS
Landiolol (Ultra-short acting β1-selective blocker)	See beta-blocker	VT, electrical storm	No oral use 100 μg/kg bolus in 1 min, infusion 10–40 μg/kg/min (max 80 μg/kg/ min; max 24 h total dose 57.6 mg/kg/day)	See beta-blocker	*Contraindications:* See beta-blocker. Bradycardia, hypotension *Other considerations:* Limited experience with its use beyond 24 h
Nadolol (Non-selective β1β2 blocker)	See beta-blocker	PVC, VT (LQTS, CPVT)	40–120 mg	See beta-blocker	*Contraindications:* See beta-blocker *Other considerations:* Plasma half-life 20–24 h
Propranolol (Non-selective β1β2 blocker)	See beta-blocker	PVC, VT (electrical storm, LQTS, CPVT)	80–320 mg (160 mg/24 h)	See beta-blocker	*Contraindications:* See beta-blocker
Disopyramide	Increases sinus node frequency and prolongs PR interval, QRS duration, and QT interval[a]	PVC, VT	250–750 mg	*Cardiac:* Negative inotrope, AV block, pro-arrhythmia (MVT, occasional TdP)	*Contraindications:* Severe sinus node dysfunction, severe AV conduction disturbances, severe intraventricular

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				Extracardiac: Anticholinergic effects	conduction disturbances, prior MI, significant SHD, hypotension *Other considerations:* Reduces LV outflow tract obstruction and symptoms in HCM
Flecainide	Prolongs PR interval, QRS duration, and QT interval[a]	PVC, VT (unmasking BrS ECG[b])	200–400 mg (1–2 mg/kg over 10 min)	*Cardiac:* Pro-arrhythmia (MVT, occasional TdP), negative inotrope, sinus bradycardia, AV block, 1:1 AV conduction during flutter *Extracardiac:* Central nervous system effects (e.g. drowsiness, diplopia, headache)	*Contraindications:* Prior MI, significant SHD, BrS, severe sinus node dysfunction, severe AV or intraventricular conduction disturbances, inherited LQTS (other than LQTS3), severe kidney disease (CrCl $<$35 mL/min/1.73 m^2) *Other considerations:* Discontinue if QRS widening $>$25% or bundle branch block
Isoproterenol	Increases sinus node frequency, shortens QT interval	(Electrical storm in BrS, idiopathic VF, and ERS, TdP, beta-blocker overdose; acquired LQTS)	No oral use (0.5–10 μg/min)	*Cardiac:* Sinus tachycardia, vasodilation *Extracardiac:* Headache, sweating, tremor	*Contraindications:* ACS, LQTS *Other considerations:* Short plasma half time (2 min)
Lidocaine	No significant effects	(VT/VF associated with ACS)	No oral use (50–200 mg bolus, then 2–4 mg/min)	*Cardiac:* Sinoatrial arrest *Extracardiac:* Central nervous system effects (e.g. drowsiness, dizziness)	*Precautions:* Reduced dose with reduced liver blood flow (e.g. shock, β-blockade, severe heart failure) *Other considerations:* More effective with high potassium level. Few haemodynamic side effects
Mexiletine	No significant effects	PVC, VT (LQT3)	600–1200 mg Loading dose: 400 mg initially followed by 600 mg in the first 24 h	*Cardiac:* Sinus bradycardia in sinus node dysfunction, hypotension *Extracardiac:* Central nervous system effects (e.g. tremor, dysarthria, dizziness), gastrointestinal complaints	*Contraindications:* Sinus node dysfunction, severe AV conduction disturbances, severe heart failure
Procainamide	Prolongs PR interval, QRS duration, and QT interval[a]	VT	(100 mg bolus, can be repeated after 5 min if no effect, max 500–750 mg [max 50 mg/min]. Then, 2–6 mg/min)	*Cardiac:* Sinus bradycardia, hypotension, TdP *Extracardiac:* Rash, myalgia, vasculitis, systemic lupus, agranulocytosis	*Contraindications:* Severe sinus node dysfunction, severe AV conduction disturbances, severe intraventricular conduction disturbances, severe LV dysfunction hypotension, BrS
Propafenone	Prolongs PR interval, QRS duration, and QT interval[a]	PVC, VT	450–900 mg	*Cardiac:* Sinus bradycardia, AV block, negative inotrope, pro-arrhythmia (MVT, occasional TdP) *Extracardiac:* Gastrointestinal disturbances, headache, dry mouth	*Contraindications:* Prior MI, significant SHD, BrS, severe sinus node dysfunction, severe AV or intraventricular conduction disturbances, LQTS, significant renal or liver disease *Other considerations:* Discontinue if QRS widening $>$25% or bundle branch block

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Quinidine	Increases sinus node frequency and prolongs PR interval, QRS duration, and QT interval[a]	(VF[c], BrS, SQTS)	600–1600 mg Loading dose: Start 200 mg every 3 h until effect, max. 3 g in first 24 h	*Cardiac:* Hypotension, TdP[d] *Extracardiac:* Gastrointestinal disturbances, auditory and visual disturbances, confusion, leukopenia, haemolytic anaemia, thrombocytopenia, anaphylaxis	*Contraindications:* Severe sinus node dysfunction, severe AV or intraventricular conduction disturbances, previous MI, significant SHD, hypotension, LQTS
Ranolazine	Decreases sinus node frequency, prolongs QT interval[a]	VT (LQTS3)	750–2000 mg	*Cardiac:* Sinus bradycardia, hypotension *Extracardiac:* Dizziness, nausea, constipation, gastrointestinal disturbance, headache, rash	*Contraindications:* Severe sinus node dysfunction, severe heart failure, LQTS (other than LQTS3) *Precautions:* Concomitant treatments associated with QT interval prolongation
Sotalol	Decreases sinus node frequency, prolongs QT interval[a]	VT	160–640 mg (0.5–1.5 mg/kg in 10 min. If necessary, can be repeated after 6 h)	See beta-blockers, TdP[d] (>2% of patients, close monitoring of QT interval and CrCl)	*Contraindications:* Severe sinus node dysfunction, severe AV conduction disturbances, severe heart failure with reduced LVEF, significant LVH, CrCl <30 ml/min, coronary vasospasm, LQTS *Precautions:* Concomitant treatments associated with QT interval prolongation, hypokalaemia *Other considerations:* Potassium channel blocker effects require higher dose than beta-blocker effects
Verapamil	Prolongs PR interval	(LV fascicular tachycardia)	120–480 mg (5–10 mg in slow bolus. If necessary, can be repeated in 30 min)	*Cardiac:* Sinus bradycardia in sinus node dysfunction, AV block, negative inotrope, hypotension *Extracardiac:* Gastrointestinal disturbances, peripheral oedema, flushing	*Contraindications:* Heart failure with reduced LVEF, severe sinus node dysfunction, and severe AV conduction disturbances, VT of unknown origin, ACS, WPW syndrome *Other considerations:* Increase the risk of myopathy when used with statins

ACS, acute coronary syndrome; AF, atrial fibrillation; AV, atrioventricular; BrS, Brugada syndrome; CPVT, catecholaminergic polymorphic ventricular tachycardia; CrCl, creatinine clearance; ECG, electrocardiogram; ERS, early repolarization syndrome; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; LV, left ventricular; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; MVT, monomorphic ventricular tachycardia; PVC, premature ventricular complex; SHD, structural heart disease; SQTS, short QT syndrome; TdP, torsades de pointes; VF, ventricular fibrillation; VT, ventricular tachycardia; WPW, Wolff–Parkinson–White.

[a]Precaution with concomitant conditions or drugs that prolong QT interval. Should be discontinued if QTc >500 ms. See *Figure 13* Algorithm for evaluation before initiation and follow-up of patients requiring drugs associated with QT prolongation.

[b]If ajmaline not available.

[c]Subacute MI, multifocal ectopic Purkinje-related premature contractions, ERS, idiopathic VF.

[d]Proarrhythmic side effects require strong indication in patients without ICD.

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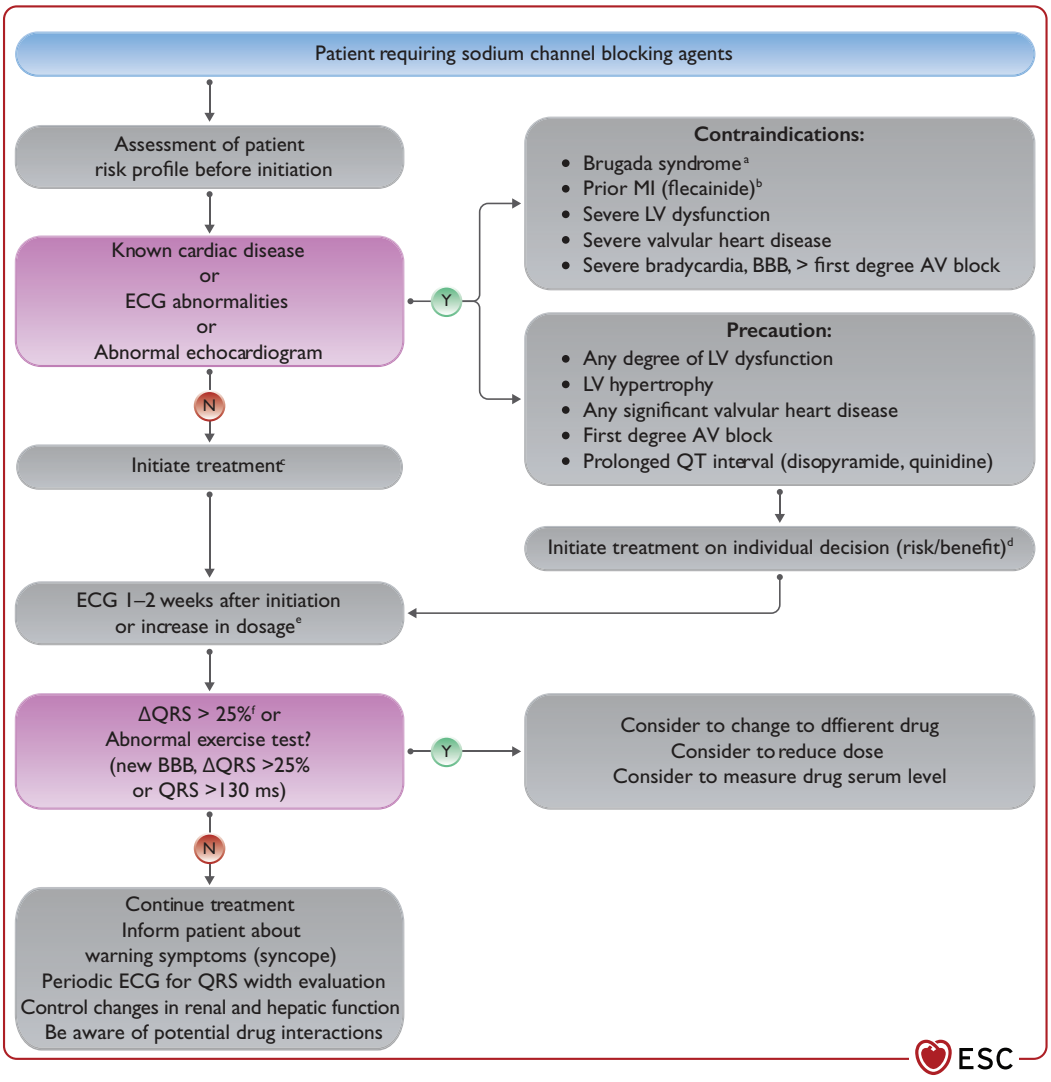

Figure 12 Algorithm for evaluation before initiation and follow-up of patients requiring sodium channel blocking agents. AV, atrioventricular; BBB, bundle branch block; ECG, electrocardiogram; LV, left ventricular; MI, myocardial infarction; N, No; Y, Yes. [a]http://www.brugadadrugs.org. [b]Flecainide, encainide. [c]Co-administration of drugs with AV nodal blocking effect in patients with atrial fibrillation or atrial flutter. [d]In implantable cardioverter defibrillator carriers, a higher risk of drug-induced pro-arrhythmia might be accepted. [e]According to the 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation.[348] [f]A ΔQRS >25% is not an absolute cut-off value but dependent on QRS width before drug initiation and individualized patient risk–benefit considerations.

Modification of risk factors, when possible, is important for prevention of pro-arrhythmia. In patients who require a potentially arrhythmia-inducing drug, regular ECG and other tests according to the patient's profile and AAD characteristics are recommended (*Figures 12* and *13*).

6.2.2. Device therapy

6.2.2.1. Implantable cardioverter defibrillator

ICD is an integral part of treating patients surviving a CA due to a VA or those deemed to be at high risk thereof. Drawbacks are the high up-front device costs, device-associated complications, and the relatively high number-to-treat needed to prevent one SCD in primary prevention.

A patient-level meta-analysis of the three early ICD trials[349–351] comparing ICD to medical therapy for secondary prevention of SCD demonstrated a 28% mortality reduction (HR 0.72; 95% CI 0.6–0.87; $P = 0.0006$) almost entirely due to reduction of arrhythmic death (HR 0.5; 95% CI 0.37–0.67; $P < 0.0001$) in the ICD group.[352] Therefore, the use of an ICD for secondary prevention of SCD that occurred in the absence of reversible causes is widely accepted.

Several randomized controlled trials[353–356] have established the role of the ICD for primary prevention of SCD in heart failure patients with an LVEF ≤35%. The reported mortality reduction has recently been supported by two large contemporary prospective registries enrolling more than 5000 patients.[357,358] In the EU-CERT-ICD trial, primary prevention ICD implantation was associated with a 27% lower mortality with similar results in CAD and DCM.[357] Results of the DANISH trial, however, indicate that the mortality benefit may be less clear in contemporary patients with non-ischaemic heart failure (see *Section 7.1.3.1*).[359]

In the work-up for ICD therapy, it is of paramount importance to consider the patient's life expectancy, quality of life, and comorbidities, and to reassess and discuss these issues with the patient at the time of generator change. There is evidence that patients with end-stage renal disease, with diabetes, and elderly patients benefit less or not at all from

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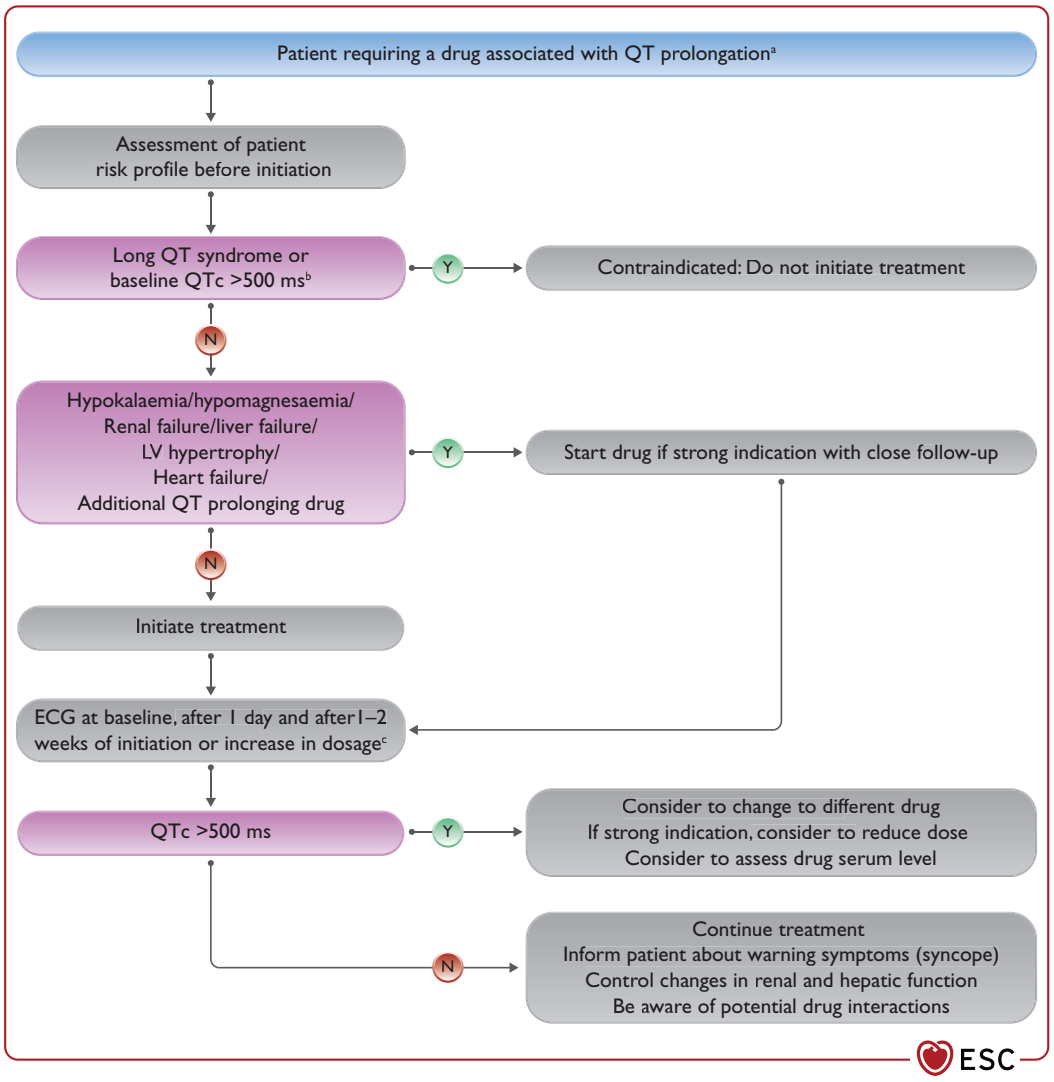

Figure 13 Algorithm for evaluation before initiation and follow-up of patients requiring drugs associated with QT prolongation. ECG, electrocardiogram; LV, left ventricular; N, No; Y, Yes. [a]http://www.crediblemeds.org. [b]If strong indication and no alternative treatment, consult a specialist. [c]According to the 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation.[348]

a primary prevention ICD.[357,360–362] Women have been underrepresented in all primary prevention trials and data suggest that they may benefit less.[361] In general, the SCD risk needs to be weighed against the individual's competing risk of a non-arrhythmic death.[363,364]

In the context of patient-centred medicine, physicians and healthcare professionals should engage ICD candidates and recipients in a joint decision process. Communication of relevant information, ensuring a good understanding of the benefits, risks, and potential consequences of different options, to enable the patient to partake in decision-making is mandatory. This shared decision-making process should discuss the different scenarios including primary prevention ICD implantation, consideration of ICD generator replacement, and end-of-life care. Importantly, the perception of 'good quality of life' depends on numerous factors that are weighed differently by people with different cultural, religious, and socioeconomic backgrounds. Although clinical prediction scores, such as the MADIT-ICD benefit score,[365] may provide helpful additional information, clinical decision-making should not only rely on such scores.

Complications of ICD therapy include inappropriate therapies, lead fractures, and device-related infections. A subcutaneous implantable cardioverter defibrillator (S-ICD) has been introduced to address problems related to transvenous leads. S-ICD has no intravascular lead and therefore cannot deliver ATP. In the PRAETORIAN trial, 849 patients with an ICD but no pacing indication were randomized to an S-ICD or a transvenous ICD.[366] Over a mean follow-up of 49 months, non-inferiority was shown for the primary endpoint of device-related complications and inappropriate shocks. The rate of inappropriate shocks was 9.7% in the S-ICD group and 7.3% in the ICD group (HR 1.43; 95% CI 0.89–2.30) and the rate of device related complications was 5.9% in the S-ICD and 9.8% in the ICD group (HR 0.69; 95% CI 0.44–1.09). There was also no difference in the secondary endpoint of death and appropriate shocks, but the trial had not been powered to show non-inferiority for this secondary endpoint. Of note, more than 80% of the included patients were in NYHA class I and II and the included patients were younger than in prior ICD trials.

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Recommendation Table 11 — Recommendations for implantable cardioverter defibrillator implantation (general aspects)

Recommendations	Class[a]	Level[b]
Implantation of a cardioverter defibrillator is only recommended in patients who have an expectation of good quality survival >1 year.	I	C
It is not recommended to implant an ICD in patients with incessant VAs until the VA is controlled.	III	C

ICD, implantable cardioverter defibrillator; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.

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Recommendation Table 12 — Recommendations for secondary prevention of sudden cardiac death*

Recommendations	Class[a]	Level[b]
ICD implantation is recommended in patients with documented VF or haemodynamically not-tolerated VT in the absence of reversible causes.[349–352]	I	A
In patients with VT/VF, an indication for ICD, and no contraindication for amiodarone, amiodarone may be considered when an ICD is not available, contraindicated for concurrent medical reasons, or declined by the patient.	IIb	C
In patients with SMVT or SPVT/VF triggered by a PVC with similar morphology and an indication for ICD, catheter ablation may be considered when an ICD is not available, contraindicated for concurrent medical reasons, or declined by the patient.	IIb	C

ICD, implantable cardioverter defibrillator; PVC, premature ventricular complex; SMVT, sustained monomorphic VT; SPVT, sustained polymorphic VT; VF, ventricular fibrillation; VT, ventricular tachycardia.
*For primary prevention and specific aspects of secondary prevention, go to *Section 7*.
[a]Class of recommendation.
[b]Level of evidence.

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Recommendation Table 13 — Recommendations for subcutaneous implantable cardioverter defibrillator

Recommendations	Class[a]	Level[b]
Subcutaneous defibrillator should be considered as an alternative to transvenous defibrillator in patients with an indication for an ICD when pacing therapy for bradycardia, cardiac resynchronization, or ATP is not needed.[366]	IIa	B

ATP, anti-tachycardia pacing; ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

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6.2.2.2. Adding cardiac resynchronization therapy[2]

Cardiac resynchronization therapy (CRT) does reduce mortality in heart failure,[367] and careful evaluation of the potential benefit of CRT in patients with ICD indication before implantation is mandatory.[2] The role of the addition of a defibrillator is less well established.[368,369] The ongoing randomized controlled RESET-CRT trial aims to determine the impact of CRT-defibrillator on overall mortality and SCD in heart failure patients with a CRT indication.

Recommendation Table 14 — Recommendations for adding cardiac resynchronization therapy to implantable cardioverter defibrillator

Recommendations	Class[a]	Level[b]
When an ICD is indicated, it is recommended to evaluate whether the patient could benefit from CRT-defibrillator.[367]	I	C

CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

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6.2.2.3. Wearable cardioverter defibrillator

The wearable cardioverter defibrillator (WCD) is an external defibrillator that has been shown to successfully detect and treat VT and VF.[370] It is therefore suitable for patients who are at risk but temporarily not candidates for an ICD owing, for example, to extraction of an infected device and subsequent antibiotic treatment.[371] An unsolved problem is the protection of patients in the early phase (40 days) after an MI. The VEST trial enrolled 2302 patients with acute MI and an LVEF ≤35% and randomized them early in a 2:1 fashion to receive a WCD or not under guideline-directed optimal medical treatment (OMT).[372] After a follow-up of 90 days there was no difference in the primary endpoint of arrhythmic death (1.6 vs. 2.4%; RR 0.67; 95% CI 0.37–1.21; $P = 0.18$). Concern was raised regarding the low median wear time of 18 h (IQR 3.8–22.7). The median wear time was higher (23.4 h, IQR 22.2–23.8) in a recent multicentre registry after structured patient education.[371] However, based on the available data, the task force does not recommend routine use of the WCD in the early post-MI phase. Nevertheless, the use of the device may be considered in selected post-MI patients deemed to be at high risk for SCD.

Data on the benefit of the WCD for primary prevention of SCD in other clinical situations (e.g. acute myocarditis, primary prevention indication during pregnancy) are sparse and no recommendations can be currently made.

Recommendation Table 15 — Recommendations for wearable cardioverter defibrillator

Recommendations	Class[a]	Level[b]
The WCD should be considered for adult patients with a secondary prevention ICD indication, who are temporarily not candidates for ICD implantation.	IIa	C

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The WCD may be considered in the early phase after MI in selected patients.[371,372]	IIb	B

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ICD, implantable cardioverter defibrillator; WCD, wearable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

6.2.3. Special aspects of device therapy

6.2.3.1. Optimization of device programming

Optimization of ICD programming is essential to minimize the burden of ICD therapy and to improve patient outcome.[373–375] Detailed recommendations are available in expert consensus papers.[376,377] Bradycardia mode should be customized to prevent unnecessary RV pacing, thus reducing heart failure hospitalizations and all-cause mortality[378–380] (ESC CardioMed chapter 43.21).[381] A tachycardia detection programming strategy incorporating prolonged settings and high rate thresholds (≥188 b.p.m. Advance III trial,[382] ≥200 MADIT-RIT[383]) reduces ICD therapies and all-cause mortality without increasing the risk of syncope.[373,382,383] The evidence is stronger for primary prevention compared to secondary prevention indications[382] (ESC CardioMed chapter 43.21).[381] Consistent use of SVT/VT discriminators even in rates up to 230 b.p.m. is recommended in ICD recipients without complete heart block to reduce inappropriate therapies.[383–385] Proper atrial sensing is a prerequisite for activation of dual-chamber discriminators[376] (ESC CardioMed chapter 43.21).[381] In general, a multi-zone detection programming is favoured to enable tailored use of detection and therapy settings at different tachycardia rates.[383,386] A single-zone programming with a high cut-off rate may be considered in patients with a high likelihood of VF only (e.g. primary electrical diseases).[387] In subcutaneous ICDs, a dual-zone configuration should be adopted. Standardized programming including a lower 'conditional shock' zone with activated discrimination algorithms and a higher 'shock zone' based on rate criteria only has been shown to reduce inappropriate shock rates without compromising patient safety.[388–390] Systematic use of ATP before shock delivery, also for very fast ventricular tachyarrhythmias, has been shown to reduce shock therapy without increase in arrhythmic syncope.[375,384,391] Burst ATP is preferred over ramp due to increased efficacy in first tachycardia termination.[392] Incorporation of remote monitoring into follow-up practice of ICD recipients should be promoted to optimize surveillance of device integrity, to enable prompt detection and management of actionable events, and to prevent occurrence of inappropriate shocks[393–396] (ESC CardioMed chapter 43.21).[381] The proposed recommendations for optimal device programming are applicable to the majority of ICD recipients. Customization may be needed in individual patients.

Recommendation Table 16 — Recommendations for optimization of device programming

Recommendations	Class[a]	Level[b]
Optimization of ICD programming is indicated to avoid inappropriate and unnecessary therapies and to reduce mortality.[373–375]	I	A
In single- or dual-chamber ICD patients without bradycardia pacing indications, it is recommended to minimize ventricular pacing.[378–380]	I	A
Programming of prolonged detection settings is indicated (duration criteria of at least 6–12 s or 30 intervals).[373,382,383]	I	A
It is recommended to program the slowest tachycardia therapy zone limit ≥188 b.p.m. in primary prevention ICD patients.[382,383]	I	A
In patients with SHD, programming of at least one ATP therapy is recommended in all tachyarrhythmias zones.[375,384,391]	I	A
It is recommended to program algorithms for SVT vs. VT discrimination for tachycardias with rates up to 230 b.p.m.[383–385]	I	B
It is recommended to activate lead failure alerts.[397–399]	I	B
Remote monitoring is recommended to reduce the incidence of inappropriate shocks.[395]	I	B
Programming of burst ATP as first attempt is recommended over ramp ATP.[392]	I	B
For S-ICDs, a dual detection zone configuration is recommended with activation of discrimination algorithm in the lower conditional shock zone.[388–390]	I	B
For routine ICD programming, activation of more than one tachycardia detection zone should be considered.[383,386]	IIa	B

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ATP, anti-tachycardia pacing; ICD, implantable cardioverter defibrillator; SHD, structural heart disease; S-ICD, subcutaneous ICD; SVT, supraventricular tachycardia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

6.2.3.2. Concomitant treatment to avoid inappropriate implantable cardioverter defibrillator therapy

Apart from optimization of device programming, pharmacological and/or invasive management may prevent inappropriate ICD therapy. Beta-blockers (carvedilol superior to metoprolol in MADIT-CRT) should be titrated to the maximal tolerated dose in heart failure patients to reduce the risk of inappropriate therapy.[400] In patients with inappropriate therapies due to recurrent SVT, catheter ablation should be first-line treatment, given its high success and low complication rate.[302,401–403] In case of AF-related inappropriate therapies, unresponsive to optimized pharmacological rate control treatment, individualized treatment strategy (rate vs. rhythm) dependent on patient characteristics is suggested.[348] In patients with early AF, adoption of a rhythm control strategy improved patient outcome in the EAST-AFNET 4 trial.[404] In CRT-defibrillator patients, AV node ablation has been associated with reduced inappropriate ICD shocks and lower hospitalization rates compared to drug treatment[405] (ESC CardioMed chapter 41.14).[406]

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Recommendation Table 17 — Recommendations for concomitant treatment to avoid inappropriate implantable cardioverter defibrillator therapy

Recommendations	Class[a]	Level[b]
Catheter ablation is recommended for ICD patients with recurrent SVT resulting in inappropriate ICD therapies.[401,402]	I	C
Pharmacological treatment or catheter ablation is recommended in patients with AF-related inappropriate ICD therapies despite optimal ICD programming.[401,405,407]	I	C

AF, atrial fibrillation; ICD, implantable cardioverter defibrillator; SVT, supraventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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6.2.3.3. Psychosocial impact of implantable cardioverter defibrillator treatment

Almost 20% of ICD recipients suffer from anxiety and depression that are associated with increased mortality.[408–411] In ICD patients, psychological distress is mainly caused by the concern of potentially receiving ICD shocks rather than by having experienced an ICD shock.[412,413] Thus, assessment of ICD concerns is recommended in all ICD patients before ICD shocks occur. Systematic screening of ICD patients for psychological distress is feasible with the use of specific questionnaires.[413–416]

A significant proportion of ICD patients with clinically relevant symptoms of anxiety and depression remains undertreated.[417] Communication with all ICD recipients is needed to clarify misconceptions about the device function, to discuss concerns about sexual functioning, driving restrictions, and to recommend an action plan in case of shock therapy.[418,419] Referral to mental health professionals may be needed for specific interventions.[418,420] Cognitive behavioural therapy intervention may also be provided by trained cardiac nurses to alleviate anxiety.[421] Web-based interventions may also prove useful in improving psychosocial well-being in ICD patients with increased psychosocial distress.[422]

Recommendation Table 18 — Recommendations for psychosocial management after implantable cardioverter defibrillator implantation

Recommendations	Class[a]	Level[b]
Assessment of psychological status and treatment of distress is recommended in ICD patients.[421–423]	I	C
Communication between patient and physician/healthcare professional is recommended to address ICD-related concerns and to discuss quality-of-life issues before ICD implantation and during disease progression.[412,424]	I	C

ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

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6.2.3.4. Patients with left ventricular assist devices

VAs are common among left ventricular assist device (LVAD) carriers.[425–428] VAs are usually well-tolerated, as LVADs maintain adequate cardiac output and prevent circulatory collapse.[429] However, sustained untreated VAs may lead to circulatory collapse even in the presence of an LVAD, especially early after device implantation and in patients with higher pulmonary vascular resistance.[430] VAs pre- and post-LVAD implantation are associated with an increased risk of cardiovascular and all-cause mortality, while ICD can significantly reduce sustained VA.[425,426,431–434] These data support ICD implantation for secondary prevention in LVAD recipients with symptomatic VA.

Observational studies in patients with previous-generation, pulsatile LVADs reported a longer survival with ICD[435–437] (ESC CardioMed chapter 37.32).[438]

Recent registries enrolling continuous-flow LVAD carriers have questioned ICD mortality reduction, but available data are inconsistent.[425,426,428,439,440] An analysis of the INTERMACS registry, enrolling the largest continuous-flow LVAD cohort, showed that ICD presence was not associated with prolonged survival.[428] The lack of documented survival benefit among continuous-flow LVAD carriers, in conjunction with the likelihood of VA tolerance and the associated risks of ICD placement in these patients (risk of infection, device interaction), favours an individualized approach.

Recommendation Table 19 — Recommendations for implantable cardioverter defibrillator implantation in left ventricular assist device recipients

Recommendations	Class[a]	Level[b]
ICD implantation should be considered in LVAD recipients with symptomatic sustained VAs.[425,431]	IIa	B

ICD, implantable cardioverter defibrillator; LVAD, left ventricular assist devices; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.

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6.2.3.5. Complications of devices

Prevention of ICD complications is important to reduce associated morbidity, mortality, and financial burden. During implantation of devices, antibiotic prophylaxis, peri-procedural patient preparation, and appropriate surgical technique should be implemented to prevent device infections and formation of pocket haematoma.[441–443] Cephalic or axillary vein access is preferred over the subclavian vein route to reduce the risk of pneumothorax and lead failure.[444–446] Proper selection of ICD systems is important. Single-chamber ICDs are recommended in primary prevention patients without atrial or AV sequential pacing indications. This reduces peri-procedural complications and generator replacements as compared to dual-chamber ICDs. This approach does not increase the risk of inappropriate shocks if optimal device programming is used.[447–450] Routine use of single-coil defibrillator leads is favoured due to reduced risk of complications during lead removal without associated differences in shock efficacy.[451,452] Use of dual-coil leads can be considered in clinical settings where a higher defibrillator threshold is suspected, e.g. HCM, right-sided implantations.[453,454]

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Recommendation Table 20 — Recommendations for prevention of implantable cardioverter defibrillator complications

Recommendations	Class[a]	Level[b]
Single-chamber ICD is recommended over dual-chamber ICD in primary prevention patients without current or expected indication for atrial or AV sequential pacing due to a lower risk of device-related complications.[447,448,450]	I	A
The use of single-coil leads over dual-coil ICD leads should be considered due to lower complication rate during transvenous lead extraction.[451]	IIa	C

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AV, atrioventricular; ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

6.2.3.6. End-of-life issues

Patients with active ICDs experience a considerable rate of shocks in the last phase of life.[455] In terminally ill patients and at the end of life, healthcare professionals can facilitate a decision by the patient and the patient's family by explaining in a sensitive and understandable manner the benefits and burdens of continued ICD therapy.[456] Patients should be informed about the options of ICD deactivation. In general, deactivation of anti-bradycardia therapy is discouraged to avoid quality-of-life impairment, and in some countries deactivation in pacemaker-dependent patients may be prohibited by law.[457] Deactivation should be discussed before device implantation and when there is significant deterioration of the patient's health status. Despite an increasing trend to address and perform device deactivation after careful consideration, current rates are still low and improved patient care is needed.[458,459]

Recommendation Table 21 — Recommendations for end-of-life issues in implantable cardioverter defibrillator carriers

Recommendations	Class[a]	Level[b]
Informed discussion with patient and family about ICD deactivation options and shared decision-making is indicated prior to implantation and in case of significant health status deterioration.[458]	I	C

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ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

6.2.4. Interventional therapy

6.2.4.1. Catheter ablation

6.2.4.1.1. Patients with structural heart disease. In patients with SHD, SMVTs are primarily due to a scar-related re-entrant mechanism.[460–465]

Because of a higher risk of SCD, an ICD implantation is usually recommended in patients with sustained VAs associated with SHD.[466–468] However, ICDs do not prevent VA, and many of these patients will experience symptomatic VT/VF recurrences resulting in syncope or ICD shocks and may require additional treatment.[330,383,419,469–471]

In patients with SHD, the choice of anti-arrhythmic agents is mostly limited to beta-blockers, sotalol, and amiodarone to help control VT/VF recurrences, and this treatment is frequently hampered by side effects.[318,472]

Owing to advances made over the last three decades, catheter ablation has become increasingly important for the management of scar-related VTs.[473] Since the early 1990s, catheter ablation of BBR-VT has been very successful[474–477] and is considered as first-line therapy[466,467] (*Figure 5*). Subsequently, catheter ablation has been shown to be very effective in controlling incessant VTs or electrical storms[330,331] and in reducing subsequent VT burden. Many observational studies have shown a positive effect of VT ablation on clinical outcome in terms of VT recurrences.[478–483] In patients with CAD, three randomized trials[471,484,485] have reported that catheter ablation, compared to conventional treatment, decreases the likelihood of subsequent ICD shocks and prevents recurrent VT episodes.

The critical part of re-entrant VT circuits, referred to as the 'protected VT isthmus', is the primary target for ablation,[460,486] but it is very challenging to unmask in haemodynamically not-tolerated VT.[487,488] Due to the high likelihood of multiple re-entry circuits in a scar and difficulties in identifying critical isthmuses, the ablation strategy has gradually evolved over the years towards more extended ablation of the arrhythmogenic substrate.[489–492] Special attention should be paid to cases of PVT/VF initiated by similar PVCs, where the triggering PVC (often related to the Purkinje network) should be targeted for ablation.[221,332,333,493]

The electrophysiological characteristics of VT circuits depend on the underlying SHD. Thus, post-infarct VTs are mainly related to an endocardial VT circuit (amenable to endocardial ablation), while the location of re-entrant VT circuits is more variable in patients with cardiomyopathies.[494–496] Here, intramural and/or epicardial involvement are more common. This significantly contributes to the difference in the clinical outcomes of VT ablation in relation to the underlying heart disease with a better outcome in CAD as compared to non-ischaemic aetiologies.[497–499]

Effective ablation requires durable ablation lesions to arrhythmogenic tissue. In some cases, such as intramural VTs, difficulties remain in achieving this objective with current catheters, regardless of the approach (endocardial/epicardial).[500] To improve the formation of myocardial lesions, new catheter-based techniques are being evaluated (e.g. bipolar/needle ablation, transcoronary alcohol ablation),[501–506] as well as radiotherapy ablation[507,508] or surgical ablation,[509] which are currently bailout treatments.

When planning VT ablation, it is important to collect all available information about the arrhythmogenic substrate, especially to identify scars (using CMR or CT scan),[510–514] and to help determine the exit site of VAs with the 12-lead ECG documentation of clinical VTs or PVCs that induce PVT/VF.

The mean long-term success rate of VT ablation varies from 30% to 70%, depending on the underlying SHD.[481,515–518] Peri-procedural complications, in particular stroke, cardiac tamponade, or death, may occur.[519–522]

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6.2.4.1.2. Patients without apparent structural heart disease. 'Idiopathic VTs' is the term for VTs that are not associated with SHD or a genetic arrhythmic syndrome. Most idiopathic VTs are mediated by triggered activity, but a re-entrant mechanism (involving the LV Purkinje network) explains verapamil-sensitive fascicular VTs.[523] Three important key features distinguish idiopathic VTs from VTs associated with SHD. First, idiopathic VTs mostly originate from a single site and specific region of the heart (namely the right or left ventricular outflow tracts,[524,525] along the valve annuli,[526–528] papillary muscle,[529] or the LV Purkinje network).[523] Second, no detectable scar is found in idiopathic VTs.[530] Finally, idiopathic VTs have a benign prognosis so that ICD implantation is generally not recommended.[466]

The earliest site of activation during VT is the ablation target for focal sources, while abnormal Purkinje tissue (with diastolic activity during VT) is the ablation target of left fascicular VTs.[531,532]

Catheter ablation is curative in most idiopathic VT patients and peri-procedural complications are rare.[533–537]

6.2.4.2. Autonomic modulation

The role of the autonomic nervous system in promoting arrhythmias has long been recognized, leading to the concept of *Coumel's triangle of arrhythmogenesis*.[538]

Sympathetic activation has been demonstrated as playing a key role in inducing VAs in some entities, such as congenital LQTS and CPVT,[539,540] and left cardiac sympathetic denervation was shown to be associated with a decrease in the frequency of arrhythmogenic syncope in congenital LQTS.[541,542] The efficacy of cardiac sympathetic blockade by different approaches (thoracic epidural anaesthesia, percutaneous stellate ganglion anaesthesia, or surgical stellate ganglion resection) in reducing the arrhythmia burden in refractory VT/VF has been recognized in several small observational studies.[326,328,340] Further studies are needed to assess which patients may benefit from a modulation of the autonomic nervous system to better control VT/VF.

7. Diagnostic evaluation, management, and risk stratification according to clinical presentation and known (likely) disease

7.1. Specific structural heart diseases

7.1.1. Coronary artery disease

7.1.1.1. Acute coronary syndromes and vasospasm

7.1.1.1.1. Acute coronary syndromes. SCD is a major cause of mortality in ACS, mostly caused by sustained VAs, in particular VF. The majority of studies have reported on patients with STEMI. Of patients with STEMI, 4–12% develop VA within the first 48 h after the onset of symptoms.[69,543,544] Pre-reperfusion VAs are more common than reperfusion-induced or post-reperfusion arrhythmias in STEMI.[545] Haemodynamic instability, cardiogenic shock, LVEF $<$ 40%, and the sum of ST-segment deviations in all leads are independent predictors of VA both in STEMI and non-STEMI.[69,546] In addition, an early repolarization pattern has been associated with increased risk of VAs and SCD in ACS.[547]

Prevention of ventricular arrhythmias in ST elevation myocardial infarction

Urgent reperfusion is the most important therapy,[292,548] as acute ischaemia triggers arrhythmias. Beta-blocker treatment is also recommended to prevent VA.[3,549] In a recent randomized trial of patients with STEMI, early intravenous metoprolol before percutaneous coronary intervention reduced the incidence of arrhythmias in the acute phase and was not associated with an increase in adverse events.[550] Prophylactic treatment with AADs has not proven beneficial, and may even be harmful.[322] Correction of electrolyte imbalances is strongly recommended.[289]

Management of sustained ventricular tachycardia and ventricular fibrillation in acute coronary syndrome

Electrical cardioversion or defibrillation is the intervention of choice to acutely terminate VAs in ACS patients (*Figure 14*).[205,339] Recurrent sustained VT, especially when polymorphic, or recurrent VF can indicate incomplete reperfusion or recurrence of acute ischaemia. In this case, immediate coronary angiography is indicated.[3] For recurrent PVT degenerating into VF, beta-blockers are recommended.[551,552] In addition, deep sedation may be helpful to reduce episodes of VT or VF.[553] Intravenous amiodarone should be considered to acutely suppress recurrent haemodynamically relevant VAs, although there is a paucity of controlled studies for amiodarone during STEMI[554] and the evidence in this setting is mainly extrapolated from studies of OHCA.[555] If treatment with beta-blockers and amiodarone is not effective, lidocaine may be considered.[322] The use of other AADs in ACS is not recommended.[549,556] In haemodynamically unstable patients with refractory VA, mechanical circulatory support may be considered.[336,557] For VA in the context of relative bradycardia or pause-related, pacing may be effective to prevent re-initiation.

The prognostic significance of early ventricular arrhythmias

Early VAs are defined as VT/VF occurring within 48 h after a STEMI. In the contemporary percutaneous coronary intervention (PCI)-based revascularization era, almost all VA occur within the first 24 h.[558] Early VA have been associated with an up to six-fold increase in in-hospital mortality, whereas long-term prognosis seems not to be significantly affected.[543,559,560] In a prospective cohort study, patients with VF during the acute STEMI phase had low and very similar incidence of late SCD as compared with VF-free patients during 5-year observation.[560] Of note, early *monomorphic* VT was associated with significantly higher incidence of adequate ICD interventions compared with early VF, and was an independent predictor of death during long-term follow-up.[561] Thus, the prognostic significance of VT and VF occurring in the acute phase of MI may be different. The impact of VA occurring late after reperfusion ($>$48 h) on late SCD is less clear.

Podolecki *et al.*[559] recently demonstrated that long-term all-cause mortality after STEMI was predicted by VA occurring late after reperfusion ($>$48 h after reperfusion), while early reperfusion VAs did not affect 5-year outcome. Further studies are required to clarify

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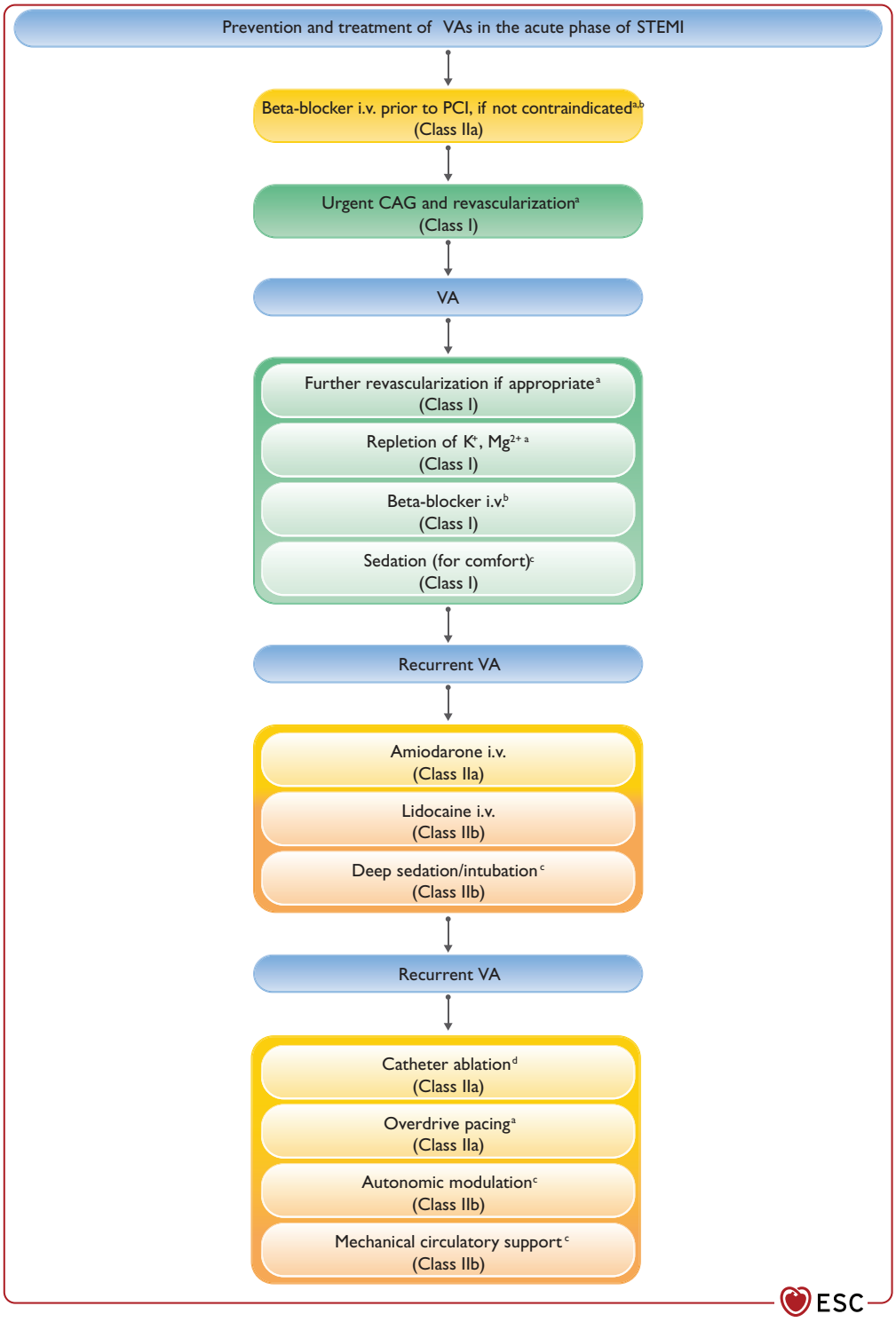

Figure 14 Algorithm for the prevention and management of ventricular arrhythmias in ST-elevation myocardial infarction. CAG, coronary angiogram; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; VA, ventricular arrhythmias. [a]The 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.[3] [b]Intravenous beta-blockers must be avoided in patients with hypotension, acute heart failure, AV block or severe bradycardia. [c]Flowchart for the management of electrical storm. [d]If similar PVC triggers recurrent polymorphic VA.

the impact of VA occurring >48 h after STEMI on late SCD in contemporary patients undergoing acute PCI.

7.1.1.1.2. Vasospasm. Coronary artery spasms might have an important role in the pathogenesis of VA. The long-term prognosis

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Recommendation Table 22 — Recommendations for treatment of ventricular arrhythmias in acute coronary syndrome and vasospasm

Recommendations	Class[a]	Level[b]
Treatment of VAs in ACS		
Intravenous beta-blocker treatment is indicated for patients with recurrent PVT/VF during STEMI unless contraindicated.[551,552]	I	B
Intravenous amiodarone treatment should be considered for patients with recurrent PVT/VF during the acute phase of ACS.[552,554,555]	IIa	C
Intravenous lidocaine may be considered for the treatment of recurrent PVT/VF not responding to beta-blockers or amiodarone, or if amiodarone is contraindicated during the acute phase of ACS.[554]	IIb	C
Prophylactic treatment with AADs (other than beta-blockers) is not recommended in ACS.[322]	III	B
Vasospasm		
In SCA survivors with coronary artery spasm, implantation of an ICD should be considered.[562–564]	IIa	C

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AAD, anti-arrhythmic drug; ACS, acute coronary syndrome; ICD, implantable cardioverter defibrillator; PVT, polymorphic ventricular tachycardia; SCA, sudden cardiac arrest; STEMI, ST elevation myocardial infarction; VA, ventricular arrhythmia; VF, ventricular fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

of patients with variant angina who survive a CA is worse than in other patients with variant angina.[562,563] In a recent multicentre European survey,[564] patients with life-threatening VAs secondary to coronary vasospasm were at high risk for recurrence, especially when insufficient medical therapy was administered. While calcium channel blockers (CCB) are capable of suppressing episodes, beta-blockers may trigger VAs. As medical intervention and multiple vasodilator drugs may not be sufficiently protective, placement of an ICD should still be considered in SCA survivors with variant angina.

7.1.1.2. Early after myocardial infarction

The first weeks after a STEMI carry the highest risk both for all-cause death and for SCD, particularly in patients with reduced LVEF.[565,566] For this reason, early assessment of LVEF, i.e. before discharge, is recommended.[567,568] Early routine prophylactic ICD implantation in the first 40 days after MI did not reduce mortality in post-MI patients with reduced LVEF in two randomized trials (DINAMIT and IRIS),[569,570] and is therefore not recommended. Early assessment by further non-invasive tests, apart from LVEF measurement, has also not proven to be useful for risk stratification with regard to SCD.[571] Limited evidence suggests that invasive risk stratification by PES in the early post-MI phase may be helpful for identification of high-risk patients with reduced LVEF.[572] However, the utility of this approach has not been confirmed so far in randomized studies. The PROTECT-ICD randomized trial (NCT03588286) is currently examining whether PES may guide the decision on ICD implantation in patients with reduced EF in the early phase after STEMI.

Reverse remodelling following an MI is associated with significantly lower rates of death, SCA, and other adverse clinical outcomes.[573,574] Therefore, assessment of the indication for prophylactic ICD implantation, usually performed by repeat echocardiography, should take place in the post-remodelling phase of the MI after the first 6 weeks in patients with a pre-discharge LVEF ≤40%. Reassessment of the LVEF before 6 weeks following MI may not discriminate between myocardial stunning and remodelling.

In the early post-MI phase, electrical storm and/or recurrent episodes of PVT or VF are immediately life-threatening conditions. In this setting, it is important to exclude ischaemia as the triggering factor for the arrhythmias. If medical treatment is not sufficient to suppress the arrhythmic episodes, catheter ablation is potentially effective particularly if the episodes are focally triggered by similar PVCs.[332,575] If PVT recurs despite beta-blocker and amiodarone treatment, suppression by quinidine therapy has been reported.[323]

Recommendation Table 23 — Recommendations for risk stratification and treatment of ventricular arrhythmias early after myocardial infarction

Recommendations	Class[a]	Level[b]
Risk stratification		
Early (before discharge) assessment of LVEF is recommended in all patients with acute MI.[567,568]	I	B
In patients with pre-discharge LVEF ≤40%, re-evaluation of LVEF 6–12 weeks after MI is recommended to assess the potential need for primary prevention ICD implantation.[568,573,574]	I	C
Treatment of VAs		
Catheter ablation should be considered in patients with recurrent episodes of PVT/VF triggered by a similar PVC non-responsive to medical treatment or coronary revascularization in the subacute phase of MI.[332]	IIa	C

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ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PVC, premature ventricular complex; PVT, polymorphic ventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

7.1.1.3. Chronic coronary artery disease

7.1.1.3.1. Primary prevention of sudden cardiac death in patients with reduced ejection fraction. Forty days after STEMI, approximately 5% of patients will have an LVEF ≤35%.[576] These patients are at risk for SCD. Therefore, in patients with LVEF ≤35% and

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heart failure symptoms NYHA class II and III, primary preventive ICD implantation is recommended.[356] ICD implantation should also be considered for asymptomatic patients with an EF ≤30%.[354] In this population, mortality reduction by an ICD has been demonstrated in four RCTs.[353–356] In patients with CAD, a reduced LVEF (≤40%), and asymptomatic NSVT, inducibility by PES identifies patients who benefit from an ICD, independent from NYHA class.[355]

Since the publication of the aforementioned trials, early revascularization strategies and modern heart failure medication have reduced the overall risk of SCD in heart failure patients.[577] Although total mortality has been reduced, the relative reduction by the ICD is a consistent 27%, which has been corroborated in two recent large prospective registry studies enrolling 2327 European patients between 2014 and 2018 (EU-CERT-ICD)[357] and 2610 Swedish patients enrolled between 2000 and 2016 (SwedeHF registry).[358]

Recommendation Table 24 — Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in chronic coronary artery disease

Recommendations	Class[a]	Level[b]
Risk stratification and primary prevention of SCD		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.[146,584]	I	C
ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.[354,356]	I	A
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.[354]	IIa	B
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT, and NSVT, if they are inducible for SMVT by PES.[355]	IIa	B
In patients with CAD, prophylactic treatment with AADs other than beta-blockers is not recommended.[556,578,579]	III	A
Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients without ongoing ischaemia with documented VF or haemodynamically not-tolerated VT occurring later than 48 h after MI.[349–351]	I	A
In patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy.[471]	I	B
The addition of oral amiodarone or beta-blocker replacement by sotalol should be considered in patients with CAD with recurrent, symptomatic SMVT, or ICD shocks for SMVT while on beta-blocker treatment.[318,581]	IIa	B
In patients with CAD and haemodynamically well-tolerated SMVT and LVEF ≥40%, catheter ablation in experienced centres should be considered as an alternative to ICD therapy, provided that established endpoints have been reached.[c,480,580]	IIa	C
ICD implantation should be considered in patients with a haemodynamically tolerated SMVT and an LVEF ≥40% if VT ablation fails, is not available, or is not desired.	IIa	C
Catheter ablation should be considered in patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite beta-blockers or sotalol treatment.[471]	IIa	C
In patients with CAD eligible for ICD implantation, catheter ablation may be considered just before (or immediately after) ICD implantation to decrease subsequent VT burden and ICD shocks.[484,485,582,583]	IIb	B

AAD, anti-arrhythmic drug; CAD, coronary artery disease; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; OMT, optimal medical therapy; PES, programmed electrical stimulation; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycardia; STEMI, ST elevation myocardial infarction; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]VT non-inducibility and elimination of electrograms consistent with conduction delay.

7.1.1.3.2. Primary prevention of sudden cardiac death in patients with preserved or mildly reduced ejection fraction. There are no data supporting primary prophylactic ICD implantation in post-infarct patients with preserved or mildly reduced LVEF. These patients are heterogeneous with regard to their potential arrhythmic substrate, and efforts are under way to identify those with the highest risk for SCD. PES is recommended in post-infarct patients in whom syncope remains unexplained after non-invasive evaluation to guide patient management (*Figure 15*).[146]

In the PRESERVE-EF study, 41 of 575 post-infarct patients with an LVEF ≥40% and one non-invasive ECG risk factor more than 40 days post-MI were inducible for VT/VF during PES and received an ICD.[151] During the 32-month follow-up period, no SCD occurred and 9 of 37 ICD patients received an appropriate ICD therapy. However, the role of appropriate ICD treatment as surrogate for SCD in patients with preserved LVEF is unknown, and randomized trials are needed. Prophylactic treatment with AADs other than beta-blockers is not indicated regardless of the LVEF.[556,578,579]

7.1.1.3.3. Secondary prevention of sudden cardiac death. The three pivotal secondary prevention ICD trials enrolled 1866 patients between 1990 and 1997.[349–351] A patient-level

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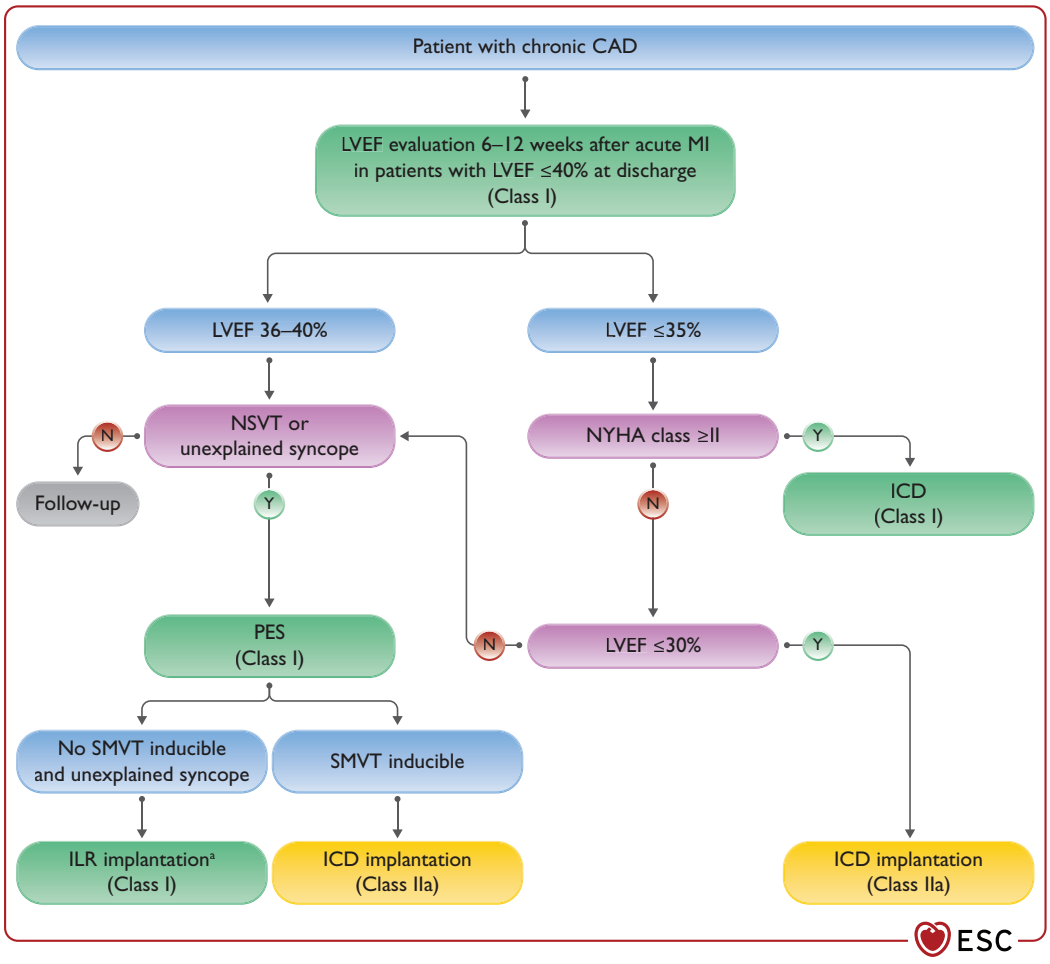

Figure 15 Algorithm for risk stratification and primary prevention of sudden cardiac death in patients with chronic coronary artery disease and reduced ejection fraction. CAD, coronary artery disease; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; LVEF, left ventricular ejection fraction; MI, myocardial infarction; N, No; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; PES, programmed electrical stimulation; SMVT, sustained monomorphic ventricular tachycardia; Y, Yes. [a]The 2018 ESC Guidelines for the diagnosis and management of syncope.[1]

meta-analysis demonstrated a 28% mortality reduction (HR 0.72; 95% CI 0.60–0.87; $P = 0.0006$) almost entirely due to reduction of arrhythmic death (HR 0.50; 95% CI 0.37–0.67; $P < 0.0001$) in the ICD group.[352] This translates to an extension of survival of 4.4 months over a mean follow-up of 6 years by the ICD. Around 80% of the study population suffered from CAD. Patients with well-tolerated SMVT were excluded from secondary prevention trials (*Figure 16*).

7.1.1.3.4. Management of patients with haemodynamically tolerated ventricular tachycardia and preserved and mildly reduced ejection fraction. With the better understanding of the mechanisms of VT after MI, as well as improved ablation and imaging technologies, catheter ablation has become an option for the treatment of haemodynamically well-tolerated VT in selected post-MI patients with preserved or mildly reduced EF, even without ICD back-up. One small monocentric retrospective trial studied patients with CAD, LVEF >40%, and haemodynamically tolerated VT who underwent catheter ablation as first-line therapy.[580] The investigators could abolish 90% of the clinical and 58% of all inducible VTs. Subsequently, 42% of the patients received an ICD. After a mean follow-up of 3.8 years, 42% of the patients died irrespective of the presence or absence of an ICD ($P = 0.47$).

A larger multicentre retrospective study looked at 166 patients with an LVEF >30% presenting with well-tolerated SMVT, which were treated by catheter ablation only, and compared the outcome to a control group of 378 patients implanted with an ICD.[480] Of the 166 patients undergoing ablation as first therapy, 55% suffered from CAD. The mean LVEF was 50%, and after a mean follow-up of 32 months, overall mortality did not differ between the groups (12%).

These data suggest that either ICD implantation or ablation in experienced centres should be considered in patients with a preserved or mildly reduced EF presenting with haemodynamically tolerated SMVT. Of note, although ICDs have been commonly implanted in this population, the secondary preventive ICD trials failed to show a survival benefit in patients with an LVEF ≥35%.[352] Although SMVT is rarely caused by ischaemia and revascularization alone

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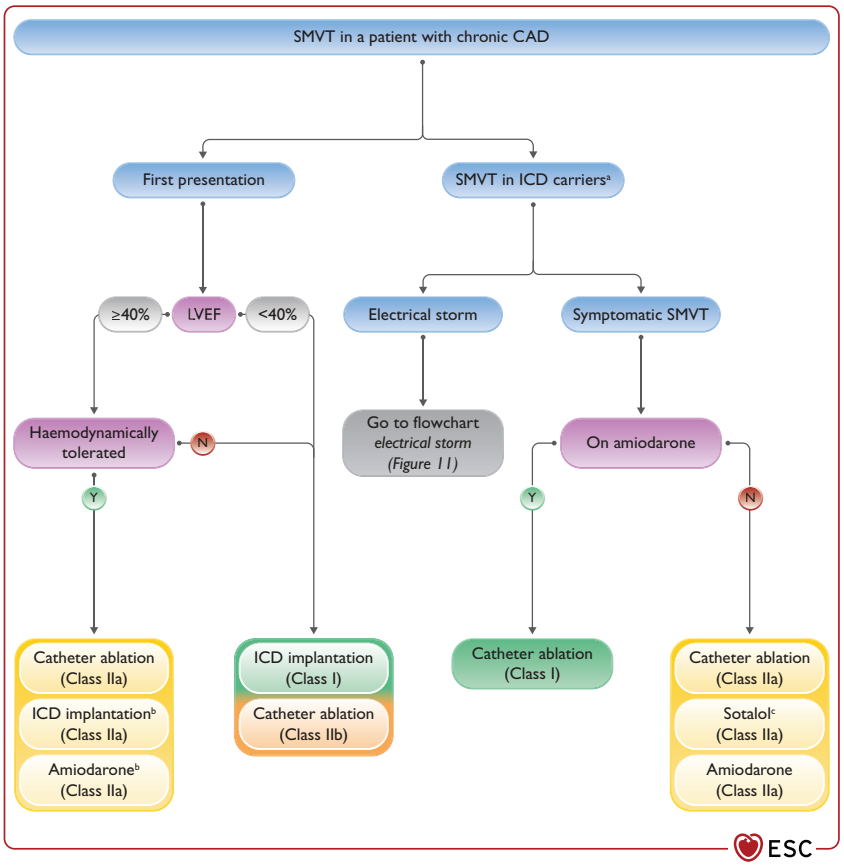

Figure 16 Algorithm for the management of sustained monomorphic ventricular tachycardia in patients with chronic coronary artery disease. CAD, coronary artery disease; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; N, No; SMVT, sustained monomorphic ventricular tachycardia; Y, Yes. [a]Incessant ventricular tachycardia in monitor zone: consider catheter ablation. [b]If catheter ablation is not available, not successful or not desired by the patient. [c]To reduce ICD shocks.

does not prevent VT recurrence, exclusion or treatment of significant CAD before catheter ablation is reasonable.

7.1.1.3.5. Management of recurrent ventricular tachycardia in implantable cardioverter defibrillator carriers. Frequent, symptomatic VT in ICD recipients should be treated medically with either amiodarone or sotalol.[318,581] In patients with CAD in whom SMVT recurs while on amiodarone treatment, catheter ablation is recommended over escalation of AAD therapy. In the VANISH trial, the composite endpoint of death, VT storm, and appropriate ICD therapy was reached significantly less often in the ablation group as compared to the escalated amiodarone-therapy group over a mean follow-up of 28 months (59% vs. 68.5%; HR 0.72; 95% CI 0.53–0.98; $P = 0.04$).[471] The ongoing VANISH2 trial (ClinicalTrials.gov Identifier: NCT02830360) addresses the question of whether catheter ablation as first-line treatment is superior to AAD therapy in post-MI patients with SMVT.

Preventive VT ablation after a first documented SMVT, which was followed by ICD implantation, reduced neither mortality nor hospitalizations for arrhythmia or worsening heart failure when compared to a deferred ablation strategy only after the third ICD shock.[582] However, in patients who present with a first VT episode and in whom an ICD is indicated, catheter ablation performed immediately before or shortly after ICD implantation may be considered to decrease subsequent VT and ICD shocks.[484,485,583]

7.1.1.4. Coronary anomalies

Anomalous aortic origin of a coronary artery, either the left or the right, arising from the opposite sinus of Valsalva, is associated with an increased risk of SCD, especially in individuals <35 years during or following vigorous exercise.[585] Anomalous aortic origin of the left coronary artery is less common but more malignant than anomalous aortic origin of the right coronary artery. Other risk factors for SCD are interarterial course between the aorta and pulmonary artery, slit-like shaped orifice, high orifice, acute-angle take-off, and intramural course and its length.[585,586] Indications for surgical intervention, especially in asymptomatic patients, are based on the evaluation of high-risk anatomy by CTA and the assessment of exercise-induced ischaemia using advanced imaging modalities.[586–588] Cardiac stress imaging is also indicated to evaluate exercise-induced ischaemia after surgical intervention, especially in patients with an aborted CA.[588]

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Recommendation Table 25 — Recommendations for sudden cardiac death prevention in patients with coronary anomalies

Recommendations	Class[a]	Level[b]
Diagnostic evaluation		
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test in patients with anomalous aortic origin of a coronary artery with an interarterial course to confirm/exclude myocardial ischaemia.[587]	I	C
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test after surgery in patients with anomalous aortic origin of a coronary artery with a history of aborted CA.	I	C
Treatment		
Surgery is recommended in patients with anomalous aortic origin of a coronary artery with CA, syncope suspected to be due to VAs, or angina when other causes have been excluded.[585,586,588]	I	C
Surgery should be considered in asymptomatic patients with anomalous aortic origin of a coronary artery and evidence of myocardial ischaemia or abnormal aortic origin of the left coronary artery with high-risk anatomy.[c,585,586,588]	IIa	C

CA, cardiac arrest; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.
[c]High-risk anatomy is defined as interarterial course, slit-like shaped orifice, high orifice, acute-angle take-off, and intramural course and its length.

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7.1.2. Idiopathic premature ventricular complexes/ventricular tachycardia and premature ventricular complex-induced cardiomyopathy

7.1.2.1. Idiopathic premature ventricular complexes/ventricular tachycardia

PVCs/VT in patients without SHD are defined as idiopathic (*Figure 17*). In patients with presumed idiopathic PVCs/VT based on a negative history and normal physical examination, 12-lead ECG and transthoracic echocardiography are important first diagnostic steps to exclude underlying SHD. Twenty-four-hour ECG Holter monitoring is usually performed to determine the PVC burden. Multiform PVCs at prolonged ECG monitoring and subtle changes on ECG or echocardiography need to be recognized.[589] CMR should be performed whenever ECG and echocardiography are inconclusive to rule out SHD, or the clinical presentation raises suspicion for SHD.[590,591]

Patients need to be treated when PVCs/VT are symptomatic or associated with deterioration of cardiac function. The clinical course and responses to different treatments have been mostly studied in those originating from the RVOT or the left fascicles.

Several drugs have been used to treat idiopathic PVCs/VT. Recommendations are based on small or non-controlled series. Beta-blockers and CCBs are the most-studied drugs and both have been shown to be effective at arrhythmia suppression.[304] The evidence for flecainide is scarce.[592] In case of a higher burden of PVCs with higher heart rate or during exercise, beta-blockers should be preferred.[593] If there is not such a correlation, the use of flecainide or CCB drugs have been associated with more effective PVC suppression. Beta-blockers should also be selected when a focal triggered activity mechanism is suspected. CCB should be the drug of choice for fascicular PVC/VT. Although data are lacking, beta-blockers or CCBs are considered first choice for PVCs with an origin outside the RVOT or the left fascicles because flecainide may have proarrhythmic side effects. Amiodarone is associated with severe systemic toxicity and should be used only if ablation or other drugs fail or cannot be used.[594] A summary of the recommendations for the treatment of idiopathic PVCs/VT and PVC-induced or aggravated cardiomyopathy with AADs is provided in *Table 9*.

A high success rate of catheter ablation of idiopathic PVCs/VT has been reported with rare complications, particularly for the RVOT and fascicular types.[535] In a randomized study including patients with RVOT PVCs, ablation was superior to AAD therapy for arrhythmia suppression with no differences in complications.[595] Ablation is therefore recommended as the first-line therapy for RVOT and fascicular PVCs/VT. The available information for other forms of idiopathic PVCs/VT is limited and mostly restricted to the acute success of ablation, which, in general, is lower and associated with more recurrences than for RVOT and fascicular PVCs/VT.[540] In addition, access to and ablation at specific locations (e.g. sinus of Valsalva, LV summit) may increase the risk for procedural complications. Therefore, when the 12-lead ECG is highly suspicious of a PVC/VT source outside the RVOT or left fascicles, the level of recommendation for ablation is lower.

In general, treatment of children should be similar to that of adults. However, ablation should be deferred in young and small children due to the risk of complications and the relatively larger size of the ablation lesion as compared to the child's heart.[596,597] Verapamil is not recommended as the first-line therapy in children <1 year old because it has been associated with hypotension in some case reports.[542] Of note, all reported patients had either heart failure, overdosing of verapamil, or other concurrent AADs at the time verapamil was given.[598]

Patients may present with asymptomatic frequent PVCs/VTs. Only a minority of patients with >1000 PVCs per day will develop ventricular dysfunction after 5 years follow-up.[599] A PVC burden of 10% seems to be the minimal threshold for development of LV dysfunction, with higher risk when the PVC burden is >20%.[535,600,601] Regular assessment of LVEF in this setting is therefore indicated. To date, there are no data supporting the benefit of arrhythmia treatment for asymptomatic patients with preserved ventricular function. In addition, PVC burden often decreases spontaneously over time, particularly in children.[599,602] In selected patients, e.g. patients who do not want to be followed, catheter ablation may be considered. In patients with PVC burden < 10%, re-evaluation may be appropriate in case of development of new symptoms or change in patient condition.

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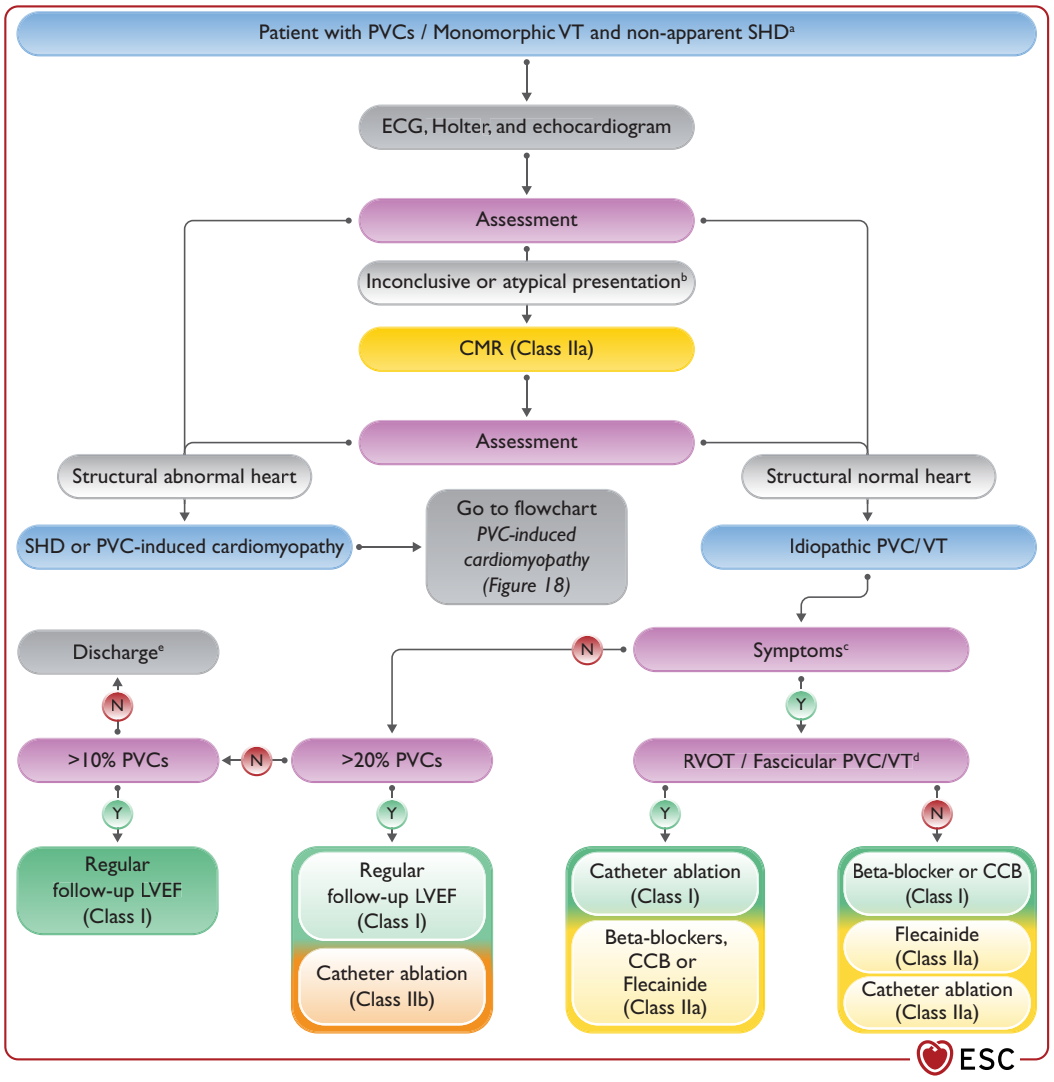

Figure 17 Algorithm for the management of patients with idiopathic premature ventricular complexes/ventricular tachycardia and non-apparent structural heart disease. CCB, calcium channel blocker; CMR, cardiac magnetic resonance; ECG, electrocardiogram; LVEF, left ventricular ejection fraction; N, No; PVC, premature ventricular complex; RVOT, right ventricular outflow tract; SHD, structural heart disease; VT, ventricular tachycardia; Y, Yes. [a]Non-apparent SHD is defined by lack of significant abnormalities in physical examination, basal ECG, and echocardiogram. [b]Atypical presentation: e.g. older age, right bundle branch block morphology, sustained monomorphic VT consistent with re-entry. [c]Symptoms should be relevant and related to PVC/VT. [d]Origin suspected by ECG or confirmed during electrophysiological evaluation. [e]Consider re-evaluation in case of new symptoms or changes in patient clinical condition.

Table 9 Summary of the recommendations for the treatment of patients with frequent idiopathic premature ventricular complexes/ventricular tachycardia or premature ventricular complex-induced cardiomyopathy

	Ablation	Beta-blocker	CCB	Flecainide	Amiodarone
RVOT/fascicular PVC/VT: Symptomatic, normal LV function	Class I	Class IIa	Class IIa	Class IIa	Class III
PVC/VT other than RVOT/fascicular: Symptomatic, normal LV function	Class IIa	Class I	Class I	Class IIa	Class III
RVOT/fascicular PVC/VT: LV dysfunction	Class I	Class IIa	Class III[a]	Class IIa[b]	Class IIa
PVC/VT other than RVOT/fascicular: LV dysfunction	Class I	Class IIa	Class III[a]	Class IIa[b]	Class IIa
PVC: Burden >20%, asymptomatic, normal LV function	Class IIb				Class III

CCB, calcium channel blocker; LV, left ventricular; PVC, premature ventricular complex; RVOT, right ventricular outflow tract; VT, ventricular tachycardia.
[a]Intravenous calcium channel blockers.
[b]In selected patients (only moderate LV dysfunction).

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Recommendation Table 26 — Recommendations for the management of patients with idiopathic premature ventricular complexes/ventricular tachycardia

Recommendations	Class[a]	Level[b]
General recommendations		
Regular assessment of ventricular function of patients with PVC burden >10% and normal ventricular function is indicated.[602,603]	I	C
In patients with PVCs/VT and a presentation not typical for an idiopathic origin,[c] CMR should be considered, despite a normal echocardiogram.[195]	IIa	C
Treatment		
Catheter ablation as first-line treatment is recommended for symptomatic idiopathic VT/PVCs from the RVOT or the left fascicles.[d,535,595,596,604]	I	B
Beta-blockers or non-dihydropyridine CCBs are indicated in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.[304,593]	I	C
Beta-blockers, non-dihydropyridine CCBs, or flecainide should be considered when catheter ablation is not available, desired, or is particularly risky in symptomatic patients with idiopathic VT/PVCs from the RVOT or the left fascicles.[304,592,593]	IIa	B
Catheter ablation or flecainide should be considered in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.[535,604,605]	IIa	C
Catheter ablation may be considered for idiopathic VT/PVCs in asymptomatic patients with repeatedly more than 20% of PVCs per day at follow-up.[535,600,601]	IIb	B
Catheter ablation of idiopathic VT/PVCs is not recommended in children <5 years of age or <10 kg weight except when previous medical therapy fails or when VT is not haemodynamically tolerated.[597]	III	C
Amiodarone as a first-line treatment is not recommended in patients with idiopathic VTs/PVCs.[594]	III	C
Verapamil is not recommended in children <1 year of age with PVC/VT, particularly if they have signs of heart failure or concurrent use of other AADs.[606]	III	C

AAD, anti-arrhythmic drug; CCB, calcium channel blocker; CMR, cardiac magnetic resonance; PVC, premature ventricular complex; RVOT, right ventricular outflow tract; SMVT, sustained monomorphic ventricular tachycardia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Including but not limited to older age, right bundle branch block (RBBB) morphology, SMVT consistent with re-entry.
[d]Level of evidence C for VT/PVCs from left fascicles.

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7.1.2.2. Premature ventricular complex-induced/-aggravated cardiomyopathy

The importance of PVC-induced cardiomyopathy as a secondary and reversible cause of LV dysfunction in patients without SHD has been recognized.[607,608] The patient's medical and family history, 12-lead ECG, Holter-ECG, and echocardiography form the cornerstones of the evaluation of patients with suspected PVC-induced cardiomyopathy (*Figure 18*). PVC burden has been shown to be the strongest independent predictor of PVC-induced cardiomyopathy in several studies.[600,609–611] Day-by-day fluctuations of PVC burden have been reported in patients undergoing 14-day monitoring, but most data are based on 24-h registrations.[611] A PVC burden of at least 10% appears to be the minimal threshold for development of PVC-induced cardiomyopathy, and the risk increases further with a PVC burden >20%.[600,611] In patients with a PVC burden <10%, other cardiomyopathy aetiologies should be suspected and further diagnostic work-up undertaken. In such patients, Holter-ECG should be repeated to assess fluctuations in PVC burden. Factors predicting adverse LV remodelling in patients with frequent PVCs include superior PVC axis, epicardial origin, NSVT, shorter coupling interval, and male gender.[535,611–613]

Frequent PVCs can also aggravate LV dysfunction in patients with SHD. In such cases, LV dysfunction can either be a direct consequence of PVCs as in PVC-induced cardiomyopathy, or due to the limiting effect of PVCs on optimal biventricular pacing in CRT patients. Parameters such as smaller LV end diastolic diameter and shorter intrinsic QRS duration might help to distinguish PVC-induced cardiomyopathy from PVC-aggravated cardiomyopathy.[614] CMR should be considered for patients suspected to have PVC-induced cardiomyopathy to exclude subtle forms of SHD.[590,615] In a patient with frequent PVCs, the presence of LGE suggests SHD with frequent PVCs rather than PVC-induced cardiomyopathy, in which LGE is mostly absent. Given that PVCs with a RBBB morphology have been reported to show a stronger association with LGE,[616] those patients should be particularly considered for CMR.

The diagnosis of PVC-induced cardiomyopathy vs. PVC-aggravated cardiomyopathy can be confirmed only after LVEF improvement/normalization (reverse remodelling) following suppression of the PVCs.

Catheter ablation of the PVCs is very efficient, with reported success rates of 75–90%, and is considered first-line treatment for PVC-induced cardiomyopathy.[535,600,609,610,612,617–620] Factors affecting acute ablation success and clinical outcome include the site of origin of PVCs (highest for outflow tract PVCs), the number of PVC morphologies, and the absence of LGE on CMR.[535,610,614] In patients with SHD, catheter ablation of frequent monomorphic PVCs has also been shown to improve LVEF in patients with both CAD and cardiomyopathies with and without CRT.[609,617,621–623] Similarly, the use of anti-arrhythmic medications for PVC suppression has been shown to improve LVEF. In one RCT, amiodarone resulted in a better PVC suppression and a higher LVEF improvement compared to placebo.[624] Sodium channel blockers can also effectively suppress PVCs.[625] In one study, flecainide reduced the PVC burden from 36% to 10% and resulted in LVEF increase from 37% to 49%.[626]

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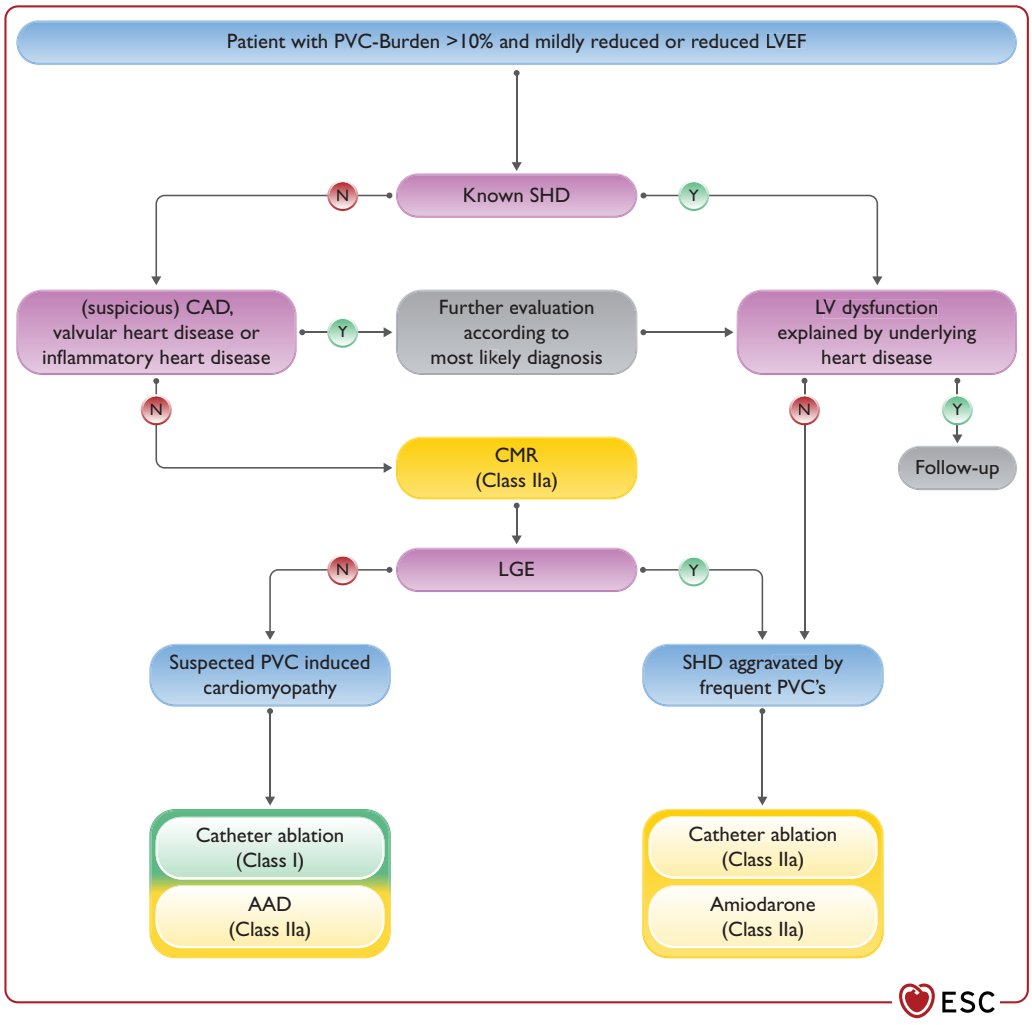

Figure 18 Algorithm for the management of patients with premature ventricular complex-induced/-aggravated cardiomyopathy. AAD, anti-arrhythmic drug; CAD, coronary artery disease; CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; N, No; PVC, premature ventricular complex; SHD, structural heart disease; Y, Yes.

While flecainide have a more favourable adverse effect profile regarding organ toxicity, increased mortality has previously been shown in patients with MI.[556] For selected patients with suspected PVC-induced cardiomyopathy and PVC-aggravated cardiomyopathy, flecainide can still be considered, particularly if an ICD is in place (*Table 9*).

A rare monogenetic cause of PVC-induced cardiomyopathy, referred to as multifocal ectopic Purkinje-related premature contractions, has been reported. It is characterized by a DCM phenotype and the presence of numerous PVCs with RBBB and/or left bundle branch block (LBBB) morphologies and an increased risk of SCD.[627] Pathogenic mutations in the *SCN5A* gene lead to a gain of function of the sodium channel responsible for hyperexcitability of the fascicular Purkinje system.[627,628] Limited data suggest that patients with multifocal ectopic Purkinje-related premature contractions do not respond to beta-blockers but might benefit from therapy with flecainide, quinidine, or amiodarone.[627–631]

Recommendation Table 27 — Recommendations for the management of patients with premature ventricular complex-induced or premature ventricular complex-aggravated cardiomyopathy

Recommendation	Class[a]	Level[b]
Diagnostic evaluation		
In patients with an unexplained reduced EF and a PVC burden of at least 10%, PVC-induced cardiomyopathy should be considered.[600,609,610]	IIa	C
In patients with suspected PVC-induced cardiomyopathy, CMR should be considered.[590,615]	IIa	B
Treatment		
In patients with a cardiomyopathy suspected to be caused by frequent and predominately monomorphic PVCs, catheter ablation is recommended.[535,600,609,612,617,618,620]	I	C

Continued

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In patients with a cardiomyopathy suspected to be caused by frequent and predominately monomorphic PVCs, treatment with AADs[c] should be considered if catheter ablation is not desired, suspected to be high-risk, or unsuccessful.[624,626]	IIa	C
In patients with SHD in whom predominately monomorphic frequent PVCs are suspected to be contributing to the cardiomyopathy, AAD (amiodarone) treatment or catheter ablation should be considered. [617,621,622,624]	IIa	B
In non-responders to CRT with frequent, predominately monomorphic PVCs limiting optimal biventricular pacing despite pharmacological therapy, catheter ablation or AADs should be considered.[623]	IIa	C

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AAD, anti-arrhythmic drug; CMR, cardiac magnetic resonance; CRT, cardiac resynchronization therapy; EF, ejection fraction; ICD, implantable cardioverter defibrillator; LV, left ventricular; PVC, premature ventricular complex; SHD, structural heart disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]Flecainide only in selected patients (ICD recipients, only moderate LV dysfunction).

7.1.3. Cardiomyopathies

7.1.3.1. Dilated cardiomyopathy and hypokinetic non-dilated cardiomyopathy

DCM is characterized by LV dilatation and systolic dysfunction unexplained by CAD or abnormal loading conditions.[632] The true prevalence is difficult to estimate. Older studies reported a prevalence of 1 in 2700 individuals.[633]

Historic data in adults with DCM showed a 1-year mortality of 20–25% and a 50% survival at 5 years.[634] Recent trials of DCM patients with systolic heart failure and OMT report 5-year mortality rates in the range of 21–28%.[356,359] SCD occurs in up to 12% of patients with DCM and still accounts for 25–35% of all deaths.[359,634,635]

In children, the annual incidence of DCM is 0.57 cases per 100 000.[636] The prognosis in children is poor, with a 5-year incidence of heart transplantation or heart failure-related death of 40%. However, in contrast to adults, the incidence of SCD in paediatric DCM patients is much lower, with a 5-year incidence of 2.4–3% as reported in two large paediatric cardiomyopathy registries from the United States and Australia.[637,638]

Causes of DCM can be genetic or acquired.[639] Genetic predisposition may also interact with extrinsic factors such as in peri-partum, alcoholic, or chemotherapy-related cardiomyopathies.[639] The phenotype, particularly of genetic aetiologies, can change over time and/or may not meet standard disease criteria at the time of disease manifestation. As a consequence, a new category of a hypokinetic non-dilated cardiomyopathy (HNDCM) has been proposed.[639]

7.1.3.1.1. Diagnostic evaluation and risk stratification. An algorithm for risk stratification and primary prevention of SCD in patients with DCM/HNDCM is presented in *Figure 19*.

Careful diagnostic work-up, including genetic testing and CMR, should be considered to identify the underlying cause for aetiology-oriented risk stratification and treatment.[341,639]

Pathogenic mutations are identified in 25–55% of DCM patients,[634,639,640] most often with autosomal dominant inheritance. Truncated mutations in the titin gene (*TTN*) are most frequently found, followed by *LMNA*, sarcomeric, and desmosomal mutations. Mutations in genes such as *LMNA*, *PLN*, *RBM20*, and *FLNC* are associated with a higher risk of VA and SCD.[641–645] Carriers of desmosomal and LMNA variants experienced the highest rate of VA/SCD, which was independent of the LVEF in one series.[645]

The yield of genetic testing is particularly high in DCM patients with familial forms of DCM or SCD in a first-degree relative at younger age. An inherited DCM is also more likely in patients who present at young age or with signs suspicious for a specific aetiology (e.g. prolonged AV conduction for LMNA) (*Figure 20*).[634,639,640,646] First-degree relatives of DCM/HNDCM patients should undergo clinical diagnostic evaluation, especially if an inherited cause is suspected.

Discrimination between high- and low-risk patients for SCD remains challenging. Beyond LVEF and NYHA class,[357,359,635,647–650] recent data suggest that both genetic and CMR findings can contribute to risk stratification. A meta-analysis of 29 studies combining 2948 patients studied the role of CMR in patients with DCM.[129] LGE was significantly associated with the arrhythmic endpoint, even when including only studies that performed multivariate analysis (HR 6.7; $P < 0.001$). Interestingly, the association between LGE and the arrhythmic endpoint remained significant among patients with mean LVEF >35%. Similarly, a recent study of 1020 consecutive patients with DCM and CMR observed that LGE and LVEF were both risk markers for all-cause mortality and cardiac death, but only LGE was significantly associated with SCD risk.[651]

SCD risk stratification has been refined in the subgroup of patients with *LMNA* mutations, which represent 5–10% of all DCM patients. LMNA mutations are associated with early atrial and ventricular arrhythmias, premature conduction disease, a high risk of SCD, and progression to end-stage heart failure.[80,642,652,653] In a multicentre registry of 269 *LMNA* mutation carriers, NSVT, LVEF <45% at first evaluation, male sex, and non-missense mutations were identified as independent risk factors for VA.[652] VA occurred only in persons with at least two of these risk factors. The risk stratification was subsequently externally validated.[653] Another study, which involved 589 *LMNA* mutation carriers, identified AV block as an additional predictor. Recently a risk calculator has been developed (https://lmna-risk-vta.fr/) to predict the risk of life-threatening VA (C-index of 0.776 [95% CI: 0.711–0.842]).[80] In patients with a 5-year estimated risk ≥10% *and* a manifest cardiac phenotype (NSVT, LVEF < 50%, or AV conduction delay), a primary prevention ICD implantation should be considered to avoid potential over-implantation in mutation carriers without a cardiac phenotype. In *LMNA* mutation carriers with a DCM phenotype, high-intensity exercise has been associated with a high risk of SCD and impaired LVEF and is therefore not recommended.[654,655]

A risk score for VA prediction has been recently proposed for patients with DCM or ARVC related to the p.Arg14del mutation in the *PLN* gene.[656] Validation studies are needed before it can be recommended for clinical use.

Beyond genetics and CMR, additional SCD predictors have been suggested, often derived from small cohorts with no or few replication studies. An unexplained syncope requires further evaluation and PES may determine the underlying cause. The risk for arrhythmic

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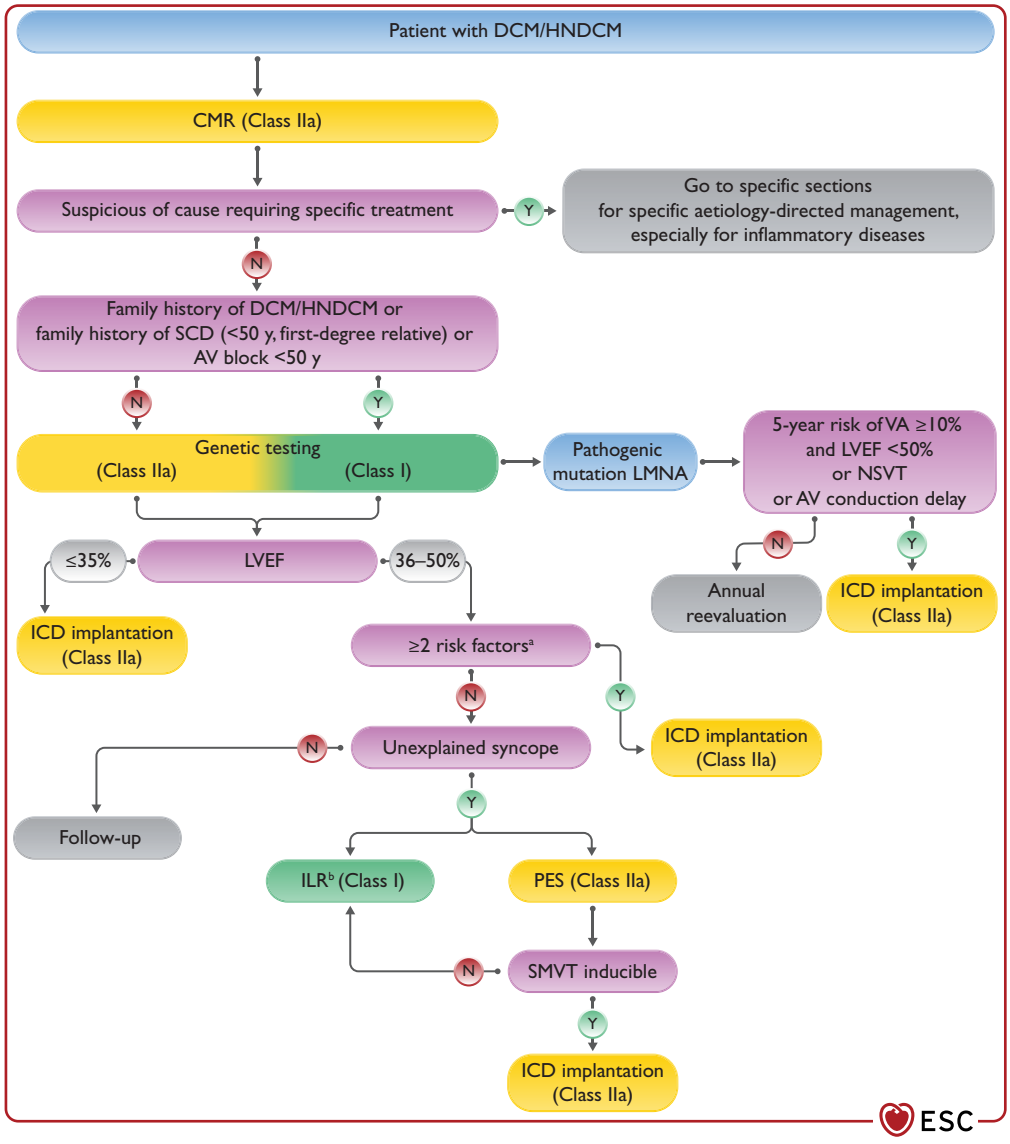

Figure 19 Algorithm for risk stratification and primary prevention of sudden cardiac death in patients with dilated cardiomyopathy/hypokinetic non-dilated cardiomyopathy. AV, atrioventricular; CMR, cardiac magnetic resonance; DCM, dilated cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; LMNA: lamin A/C gene; LVEF, left ventricular ejection fraction; N, No; NSVT, non-sustained ventricular tachycardia; PES, programmed electrical stimulation; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmias; Y, Yes. [a]Risk factors: unexplained syncope, pathogenic variants in PLN, FLNC, or RBM20, LGE on CMR, inducible SMVT at PES. [b]The 2018 ESC Guidelines for the diagnosis and management of syncope.[1]

events in DCM patients with a low LVEF and an unexplained syncope was similar to those with prior CA[657] and high, independent from the outcome of PES.[148] However, data in DCM patients with a mildly reduced EF suggest an incremental value of PES. Among DCM patients with an EF ≥40% and an unexplained syncope, who underwent ICD implantation after a positive PES, 80% had appropriate ICD therapy during follow-up. No SCD or symptomatic VA occurred in non-inducible patients.[146]

7.1.3.1.2. Primary prevention of sudden cardiac death. In patients with DCM/HNDCM, OMT according to current 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure is mandatory.[342] Re-evaluation of cardiac function and clinical status after 3 months' OMT is required before primary prevention ICD implantation. LV function is more likely to improve in DCM caused by myocarditis or *TTN* mutations.

The efficacy of primary prevention ICDs in DCM patients with HFrEF has been addressed in six RCTs.[635]

Five studies were published between 2002 and 2005 (CAT, AMIOVIRT, DEFINITE, COMPANION, and SCD-HeFT). The first three were smaller studies enrolling only DCM patients, whereas SCD-HeFT and COMPANION were larger and

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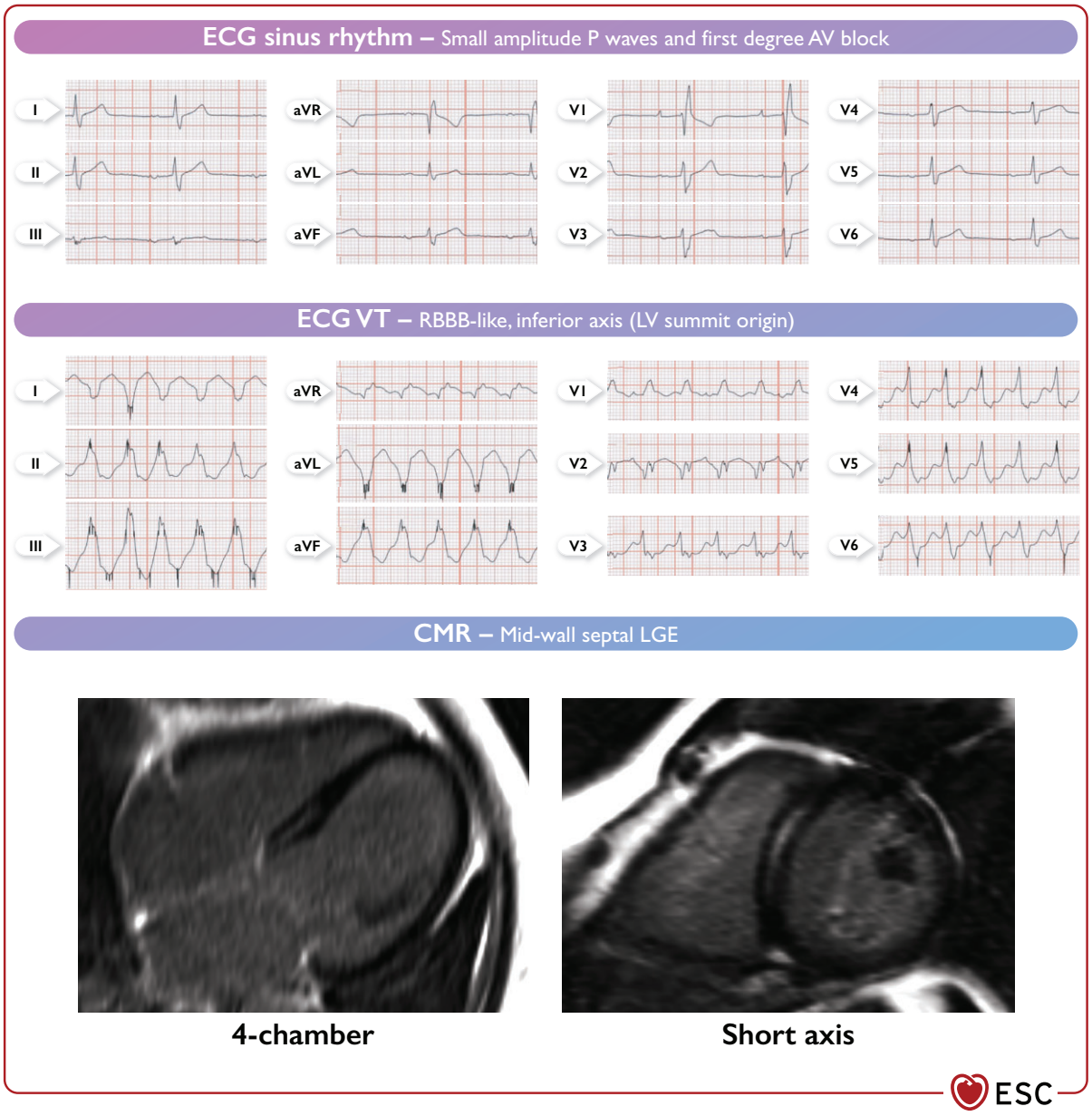

Figure 20 Typical features of dilated cardiomyopathy associated with lamin A/C gene mutation with ventricular arrhythmias. AV, atrioventricular; CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; LV, left ventricle; RBBB, right bundle branch block; VT, ventricular tachycardia.

included patients with CAD and DCM. The COMPANION study differed from the others as it compared CRT-defibrillator, CRT-pacemaker, and OMT. A meta-analysis of the five trials (1854 patients with DCM) demonstrated a 31% reduction in all-cause mortality with ICD relative to medical therapy (RR 0.69 [95% CI 0.55, 0.87], $P < 0.002$).[658] This effect persisted when COMPANION was excluded.

More recently, the DANISH trial enrolled 1116 symptomatic patients (NYHA class II or III) with non-ischaemic systolic heart failure (LVEF $\leq$ 35%). Patients were randomized to ICD or no ICD after OMT.[359] No reduction in the primary endpoint of all-cause death for patients randomized to ICD therapy (HR 0.87; 95% CI 0.68–1.12; $P = 0.28$) was observed, despite a significant reduction in SCD in the ICD group (HR 0.50; 95% CI 0.31–0.82; $P = 0.005$). Potential explanations are the low SCD rate in the trial (4.3% in the ICD group and 8.2% in the control group), the excellent medical treatment (>90% of patients on ACE inhibitors and beta-blockers, >50% on MRA), and the high prevalence (58%) of CRT. A meta-analysis of all six primary prevention trials still demonstrated a reduction, although lower, in overall mortality with ICD therapy (RR 0.76; 95% CI 0.65–0.91; $P = 0.002$).[635] In a sensitivity analysis, the benefit of ICD therapy was maintained after the removal of any single study from the pooled analysis.

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The results of the DANISH trial emphasize the need for further refining the indication for primary prevention ICDs in contemporary DCM patients. Age and comorbidity need to be considered.[635] In the DANISH trial, ICD implantation was associated with a significantly lower rate of death in younger patients.[359] A further analysis of the DANISH data[647] showed an association between reduced all-cause mortality and ICDs in patients ≤70 years of age (HR, 0.70; 95% CI 0.51–0.96; $P = 0.03$), but not in patients >70 years of age.

Prospective studies evaluating the benefit of ICDs in DCM/HNDCM patients with intermediate LV dysfunction, but with risk factors that have been associated with VA and SCD (including LGE on CMR, pathogenic mutations in *PLN*, *FLNC*, *RBM20*, unexplained syncope, and inducibility of SMVT), are lacking.[129,641,643,644,659–662] Given the limitation of LVEF as the only risk marker in DCM/HNDCM, this panel of experts shares the opinion that in the presence of a combination of risk markers an ICD should be considered.

7.1.3.1.3. Secondary prevention of sudden cardiac death and management of ventricular arrhythmias. Three randomized trials (AVID, CASH, and CIDS) have compared ICD therapy and medical treatment for secondary prevention in patients after aborted CA or not-tolerated VT.[349,351,352] The three trials enrolled a total of 1963 patients, of whom only 292 (14.8%) had non-ischaemic aetiologies. A significant reduction in death from any cause in patients with ICDs was demonstrated, which was almost entirely due to a 50% reduction in arrhythmic death.[352] In the subgroup of patients with cardiomyopathies there was a similar but non-significant trend in the reduction of death.[352] RCTs have excluded patients with haemodynamically tolerated VT. In DCM patients the VT substrate is less well defined, and disease progression needs to be considered. Therefore, despite the lack of data, this panel of experts shares the opinion that an ICD should also be considered in DCM patients with haemodynamically tolerated VT.

Optimization of ICD programming (see *Section 6.2.3.1*) can reduce ICD shocks delivered in response to VT, but additional therapy to reduce symptomatic VA episodes is often required. In the OPTIC trial, 412 patients with ICD implantation within 21 days of VT/VF were randomized to amiodarone plus beta-blockers, sotalol alone, or beta-blocker alone. ICD shock rates after one year were 10.3%, 24.3%, and 38.5%, respectively. The higher efficacy of amiodarone plus beta-blockers compared to sotalol needs to be weighed against the higher rate of medication-related adverse events on an individual basis.[318] Although only limited data are available, sodium channel blockers may control VT in SHD and may be beneficial in ICD recipients without advanced heart failure. The majority of SMVT is due to scar-related re-entry, which can be targeted by catheter ablation. Acute ablation outcome has been reported to be similar for CAD and DCM.[497,663] However, VT recurrence rates are usually higher in DCM patients (VT-free survival 40.5% in DCM vs. 57% in CAD at 1 year).[497] After multiple procedures in 36% of the patients, long-term freedom of VT could be achieved in 69% of cases in a retrospective, single-centre cohort of 282 patients treated between 1999 and 2014.[664]

Epicardial ablation is needed in 27–30% of the procedures.[497,664] Outcome is particularly poor, and bailout strategies (transcoronary ethanol ablation, bipolar ablation, surgical ablation) may be required in patients with pathogenic mutations (*LMNA* gene) and in those with deep intramural, anteroseptal substrate locations.[499,665,666] Considering the complexity of the ablation procedure, DCM patients should therefore be treated only in specialized centres.

Recommendation Table 28 — Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in dilated cardiomyopathy/hypokinetic non-dilated cardiomyopathy

Recommendation	Class[a]	Level[b]
Diagnostic evaluation and general recommendations		
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) is recommended in patients with DCM/HNDCM and AV conduction delay at <50 years, or who have a family history of DCM/HNDCM or SCD in a first-degree relative (at age <50 years).[641–645]	I	B
CMR with LGE should be considered in DCM/HNDCM patients for assessing the aetiology and the risk of VA/SCD.[129,651,667]	IIa	B
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) should be considered for risk stratification in patients with apparently sporadic DCM/HNDCM, who present at young age, or with signs suspicious for an inherited aetiology.[641–645]	IIa	C
Participation in high-intensity exercise including competitive sports is not recommended for individuals with DCM/HNDCM and a *LMNA* mutation.[655]	III	C
Risk stratification and primary prevention of SCD		
ICD implantation should be considered in patients with DCM/HNDCM, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% after ≥3 months of OMT.[357,359,635,650]	IIa	A
ICD implantation should be considered in DCM/HNDCM patients with a pathogenic mutation in *LMNA* gene, if the estimated 5-year risk of life-threatening VA is ≥10%[c] *and* in the presence of NSVT or LVEF < 50% or AV conduction delay.[80,652,653]	IIa	B
ICD implantation should be considered in DCM/HNDCM patients with a LVEF <50% and ≥2 risk factors (syncope, LGE on CMR, inducible SMVT at PES, pathogenic mutations in *LMNA*,[d] *PLN*, *FLNC*, and *RBM20* genes).	IIa	C
In DCM/HNDM patients, electrophysiological evaluation should be considered when syncope remains unexplained after non-invasive evaluation.[661,668]	IIa	C

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Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients with DCM/HNDCM, who survive SCA due to VT/VF or experience haemodynamically not-tolerated SMVT.[349,351,352]	I	B
Catheter ablation in specialized centres should be considered in patients with DCM/HNDCM and recurrent, symptomatic SMVT or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.[481,497,664,669]	IIa	C
The addition of oral amiodarone or replacement of beta-blockers by sotalol should be considered in patients with DCM/HNDCM and an ICD who experience recurrent, symptomatic VA despite optimal device programming and beta-blocker treatment.[318]	IIa	B
ICD implantation should be considered in patients with DCM/HNDCM and haemodynamically tolerated SMVT.	IIa	C
Management of relatives of a patient or SCD victim with DCM/HNDCM		
In a first-degree relative of a DCM/HNDCM patient, an ECG and an echocardiogram are recommended if: • the index patient was diagnosed <50 years of age or has clinical features suggestive of an inherited cause, or • there is family history of DCM/HNDCM, or premature unexpected SD.[646]	I	C
In a first-degree relative of a patient with apparently sporadic DCM/HNDCM, an ECG and an echocardiogram may be considered.[646]	IIb	C

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AAD, anti-arrhythmic drug; AV, atrioventricular; CMR, cardiac magnetic resonance; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; OMT, optimal medical therapy; PES, programmed electrical stimulation; SCA, sudden cardiac arrest; SCD, sudden cardiac death; SD, sudden death; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Based on the risk calculator https://lmna-risk-vta.fr/
[d]See specific recommendations for LMNA.

7.1.3.2. Arrhythmogenic right ventricular cardiomyopathy

ARVC is an inherited disease characterized by fibrofatty myocardial replacement.[670] The prevalence ranges from 1:1000 to 1:5000 individuals, with male predominance among probands.[671] Patients with SCD/VF at first presentation are typically younger (median age 23 [range 13–57]) compared to those who present with a SMVT (median age 36 years [range 14–78]).[672]

ARVC is caused by pathogenic mutations in desmosomal genes and less commonly in non-desmosomal genes. Genetic testing is indicated and identification of a mutation (in up to 73% of probands) is a major criterion for the diagnosis.[116,671] In 4–16% compound/digenic mutations are found, which have been associated with an increased risk of VA at younger age.[672,673] The disease penetrance in first-degree relatives is 28–58%,[674,675] supporting regular clinical evaluation of relatives.

ARVC is characterized by a predominant RV involvement. The 2010 revised international diagnostic task force criteria are based on a multiparametric strategy[116] (*Figure 21*). Tissue characterization by CMR was not included. However, RV fatty infiltration and LV LGE are frequently observed (in 29–53% and 35.5–45% of probands, respectively) and may be present before patients meet major task force imaging criteria.[676–678] Both wall motion alterations and pre-/post-contrast signal abnormalities have been suggested to enhance the diagnostic accuracy of CMR for ARVC.[679] The identification of biventricular and left-dominant involvement in ARVC patients[680,681] has recently led to the proposed term 'arrhythmogenic cardiomyopathy'.[682]

Restriction from high-intensity exercise is regarded as a preventive tool in clinically affected ARVC patients to reduce the risk of VAs and disease progression.[683–685] Whether sport restriction is beneficial in all mutation carriers without disease expression has not been evaluated in prospective cohorts, but avoidance of competitive, high-intensity exercise seems to be reasonable.[686,687] SCD and VA occur disproportionately during exercise in affected patients, and high-dose isoproterenol infusion may provoke PVT in >90% of ARVC patients, supporting the role of sympathetic stimulation for arrhythmogeneity.[152,688,689] Whether beta-blockers can prevent spontaneous VA is, however, unclear. Limited data suggest a potential beneficial role of atenolol.[690]

7.1.3.2.1. Risk stratification. In ARVC patients not implanted with ICDs, CA occurs in 4.6–6.1%, while 23% of patients experience a non-fatal SMVT during an average follow-up of 8–11 years.[691–694] Whether a SMVT is acutely life-threatening depends on the VT cycle length, cardiac function, and the circumstances under which VT occurs. Among definite/probable ARVC patients considered at high risk for VA, 23–48% will experience appropriate ICD intervention during a mean follow-up of 4.7 years. In 16–19% of cases, ICD intervention is triggered by fast VT ≥250 b.p.m. or VF, which is considered as surrogate for a life-threatening event.[695–698] In a large cohort of 864 ARVC patients (38.8% with a prior VA), 43% had VT/VF during a median follow-up of 5.75 years, but only 10.8% a potentially life-threatening event. Thus, in 3 out of 4 ARVC patients, ICD therapy is appropriate but may not be considered acutely life-saving. This is relevant because risk prediction algorithms and models are based on combined arrhythmic endpoints, which are often equated with ICD indications to prevent SCD. This is particularly important for the young ARVC patients with a lifetime risk of ICD-related complications.[695,699]

Randomized studies of ICD therapy for secondary prevention are lacking, but the high rates of appropriate ICD therapy triggered by fast VT/VF episodes in patients implanted after CA or haemodynamically poorly tolerated VT strongly suggest a survival benefit from ICD.[700] In patients who present with a haemodynamically tolerated VT, the survival benefit from ICD is less clear.[691,700–702] Identification of ARVC patients at risk for SCD is difficult, and the evidence supporting risk factors for life-threatening VAs is limited. Arrhythmic syncope was a predictor for subsequent events in most series of patients with definitive ARVC (pooled HR 3.67; CI 2.75–4.9)[81,696,701,703] and, in these patients, an ICD should be considered. RV and LV dysfunction have been associated with a higher arrhythmic risk.[675,704] Cut-off values are difficult to determine but, in

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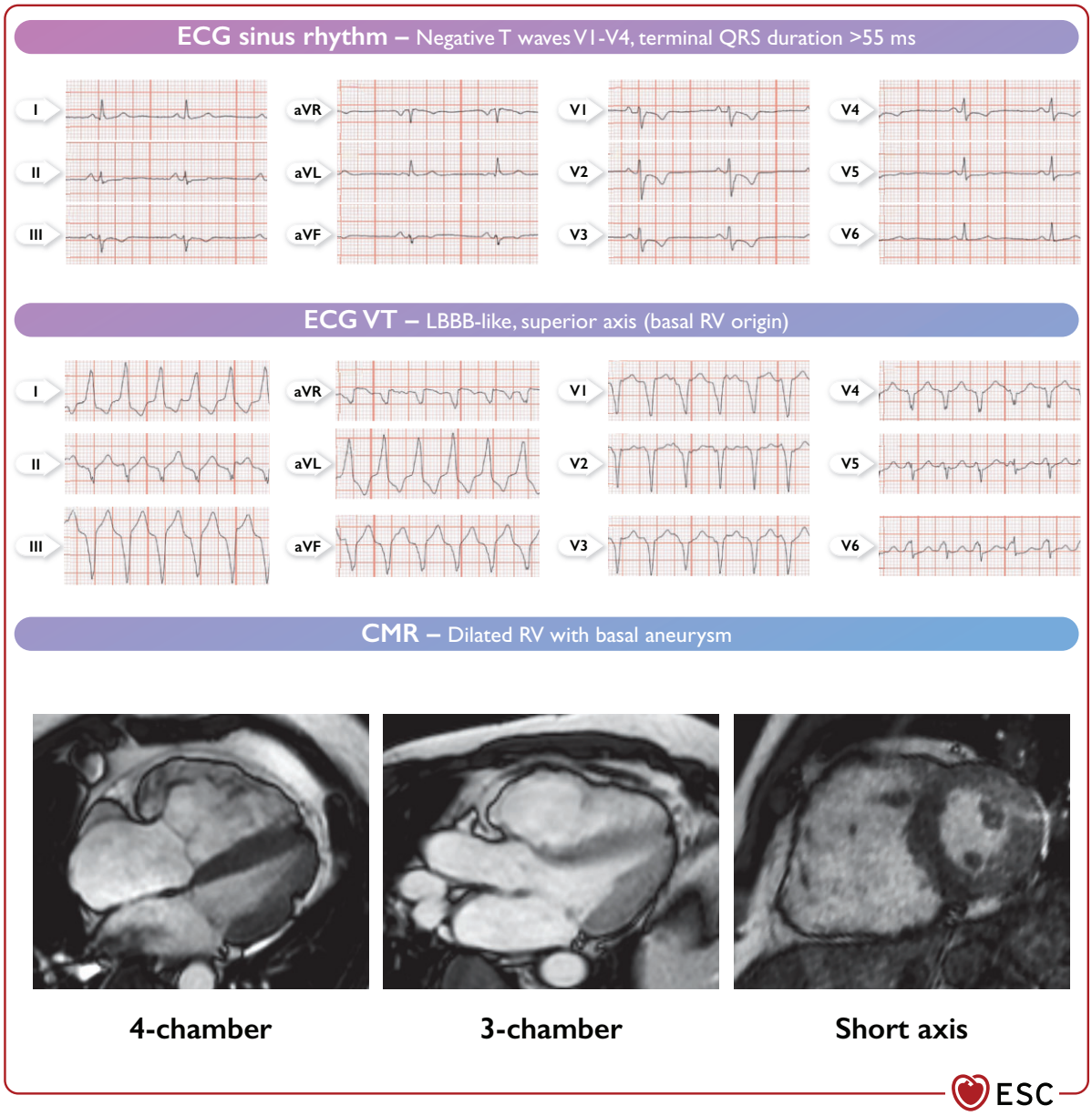

Figure 21 Typical features of arrhythmogenic right ventricular cardiomyopathy associated with ventricular arrhythmias. CMR, cardiac magnetic resonance; ECG, electrocardiogram; LBBB, left bundle branch block; RV, right ventricle; VT, ventricular tachycardia.

patients with *severe RV dysfunction* (RV fractional area change ≤17% or RV ejection fraction ≤35%), an ICD should be considered. Likewise, ARVC patients with significant LV involvement (LVEF ≤ 35%) should be treated according to the current DCM recommendation regarding ICD implantation. There are conflicting data on the *independent* predictive value of NSVT for subsequent sustained arrhythmic events.[695,696,701] Likewise, the role of PES in risk stratification, particularly in asymptomatic patients, is not well defined.[695,696,705] In one series including mainly symptomatic patients, both NSVT and a positive PES independently predicted arrhythmic events, while others report a low diagnostic accuracy.[696] Risk prediction based on a single parameter does not consider the potential combined effect and interactions between factors. Therefore, although supporting data are lacking, this panel of experts supports that an ICD should be considered[706] in symptomatic ARVC patients with moderate RV (<40%) and/or LV dysfunction (<45%) and who have *either* NSVT *or* have SMVT inducible at PES. An internally validated risk model has recently been developed from 528 patients with definite ARVC and no prior VA, including age, sex, arrhythmic syncope, NSVT, PVC burden, leads with T-wave inversion and RV ejection fraction, to predict *any sustained VA* (c-index 0.77).[81] In addition, a prediction model for specifically life-threatening VA has been promoted based on 864 ARVC patients, with predictors including male sex, age, 24 h PVC count, and leads with T-wave inversion (c-index 0.74).[702] However, validation studies are needed before these risk models can be recommended for clinical use.

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7.1.3.2.2. Treatment. Up to 97.4% of all VA episodes in ARVC ICD recipients are SMVT. The very high termination rate by ATP (92% of all episodes) independent from VT cycle length strongly supports devices with the capability for ATP.[698] S-ICDs reduce lead-related complications and have been proven to effectively shock terminate VA in small cohorts of ARVC patients during short-term follow-up.[707]

Additional treatment to supress VA is often required. Although not confirmed by clinical data, beta-blockers are recommended as first-line therapy in symptomatic patients.

Data on AADs to prevent VT recurrence are limited to small observational studies and registries. In general, AAD therapy has limited efficacy. Although sotalol was effective to prevent inducibility of VT,[708] it did not supress clinically relevant arrhythmias.[690,708] Treatment with amiodarone or class 1 drugs was associated with a trend to lower VT recurrence as compared with sotalol.[709] The addition of flecainide to beta-blockers/sotalol was beneficial in a small cohort.[710] Catheter ablation provides an alternative. Endocardial and adjuvant epicardial substrate ablation, if needed, has been associated with promising VT-free survival. Potential procedural risks, drug side effects, and the patient's preference need to be taken into consideration.[482]

Recommendation Table 29 — Recommendations for diagnostic, risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy

Recommendations	Class[a]	Level[b]
Diagnostic evaluation and general recommendations		
In patients with suspected ARVC, CMR is recommended.[676–678]	I	B
In patients with a suspected or definite diagnosis of ARVC, genetic counselling and testing are recommended.[672,673]	I	B
Avoidance of high-intensity exercise is recommended in patients with a definite diagnosis of ARVC.[683–685]	I	B
Avoidance of high-intensity[c] exercise may be considered in carriers of ARVC-related pathogenic mutations and no phenotype.[683,687]	IIb	C
Beta-blocker therapy may be considered in all patients with a definite diagnosis of ARVC.	IIb	C
Risk stratification and primary prevention of SCD		
ICD implantation should be considered in patients with definite ARVC and an arrhythmic syncope.[696,701,711–713]	IIa	B
ICD implantation should be considered in patients with definite ARVC and severe RV or LV systolic dysfunction.[675,691]	IIa	C
ICD implantation should be considered in symptomatic[d] patients with definite ARVC, moderate right or left ventricular dysfunction, and either NSVT or inducibility of SMVT at PES.[695,696,701,703,705]	IIa	C
In patients with ARVC and symptoms highly suspicious for VA, PES may be considered for risk stratification.[695,705]	IIb	C
Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in ARVC patients with haemodynamically not-tolerated VT or VF.[700]	I	C
In patients with ARVC and non-sustained or sustained VAs, beta-blocker therapy is recommended.	I	C
In patients with ARVC and recurrent, symptomatic SMVT or ICD shocks for SMVT despite beta-blockers, catheter ablation in specialized centres should be considered.[482,709,714]	IIa	C
In ARVC patients with indication for ICDs, a device with the capability of ATP programming for SMVT up to high rates should be considered.[698]	IIa	B
ICD implantation should be considered in ARVC patients with a haemodynamically tolerated SMVT.[692]	IIa	C
In patients with ARVC and recurrent, symptomatic VT despite beta-blockers, AAD treatment should be considered.[709,710]	IIa	C
Management of relatives of a patient with ARVC		
In a first-degree relative of a patient with ARVC, ECG and echocardiogram are recommended.[675]	I	C

AAD, anti-arrhythmic drug; ARVC, arrhythmogenic right ventricular cardiomyopathy; ATP, anti-tachycardia pacing; CMR, cardiac magnetic resonance; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LV, left ventricle; NSVT, non-sustained ventricular tachycardia; PES, programmed electrical stimulation; RV, right ventricle; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]The 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease.[4]
[d]Presyncope or palpitations suggestive of VA.

7.1.3.3. Hypertrophic cardiomyopathy

HCM is characterized by increased LV wall thickness not explained by abnormal loading conditions (such as hypertension or valvular disease).[128,715] Because the natural history and management differs according to the underlying aetiology of LVH, diagnostic work-up is of paramount importance (see *Section 7.1.3.5*) and includes CMR and genetic testing.[716–725] HCM is usually caused by a mutation with autosomal dominant inheritance, supporting cardiac screening in first-degree relatives, in parallel with genetic testing in the index patient. A sarcomeric gene mutation is identified in 30–60%, most frequently in patients who are younger at diagnosis or with a family history of HCM.[646,722]

The estimated prevalence of HCM in adults is 1 in 500.[726] In children, the prevalence is much lower.

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Annual mortality related to HCM is 1–2% in most studies with contemporary management strategies,[128,715] and may be as low as 0.5%.[727] The annual rate of SCD or appropriate ICD therapy is about 0.8% but is largely dependent on age and risk profile.[85,728–730] HCM patients are at risk for heart failure, AF, and stroke.[128,715] Most HCM-related deaths at age ≤60 years occur suddenly, while older patients die more often of stroke or heart failure.[731] SCD is often related to VA, which can be a consequence of ischaemia, left ventricle outflow tract (LVOT) obstruction, or supraventricular arrhythmias. SCD may also be triggered by exercise, and participation in competitive sport has been discouraged.[732] However, recent data suggest that even vigorous exercise in HCM patients without risk markers may not be associated with VA.[733,734]

7.1.3.3.1. Risk stratification and primary prevention of sudden cardiac death. In primary prevention, the challenge remains to identify the relatively small group of patients with the highest risk of SCD. NSVT is identified on continuous (24/48 h) ambulatory ECG monitoring in 20–25% of patients.[128,715] Its prevalence increases with age and correlates with LV wall thickness and LGE on CMR.[716–721,735] The prognostic value of NSVT for SCD is more important in young patients (<30 years).[735] The relation between the duration, frequency, or rate of NSVT and HCM prognosis remains unclear.[735]

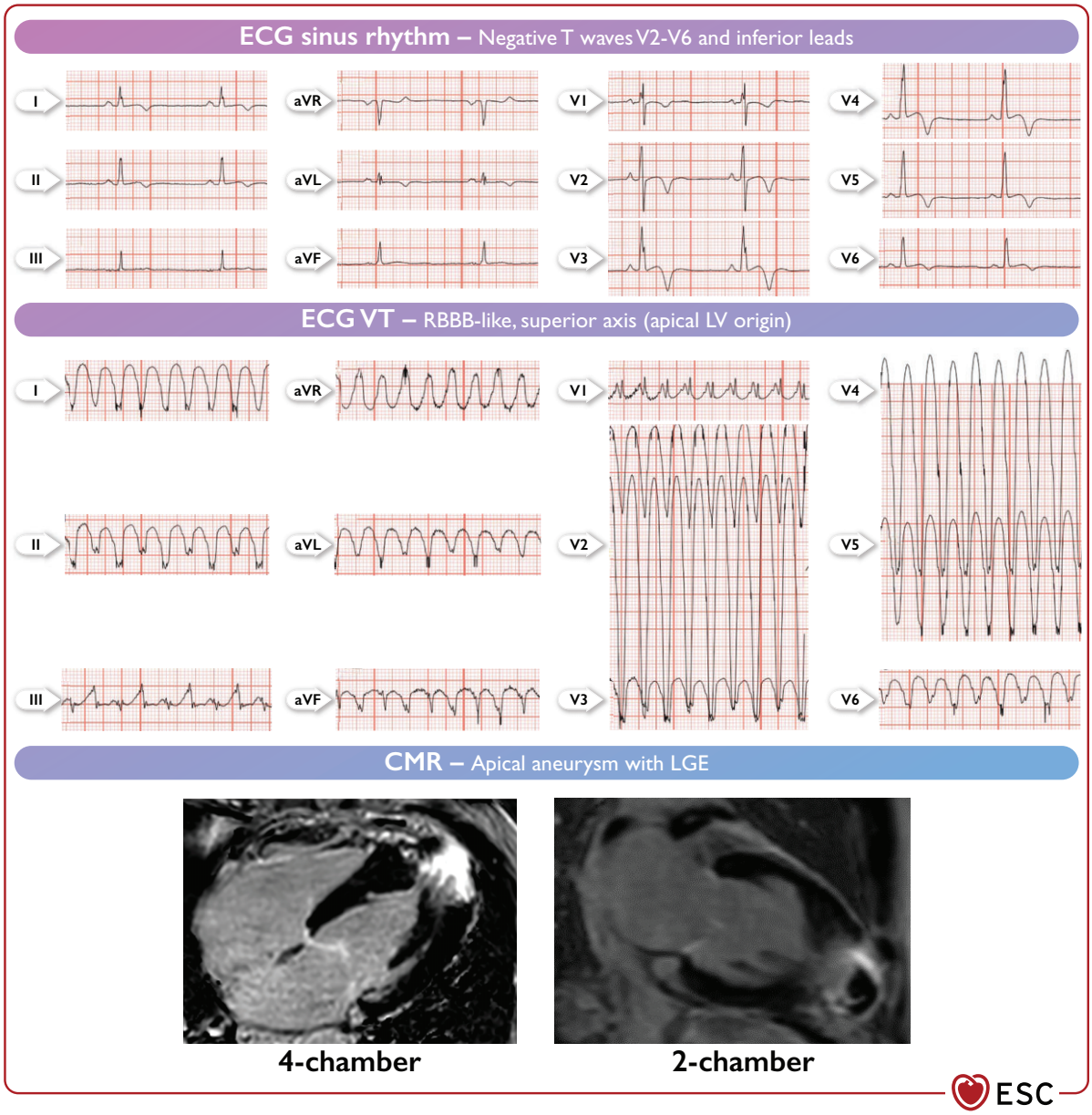

Figure 22 Typical features of hypertrophic cardiomyopathy associated with sustained monomorphic ventricular tachycardia. CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; LV, left ventricular; RBBB, right bundle branch block; VT, ventricular tachycardia.

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Documented NSVT during exercise test is very rare, but was associated with a higher risk of SCD.[732] Additional risk factors have been identified and a 5-year SCD risk stratification score based on seven factors (age, LV wall thickness, LA size, LVOT gradient, NSVT, unexplained syncope, and family history of SCD) has been developed[85] (HCM Risk-SCD: https://doc2do.com/hcm/webHCM.html) and externally validated.[85,728,729] The calculator is not intended for use in elite athletes, or in individuals with metabolic or infiltrative diseases, or after myectomy or alcohol septal ablation.[85]

Additional factors not captured by the Risk-SCD model should also be considered in patients with intermediate or low calculated risk, including LV systolic dysfunction, apical aneurysm, extensive LGE on CMR, and presence of single or multiple sarcomeric mutations (*Figure 22*).[716,717,722,736–739] Extensive LGE on CMR defined as ≥15% of LV mass has been suggested as good predictor of SCD in adults. However, thresholds may be difficult to use because LGE quantification is dependent on CMR acquisition, type, and amount of contrast.

Periodic reassessment is mandatory as part of the longitudinal evaluation of patients. VA induced by PES is considered non-specific, although conflicting results have been reported.[740,741]

In children few data on primary prevention were available until the recent development of scores and related risk calculators.[83,84] The HCM Risk-Kids score[84] has been developed and externally validated[742] specifically in children with HCM (1–16 years of age) and includes unexplained syncope, maximal LV wall thickness, large left atrial diameter, low LVOT gradient, and NSVT (https://hcmriskkids.org). In contrast to adults, including age and family history of SCD did not improve the performance of the paediatric model. Patients with prior VF or sustained VT, known inborn errors of metabolism, and syndromic causes of HCM were excluded. The predictive value of LGE in children is less defined, although preliminary data were reported.[743]

7.1.3.3.2. Treatment to prevent ventricular arrhythmia recurrence. Patients surviving a CA due to VT/VF or haemodynamically not-tolerated VT remain at high risk for future life-threatening VA, and will benefit from ICD therapy.[128,744–746]

There are no RCTs in HCM or cohort studies supporting a significant role of drugs to prevent SCD.[128,715,747] Amiodarone may reduce VA but with conflicting results regarding SCD prevention.[747,748] Disopyramide and beta-blockers are efficient to control symptoms and LVOT obstruction, but there is no evidence that they reduce the risk of SCD.[128,715] Similarly, surgical myectomy or alcohol ablation are not recommended with the aim to reduce risk of SCD in patients with LVOT obstruction.[128,715] Following ICD implantation for primary or secondary prevention, the most common documented VA subtype is SMVT, and ATP is successful in 69–76.5% of all episodes.[749–751] Although data on drug efficacy are lacking, AADs (beta-blockers, amiodarone, sotalol, sodium channel blockers) should be considered in HCM patients with symptomatic VA. Catheter ablation may also be considered in highly selected HCM patients with SMVT, in whom AADs are ineffective, contraindicated or not tolerated, as outcome after ablation is inferior compared to other non-ischaemic aetiologies.[752–754]

Recommendation Table 30 — Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in hypertrophic cardiomyopathy

Recommendation	Class[a]	Level[b]
Diagnostic evaluation and general recommendations		
CMR with LGE is recommended in HCM patients for diagnostic work-up.[716–718]	I	B
Genetic counselling and testing are recommended in HCM patients.[721–725]	I	B
Participation in high-intensity exercise may be considered for asymptomatic adult HCM patients without risk markers.[733]	IIb	C
Risk stratification and primary prevention of SCD		
It is recommended that the 5-year risk of SCD is assessed at first evaluation and at 1–3-year intervals, or when there is a change in clinical status.	I	C
ICD implantation should be considered in patients aged 16 years or more with an estimated 5-year risk of SD ≥6%.[c,85,728,729]	IIa	B
ICD implantation should be considered in HCM patients aged 16 years or more with an intermediate 5-year risk of SCD (≥4 to <6%)[c] and with (a) significant LGE at CMR (usually ≥15% of LV mass); or (b) LVEF < 50%; or (c) abnormal blood pressure response during exercise test[d]; or (d) LV apical aneurysm; or (e) presence of sarcomeric pathogenic mutation.[716,717,722,736–739]	IIa	B
In children less than 16 years of age with HCM and an estimated 5-year risk of SD ≥6% (based on HCM Risk-Kids score[e]), ICD implantation should be considered.[84,742]	IIa	B
ICD implantation may be considered in HCM patients aged 16 years or more with an estimated 5-year risk of SCD of ≥4 to <6%.[c,85,728,729]	IIb	B
ICD implantation may be considered in HCM patients aged 16 years or more with a low estimated 5-year risk of SCD (<4%)[c] and with (a) significant LGE at CMR (usually ≥15% of LV mass); or (b) LVEF < 50%; or (c) LV apical aneurysm.[716,717,722,736–739]	IIb	B
Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in HCM patients with haemodynamically not-tolerated VT or VF.[744–746]	I	B
In patients with HCM presenting with haemodynamically tolerated SMVT, ICD implantation should be considered.	IIa	C
In patients with HCM and recurrent, symptomatic VA, or recurrent ICD therapy, AAD treatment should be considered.	IIa	C

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Catheter ablation in specialized centres may be considered in selected patients with HCM and recurrent, symptomatic SMVT or ICD shocks for SMVT, in whom AAD are ineffective, contraindicated, or not tolerated.[753,754]	IIb	C
Management of relatives of a patient with HCM		
In a first-degree relative of a patient with HCM, ECG and echocardiogram are recommended.	I	C

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AAD, anti-arrhythmic drug; CMR, cardiac magnetic resonance; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LV, left ventricle; LVEF, left ventricular ejection fraction; SCD, sudden cardiac death; SD, sudden death; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Based on the HCM Risk-SCD: https://doc2do.com/hcm/webHCM.html
[d]Defined as a failure to increase systolic pressure by at least 20 mmHg from rest to peak exercise, or a fall of >20 mmHg from peak pressure.
[e]Based on the HCM kid risk score: https://hcmriskkids.org

7.1.3.4. Left ventricular non-compaction

LVNC comprises a heterogeneous group of diseases. The diagnosis is challenging, and various diagnostic criteria have been proposed. The yield of genetic tests in index patients is low.[755]

The morphological phenotype of non-compaction based on imaging parameters may also appear in a healthy population.[756]

A meta-analysis including 2501 LVNC patients revealed a risk of cardiovascular mortality similar to that of DCM patients, with no relation to the extent of trabeculation.[757] CMR-based detection of focal fibrosis using LGE in LVNC with preserved ejection was associated with serious cardiac events (aborted death, ICD therapy, heart transplantation [HTX]/LVAD) in another meta-analysis including 574 patients (OR 6.1; CI 2.1–17.5; $P < 0.001$).[758] A combination of CMR criteria with systematic genotyping may overcome current uncertainties regarding risk stratification.[759]

Recommendation Table 31 — Recommendations for implantable cardioverter defibrillator implantation in left ventricular non-compaction

Recommendations	Class[a]	Level[b]
In patients with a LVNC cardiomyopathy phenotype based on CMR or echocardiography, implantation of an ICD for primary prevention of SCD should be considered to follow DCM/HNDCM recommendations.	IIa	C

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CMR, cardiac magnetic resonance; DCM, dilated cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; LVNC, left ventricular non-compaction; SCD, sudden cardiac death.
[a]Class of recommendation.
[b]Level of evidence.

7.1.3.5. Restrictive cardiomyopathy

The phenotype of restrictive cardiomyopathy (RCM) is rare and can be the consequence of different aetiologies, including infiltrative disorders (e.g. amyloidosis) and storage disease (e.g. Andersen–Fabry disease), the identification of which is crucial for guiding therapy. Heart failure is one of the leading symptoms in primary and secondary RCM.[760]

In Fabry disease the majority of the reported cardiovascular deaths have been categorized as SCD in a recent systematic review of 13 studies including 4185 patients.[761] Higher age, male gender, LVH, LGE, and NSVT have been identified as potential risk factors associated with SCD events. However, SCD rates were reported in only 11 of the studies, including 623 patients. The retrospective, observational nature of most of these small, single-centre studies and the low absolute number of cardiovascular deaths (36/623) and SCD (30/623) do not currently allow guidance for primary prevention ICD implantation.[761]

Amyloidosis can be caused by different misfolded precursor proteins leading to deposits in tissue and organs. Cardiac amyloidosis is mainly related to light-chain amyloid or transthyretin amyloid. The latter can be subdivided into wild-type, also called senile amyloid, more often complicated by AV conduction delay and atrial arrhythmias, and amyloid due to pathogenic mutations in the *TTR* gene. Disease manifestation depends on the mutation. Despite advances in the treatment of amyloid light-chain amyloidosis, outcome is still poor in patients with manifest cardiac involvement.[762] Causes of death are progressive heart failure, autonomic dysfunction, and electromechanical dissociation.[762,763] The benefit of primary prevention ICD implantation in patients with cardiac amyloidosis is uncertain. Currently, an ICD should be considered in patients with haemodynamically not-tolerated VT after careful discussion of the competing risks of non-arrhythmic death and non-cardiac death.

Recommendation Table 32 — Recommendations for implantable cardioverter defibrillator implantation in patients with cardiac amyloidosis

Recommendations	Class[a]	Level[b]
An ICD should be considered in patients with light-chain amyloidosis or transthyretin-associated cardiac amyloidosis and haemodynamically not-tolerated VT.	IIa	C

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ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

7.1.3.6. Neuromuscular disorders

An algorithm for risk stratification, SCD prevention, and treatment of VAs in myotonic dystrophy is presented in *Figure 23*.

Arrhythmias are common and often the first manifestation of neuromuscular disorders.[764] Myotonic dystrophy is the most common muscular dystrophy in the adult population (prevalence 1 in 8000). Myotonic dystrophy is the consequence of trinucleotide repeat expansion in the end of *DMPK* gene, which results in mis-splicing of *SCN5A* and cardiac conduction system delays and arrhythmia. Duchenne dystrophy also has a high incidence (1 in 3500 male births). As most patients die before the age of 20, it is rarely seen in adulthood. Other neuromuscular disorders, such as Becker (1 in 100 000 male births) and facioscapulohumeral (1 in 100 000) dystrophies, are less common. Most of these disorders are associated with conduction and rhythm

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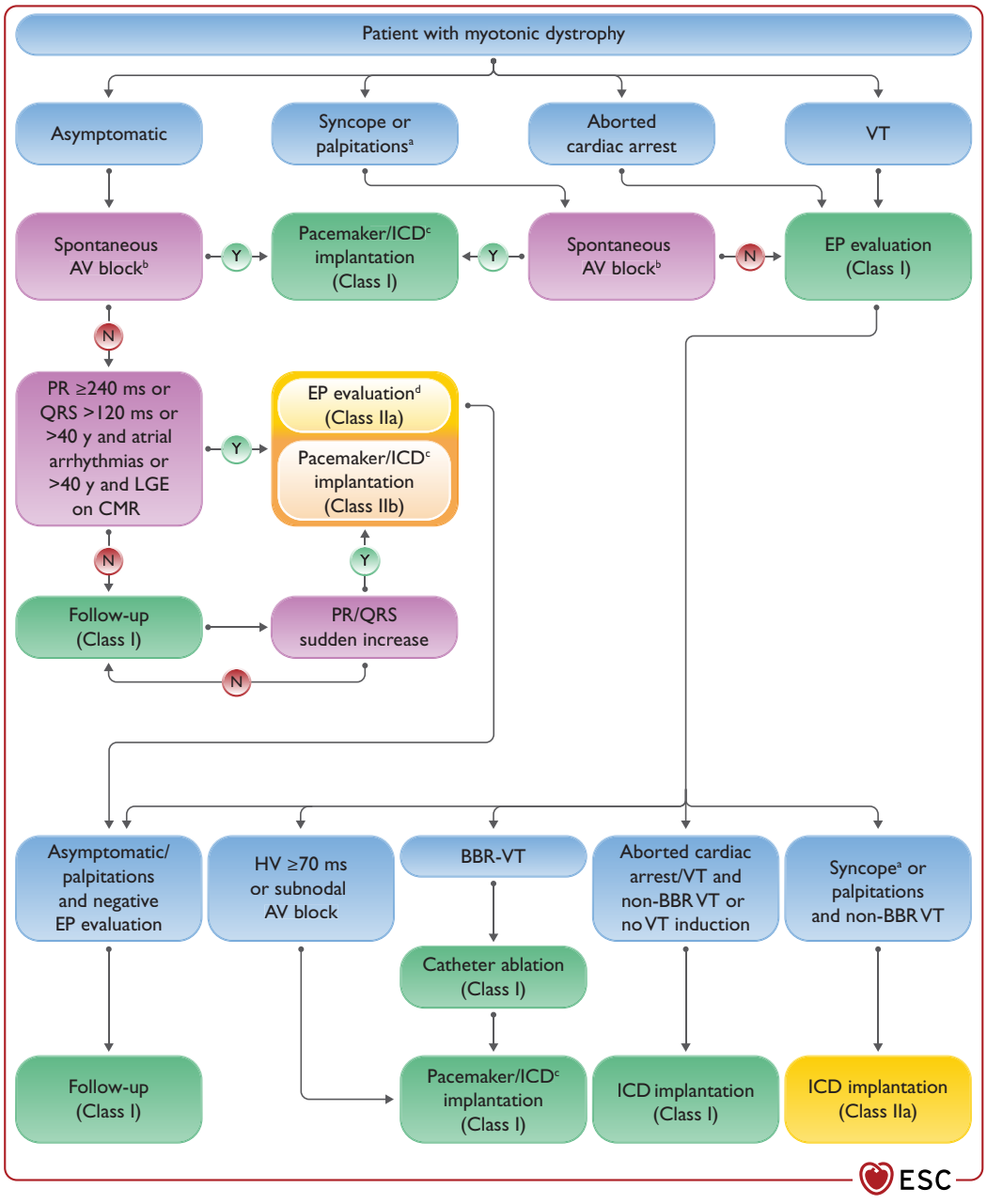

Figure 23 Algorithm for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in myotonic dystrophy. AV, atrioventricular; BBR-VT, bundle branch re-entrant ventricular tachycardia; CMR, cardiac magnetic resonance; EP, invasive electrophysiological evaluation; HV, His-to-ventricle interval; ICD, implantable cardioverter defibrillation; LGE, late gadolinium enhancement; N, No; VT, ventricular tachycardia, Y, Yes. [a]Syncope or palpitations highly suspicious of arrhythmic origin. [b]Spontaneous AV block: third or advanced second-degree AV block. [c]Factors favouring ICD implantation: age,[5,6,11] CTG expansion,[6–9,13,16] sudden death (SD) or family history of SD,[5] ECG conduction abnormalities,[16] PR prolongation,[13] left bundle branch block,[5] atrial arrhythmias,[6,16] non-sustained VT,[5] LV dysfunction,[17] significant LGE in CMR.[14,15,18] [d]Further management according to outcome of EP evaluation.

disturbances, some life-threatening, and with mechanisms amenable to specific anti-arrhythmic therapy.[17] Anti-arrhythmic therapy should be considered, as muscular function and life expectancy are often only moderately limited.[765] It is generally recommended to treat patients with neuromuscular diseases who have survived a CA or have VAs or ventricular dysfunction in the same way as patients without extracardiac manifestations. However, the benefit of ICD implantation should be balanced with the overall prognosis in some subtypes, such as Duchenne dystrophy.

Symptoms may be the result of bradycardia or tachyarrhythmias and invasive electrophysiological evaluation is warranted unless a cause, such as AV block, has been clinically documented.[153] Sudden increase of PR interval and QRS duration have been associated with AV block and SCD in myotonic dystrophy despite the absence of symptoms, and electrophysiological evaluation should be considered.[766,767] An HV interval ≥70 ms should prompt pacemaker implantation regardless of symptoms. Induction of BBR-VT in a symptomatic patient strongly supports BBR-VT (ESC CardioMed chapter 42.5)[768] as an underlying cause of symptoms, and ablation of the right bundle branch is recommended.[153] Following bundle branch ablation, the risk of AV block at follow-up is considered particularly high due to

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progressive His–Purkinje disease, and a pacemaker should be implanted. Prolonged PR or QRS intervals,[13,16,80] concurrent atrial arrhythmias,[6,16,80] and LGE at CMR[14,15,18] in patients older than 40 years have all been associated with AV block and SCD at follow-up in myotonic dystrophy. Accordingly, pacemaker implantation may be considered even in the absence of symptoms. Although data are lacking, implantation of an ICD rather than a pacemaker may be preferred in myotonic dystrophy patients, with additional risk factors for VA and SCD (*Figure 23*). Permanent pacemaker implantation may also be considered in patients with Kearns–Sayre syndrome, Emery–Dreiffus, or limb–girdle muscular dystrophy with any degree of AV block because of the substantial risk of rapid progression to total block. In patients with limb–girdle type 1B or Emery–Dreifuss muscular dystrophies who have an indication for pacing or significant LGE on CMR, ICD implantation should be considered.[769]

Implantation of an ICD rather than a pacemaker may be also considered in patients with Duchenne/Becker, when there is significant LGE on CMR.[770,771] However, the general prognosis of these diseases should be taken into consideration. In patients who have survived a CA due to a SMVT, implantation of an ICD is recommended when other than BBR-VTs (e.g. scar-related VTs) are inducible or if VT is not inducible. Myotonic dystrophy patients with a syncope likely due to a VA, even if not inducible, and those with palpitations and induction of a non-BBR-VT are considered at risk for arrhythmic SCD, and ICDs should be considered.

Due to the progressive nature, annual follow-up with an ECG is recommended, even in the concealed phase of the disease when patients are asymptomatic and the ECG is normal.[6,13] Due to slow progression and the fact that significant changes are often reflected on the surface ECG, serial electrophysiological evaluation to assess AV conduction and arrhythmia induction is not recommended in patients without arrhythmia suspicion or progression of ECG conduction disorders.[767,772]

Recommendation Table 33 — Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in neuromuscular diseases

Recommendations	Class[a]	Level[b]
General recommendations		
Annual follow-up with at least a 12-lead ECG is recommended in patients with muscular dystrophies, even in the concealed phase of the disease.[6,13]	I	C
It is recommended that patients with neuromuscular disorders who have VAs or ventricular dysfunction are treated in the same way for arrhythmia as patients without neuromuscular disorders.[17,765]	I	C
Risk stratification, primary and secondary prevention of SCD		
Invasive electrophysiological evaluation is recommended in patients with myotonic dystrophy and palpitations or syncope suggestive of VA or surviving a CA.[153]	I	C
ICD implantation is recommended in patients with myotonic dystrophy and SMVT or aborted CA not caused by BBR-VT.[766]	I	C
Invasive electrophysiological evaluation should be considered in patients with myotonic dystrophy and a sudden increase in the PR interval or QRS duration.[766,767]	IIa	B
Invasive electrophysiological evaluation should be considered in patients with myotonic dystrophy and a PR interval ≥240 ms or QRS duration ≥120 ms or who are older than 40 years and have supraventricular arrhythmias[c] or who are older than 40 years and have significant LGE on CMR.[c,5,14,16,766]	IIa	B
In myotonic dystrophy patients without AV conduction delay and a syncope highly suspicious for VA, ICD implantation should be considered.[766]	IIa	C
In myotonic dystrophy patients with palpitations highly suspicious for VA and induction of a non-BBR-VT, ICD implantation should be considered.[766]	IIa	C
In patients with limb–girdle type 1B or Emery–Dreifuss muscular dystrophies and indication for pacing, ICD implantation should be considered.[769]	IIa	C
Implantation of an ICD may be considered in patients with Duchenne/Becker muscular dystrophy and significant LGE at CMR.[770,771]	IIb	C
Implantation of an ICD over a permanent pacemaker may be considered in myotonic dystrophy patients with additional risk factors[d] for VAs and SCD.	IIb	C
In myotonic dystrophy patients, serial electrophysiological evaluation of AV conduction and arrhythmia induction is not recommended without arrhythmia suspicion or progression of ECG conduction disorders.[772]	III	C
Management of VA		
In symptomatic patients with BBR-VT, catheter ablation is recommended.[e,153,474,475,477]	I	C
In patients with myotonic dystrophy undergoing ablation for BBR-VT, pacemaker/ICD implantation is recommended.[153]	I	C

AV, atrioventricular; BBR-VT, bundle branch re-entrant ventricular tachycardia; CA, cardiac arrest; CMR, cardiac magnetic resonance; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; LGE, late gadolinium enhancement; LV, left ventricular; SCD, sudden cardiac death; SD, sudden death; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VT, ventricular tachycardia.

[a]Class of recommendation.

[b]Level of evidence.

[c]Level of evidence C.

[d]Factors favouring ICD implantation: Age,[5,6,11] CTG expansion,[6–9,13,16] SD or family history of SD,[5] ECG conduction abnormalities,[16] PR prolongation,[13] LBBB,[5] atrial arrhythmias,[6,16] non-sustained VT,[5] LV dysfunction,[17] structural abnormalities in CMR.[14,15,18]

[e]In other cardiac conditions (e.g. aortic valve replacement) with BBR-VT, catheter ablation is also recommended.

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7.1.4. Inflammatory cardiac diseases

Cardiac inflammation has been associated with altered myocardial electrical properties and arrhythmias, and has been reported in various cardiomyopathies such as, obviously, myocarditis, but also inherited cardiomyopathies or after MI.[773,774]

Inflammatory cardiomyopathies are characterized by myocardial inflammation (i.e. myocarditis) as the *primary* cause of cardiac damage, whereas *secondary* myocardial inflammations are caused by an *initial myocardial pathology*.[775,776]

Myocarditis, sarcoidosis, and Chagas' disease are among the major entities within inflammatory cardiomyopathies.

7.1.4.1. Myocarditis

The diagnosis of myocarditis can be challenging. There is no pathognomonic clinical presentation of this disease,[777] with cardiac manifestations ranging from subtle symptoms to severe heart failure, complete AV block, and SCD.[778] In young people, it is estimated that 2–12% of SCD are related to myocarditis.[779–781]

Myocarditis is diagnosed on endomyocardial biopsy by established histological, immunological, and immunohistochemical criteria, as well as polymerase chain reaction (PCR) to detect viral genomes.[782,783] This implies that endomyocardial biopsy, although not widely used, is the diagnostic gold standard for myocarditis.[778,784] In current practice, the diagnosis of myocarditis relies on clinical presentation, elevated troponin level, ECG changes, evidence of LV dysfunction, absence of significant CAD or valvular heart disease, and suggestive findings on CMR or PET-CT.

In the context of suspected or confirmed acute myocarditis, patients with a life-threatening presentation (fulminant myocarditis, sustained VAs, or complete AV block) are to be referred to a specialized centre.[785,786] A specialized centre must have the capacity to perform cardiac catheterization, endomyocardial biopsies, use mechanical circulatory support devices, and manage complex VAs.

Sustained VAs may occur in acute myocarditis. In a large series of patients,[786] in-hospital VF or CA was reported in 2.5% of cases. In another series of acute myocarditis in children,[787] sustained tachyarrhythmias were reported in 11.5% of patients, with VAs accounting for most cases (79.5%). Tachyarrhythmias were associated with a 2.3-fold increased risk of death.[787] Giant cell myocarditis, although rare, has a higher risk of life-threatening VAs, which are seen in 14% of giant cell myocarditis patients on initial presentation, and then develop as refractory arrhythmias in more than half of the patients during the course of the disease.[788,789]

The management of acute myocarditis depends on clinical presentation, viral PCR from myocardial biopsies, and histological findings. In patients with suspected myocarditis who present with mild heart failure, it is recommended to avoid exercise and use beta-blockers and ACE inhibitors.[790] Patients with VAs or AV block must be admitted to the hospital and continuously monitored.

Treatment of arrhythmias in patients with inflammatory heart disease does not differ from generally accepted clinical principles. Symptomatic VAs may require AADs such as amiodarone and/or beta-blockers.[791–793] Of note, in a retrospective observational study, patients with sustained VAs during the acute phase of myocarditis (LVEF 53 $\pm$ 10%) had a high risk (45% at 3 years) of VT/VF recurrences during follow-up.[794]

Myocarditis may resolve without sequelae, recur, or become chronic. Thus, myocarditis is often considered a precursor of DCM.[795] Development of DCM has been observed in 21% of patients with acute myocarditis over a mean follow-up period of 3 years.[796] The exact proportion of chronic DCM consecutive to the progression of acute myocarditis remains unknown, but myocarditis has been identified as the cause of DCM in up to 12% of cases in a large retrospective study.[797] In patients with SMVT of unclear aetiology, myocarditis should be suspected especially when CMR reveals subepicardial and/or intramural abnormal fibrotic myocardial tissue. The presence of LGE at CMR has also been associated with the late occurrence of VAs in patients with endomyocardial biopsy-proven viral myocarditis.[798–800]

The management of documented VAs in chronic myocarditis is similar to that of patients with DCM, including ICD implantation and the use of AADs. Catheter ablation can be effective to treat SMVT, the arrhythmogenic substrate of which is often found on the epicardium of the lateral/basal left ventricle.[752,801–803] In one publication,[802] non-inducibility of VT after catheter ablation led to avoidance of ICD implantation in one-third of patients, with subsequently no VT recurrence during follow-up.

Recommendation Table 34 — Recommendations for sudden cardiac death prevention and treatment of ventricular arrhythmias in myocarditis

Recommendations	Class[a]	Level[b]
General recommendations		
In confirmed or clinically suspected acute myocarditis, it is recommended that patients who present with life-threatening VAs are referred to a specialized centre.[786,804]	I	C
Secondary prevention of SCD and treatment of VA		
In patients with haemodynamically not-tolerated SMVT occurring in the chronic phase of myocarditis, an ICD implantation is recommended.[794,805]	I	C
In patients with haemodynamically not-tolerated sustained VT or VF during the acute phase of myocarditis, ICD implantation before hospital discharge should be considered.[788,794,806]	IIa	C
AADs should be considered (preferably amiodarone and beta-blockers) in patients with symptomatic non-sustained or sustained VAs during the acute phase of myocarditis.	IIa	C
In post-myocarditis patients with recurrent, symptomatic VT, AAD treatment should be considered.	IIa	C
Catheter ablation, performed in specialized centres, should be considered in post-myocarditis patients with recurrent, symptomatic SMVT or ICD shocks for SMVT in whom AADs are ineffective, not tolerated, or not desired.[752,801,802]	IIa	C
In patients with haemodynamically tolerated SMVT occurring in the chronic phase of myocarditis, ICD implantation should be considered.	IIa	C

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In patients with haemodynamically well-tolerated SMVT occurring in the chronic phase of myocarditis, preserved LV function and a limited scar amenable to ablation, catheter ablation may be considered as an alternative to ICD therapy, after discussion with the patient and provided that established endpoints have been reached.[c]	IIb	C

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AAD, anti-arrhythmic drug; ICD, implantable cardioverter defibrillator; LV, left ventricular; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]VT non-inducibility and elimination of electrograms consistent with conduction delay.

7.1.4.2. Cardiac sarcoidosis

Sarcoidosis is a multisystem inflammatory disease of unknown cause, with a genetic predisposition,[807] characterized by the accumulation of T lymphocytes, mononuclear phagocytes, and non-caseating granulomas leading to tissue scarring.[808] Although lung involvement is most frequent, any organ can be affected. It is estimated that 5% of patients with sarcoidosis have symptoms indicative of cardiac involvement. However, using advanced cardiac imaging modalities (CMR/PET-CT), subclinical cardiac sarcoidosis is increasingly diagnosed.[808–811]

The diagnosis of cardiac sarcoidosis is challenging. It can mimic the ARVC phenotype in the event of a predominant RV involvement[810] or the heart is the only organ affected by sarcoidosis (so-called 'isolated cardiac sarcoidosis').[812] Cardiac electroanatomical voltage mapping may help in the differential diagnosis between isolated cardiac sarcoidosis and ARVC.[813] The three usual cardiac manifestations of cardiac sarcoidosis are LV dysfunction, AV conduction abnormalities, and VAs. Complete AV block develops primarily during the acute inflammatory phase as opposed to sustained VT, which frequently develops in the advanced stage of the disease (*Figure 24*).[814]

In addition to *isolated* cardiac sarcoidosis,[812] three independent factors have been found associated with an adverse outcome and, particularly, the risk of VAs: (i) an LVEF $<35\%$[812]; (ii) documentation of high-degree AV block[815,816]; and (iii) presence of RV or LV scarring at CMR (*Figure 25*).[817–821] However, VAs and SCD may occur in patients with a mildly reduced or normal LVEF. PES,[822–825] PET-CT,[826] and LGE-CMR help stratify the risk of VAs in such patients.[827] In a series of 120 patients with biopsy-proven extracardiac sarcoidosis and preserved LV/RV systolic function, VT inducibility at PES was low (6%) but associated with the composite endpoint of VAs and SCD, which occurred in 3 patients, all with abnormal PET or CMR ($P = 0.009$).[825] In a cohort of 66 asymptomatic patients with biopsy-proven extracardiac sarcoidosis and abnormal PET-CT or CMR, 8 (11%) were inducible at PES and 6 of 8 had VA or died during follow-up, compared to 1 of 68 non-inducible patients ($P < 0.0001$). Of note, inducible patients had a lower LVEF at PES, which further deteriorated at 2-year follow-up.[823]

The benefit of ICDs, both for primary and secondary prevention, has been reported.[828–832] Data support the use of ICDs for primary prevention of SCD in patients with LVEF $\leq 35\%$.[812,830] In addition, whatever the LVEF, ICD should also be considered in patients with an indication for permanent cardiac pacing or the presence of significant scar at CMR.[833,834] Indeed, as shown in two recent meta-analyses,[821,832] the occurrence of VA is higher in patients with complete AV block (OR $= 2.19$; $P < 0.01$), and the presence of scar at CMR is associated with a higher risk of the composite endpoint of ventricular arrhythmic events and mortality (OR $= 10.74$; $P < 0.00001$). A widely accepted definition of *significant* LGE is not available. LGE in $\geq 9/29$ segments (17 LV and 12 RV segments) and LGE affecting $\geq 22\%$ of the LV mass have been associated with arrhythmic endpoints.[820,827,835]

Corticosteroid therapy is a mainstay of cardiac sarcoidosis treatment, but the effect of this treatment on the occurrence of VAs has only been ascertained from observational studies.[836–838] Obviously, based upon pathophysiology of the disease, inflammation plays a role in the development of ventricular scar in patients with cardiac sarcoidosis. However, so far there is no evidence that VAs are directly triggered by active inflammation itself. Indeed, a scar-related intramural or epicardial substrate (with a predilection in peri-valvular regions) explains most VTs in patients with cardiac sarcoidosis.[839] The VT substrate was more likely located in segments with scar transmurality at CMR and a lower degree of inflammation on PET-scan.[840] Catheter ablation may help to prevent VT,[839,841,842] in particular if AAD treatment fails,[837] but VT recurrences are still frequent,[752,839] in particular if catheter ablation is performed during active inflammation, with AADs continued in many patients.[839,843]

Recommendation Table 35 — Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in cardiac sarcoidosis

Recommendations	Class[a]	Level[b]
Risk stratification and primary prevention of SCD		
ICD implantation is recommended in patients with cardiac sarcoidosis who have a LVEF $\leq 35\%$.[812,828–830,832]	I	B
In patients with cardiac sarcoidosis who have an indication for permanent cardiac pacing related to high-degree AV block, ICD implantation should be considered, regardless of LVEF.[816]	IIa	C
In patients with cardiac sarcoidosis who have a LVEF $>35\%$ but significant LGE at CMR after resolution of acute inflammation, ICD implantation should be considered.[817–819,821,833,834]	IIa	B
In patients with cardiac sarcoidosis who have a LVEF 35–50% and minor LGE at CMR, after resolution of acute inflammation, PES for risk stratification should be considered.	IIa	C
In patients with cardiac sarcoidosis, LVEF 35–50% and inducible SMVT at PES, ICD implantation should be considered.[823–825]	IIa	C

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Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients with cardiac sarcoidosis who (1) have documented sustained VT, or (2) aborted CA.[812,828–830,832]	I	B
In patients with cardiac sarcoidosis and recurrent, symptomatic VA, AAD treatment should be considered.	IIa	C
Catheter ablation, in specialized centres, may be considered in cardiac sarcoidosis ICD-recipients with recurrent, symptomatic SMVT or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.[839,841,842]	IIb	C

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AAD, anti-arrhythmic drug; AV, atrio-ventricular; CA, cardiac arrest; CMR, cardiac magnetic resonance; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; PES, programmed electrical stimulation; SCD, sudden cardiac death; SMVT, sustained monomorphic VT; AV, ventricular arrhythmia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

7.1.4.3. Chagas' cardiomyopathy

Chagas' disease, a myocardial disease caused by the parasite *Trypanosoma cruzi*, is the most common cause of non-ischaemic cardiomyopathy in Latin America. After the incubation period, the vast majority of infected persons have minor or no symptoms, and very few (<1%) develop acute myocarditis.[845] However, people are infected for life, and years to decades after the initial infection 20–30% of them will develop cardiomyopathy,[846] which can lead to heart failure, heart block and atrial and ventricular arrhythmias. SCD, particularly due to VF, is the most common cause of death in patients with Chagas' cardiomyopathy.[847,848] A risk score developed by Rassi *et al.*[849] as well as the presence of myocardial fibrosis at LGE-CMR[850] are useful in assessing the risk of death in Chagas' disease patients. However, whether such risk stratification can translate into clinical benefit through ICD treatment needs to be assessed in prospective trials, also considering the high annual mortality in Chagas patients with ICDs.[851]

Although ICD implantation may seem reasonable for the secondary prevention of SCD in patients with Chagas' cardiomyopathy, there are controversial studies[851–856] about the benefits and risks

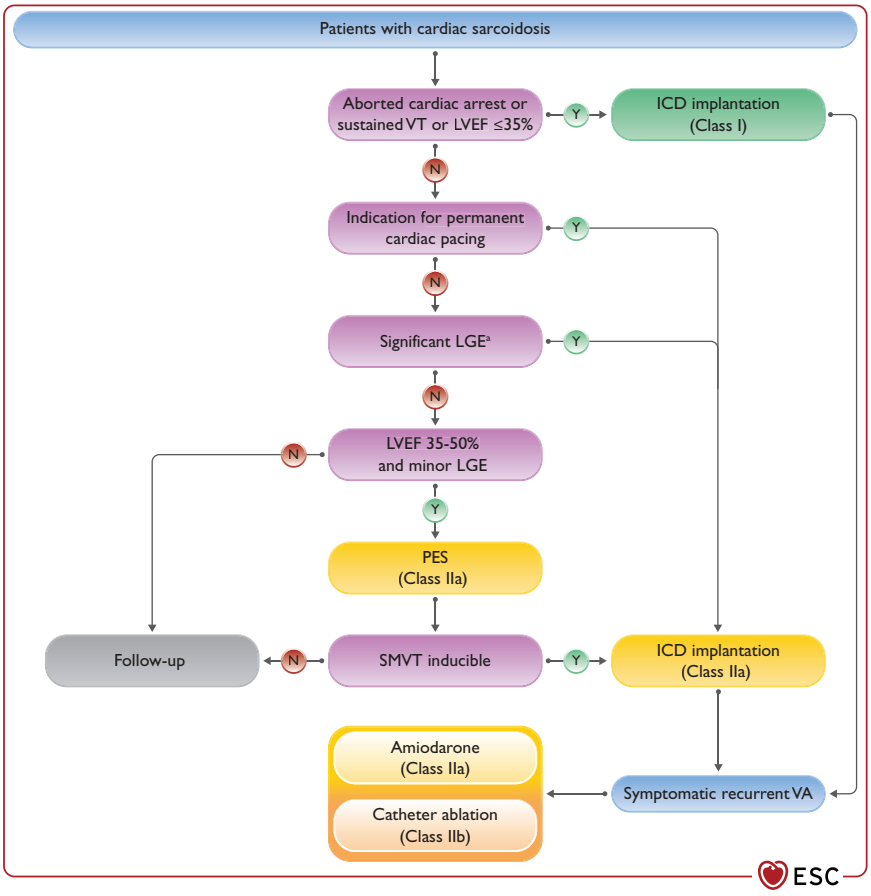

Figure 24 Algorithm for sudden cardiac death prevention and treatment of ventricular arrhythmia in patients with cardiac sarcoidosis. ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; N, No; PES, programmed electrical stimulation; SMVT, sustained monomorphic ventricular tachycardia; VA, ventricular arrhythmia; VT, ventricular tachycardia; Y, Yes. [a]LGE affecting ≥9/22 segments or ≥22% of the LV mass has been associated with arrhythmic endpoints.

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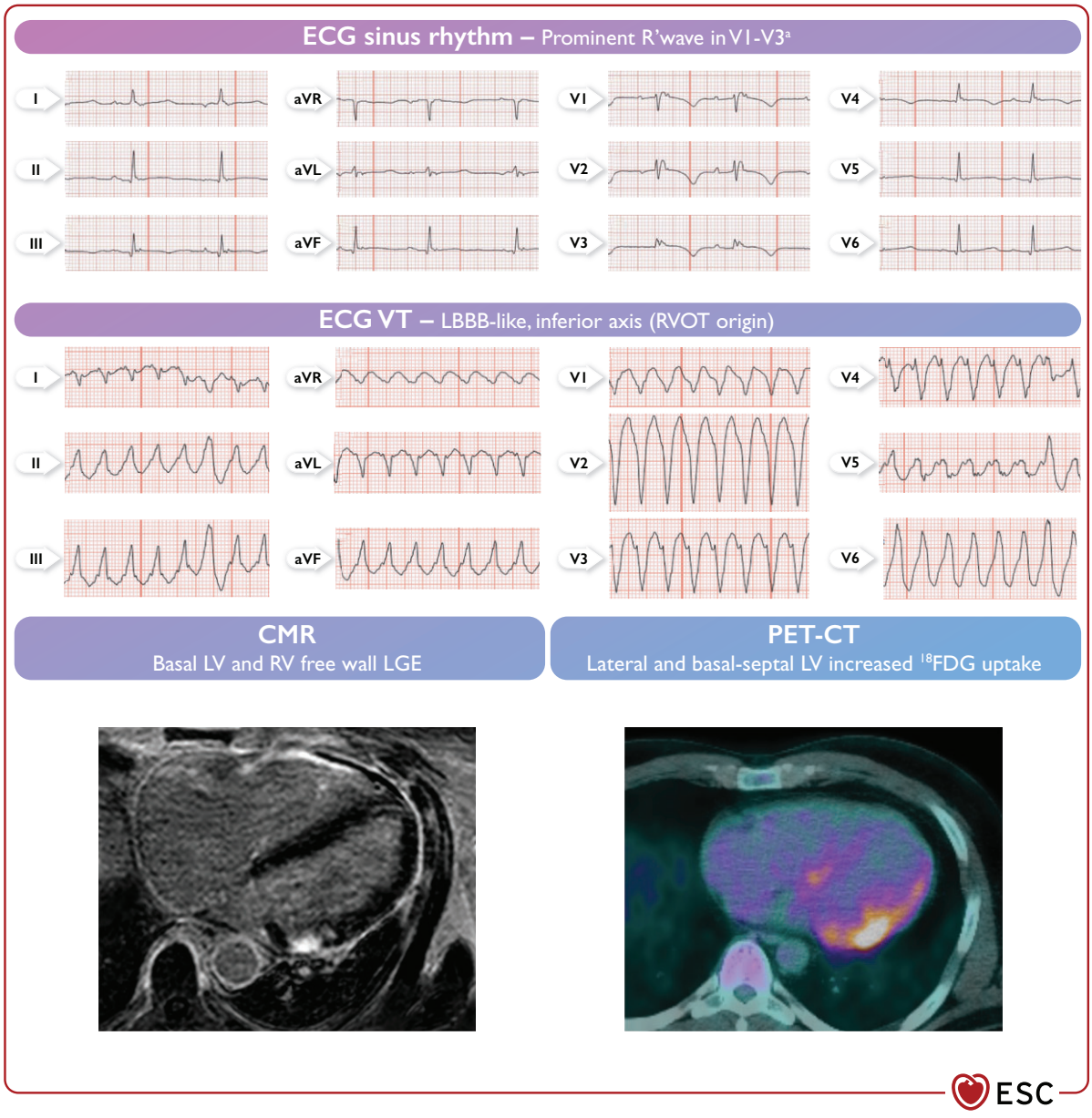

Figure 25 Typical features of cardiac sarcoidosis associated with sustained monomorphic ventricular tachycardia. CMR, cardiac magnetic resonance; ECG, electrocardiogram; LBBB, left bundle branch block; LGE, late gadolinium enhancement; LV, left ventricle; PET-CT, positron emission tomography CT; RV, right ventricle; RVOT, right ventricular outflow tract; VT, ventricular tachycardia. [a]Note the prominent R′ in V1 to V3, a pattern frequently found in cardiac sarcoidosis with RV involvement.[844]

of ICD implantation in these patients. Indeed, a meta-analysis of observational studies found no benefit of ICD ($n = 483$) vs. amiodarone ($n = 115$) for the secondary prevention of SCD in patients with Chagas' disease as all-cause annual mortality rates were comparable in both groups (9.7% and 9.6%, respectively).[856] Another meta-analysis found a 4.7% annual incidence of inappropriate shocks and a high 9.0% annual mortality rate in 1041 ICD patients with Chagas' disease.[851]

Amiodarone[857] and catheter ablation[858–860] have been successfully used to control recurrent VAs in some patients. As with various forms of myocarditis, the arrhythmogenic substrate is often found at the epicardium in Chagas' cardiomyopathy.

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Recommendation Table 36 — Recommendations for the treatment of ventricular arrhythmias in Chagas' cardiomyopathy

Recommendations	Class[a]	Level[b]
Amiodarone should be considered to reduce arrhythmia burden in patients with Chagas' cardiomyopathy who present with symptomatic PVCs or VT.[857]	IIa	C
In patients with Chagas' cardiomyopathy and recurrent, symptomatic SMVT or ICD shocks for SMVT in whom AADs are ineffective, contraindicated, or not tolerated, catheter ablation in specialized centres should be considered.[859,860]	IIa	C
In patients with Chagas' cardiomyopathy and symptomatic VT in whom AADs (amiodarone and beta-blockers) are ineffective or not tolerated, ICD implantation may be considered.[851,854–856]	IIb	C

AAD, anti-arrhythmic drug; ICD, implantable cardioverter defibrillator; PVCs, premature ventricular complexes; SMVT, sustained monomorphic ventricular tachycardia; VT, ventricular tachycardia.

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7.1.5. Valvular heart disease

Valvular heart diseases predispose to SCD both in the pre-operative period and after valvular surgery. In old cohorts of symptomatic, non-operated patients with severe aortic stenosis or severe mitral regurgitation, the incidence of SCD was 50–60%. In these studies, the rate of SCD secondary to VA was not specified.[861,862]

Rates of SCD in patients with prosthetic valves range from 15% to 30%, with an estimated annual risk of 0.2–0.9%.[863] In a large series of 1533 patients who underwent aortic or mitral valve replacement, 6% of deaths were caused by arrhythmias.[864] A recent report of 3726 patients undergoing transcatheter aortic valve implantation (TAVI) showed 5.6% SCD during 22 months of follow-up, emphasizing the remaining SCD risk also after valve replacement.[865]

Small observational studies have shown that patients with residual LV dysfunction after valvular surgery who undergo ICD implantation have appropriate therapy and mortality rates similar to patients with ischaemic or dilated cardiomyopathy.[866–868] ICD implantation in these patients should therefore follow DCM/HNDCM recommendations.

In patients after TAVI, SCD has been associated with the presence of new-onset conduction disturbances (LBBB, QRS > 160 ms) and reduced LVEF ≤40%.[865] SCD in these patients may be the consequence of advanced AV block, and permanent pacing indication should follow the 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy.[2] The role of ICD implantation for prevention of SCD after TAVI is less clear. Two recent retrospective analyses including a total of 203 patients in whom the LVEF remained ≤35% did not show survival benefit from ICD implantation, probably related to the high competing risk of death from heart failure and relevant comorbidities in this population.[869,870]

In patients presenting with SMVT after aortic valve replacement, PES is indicated because of the high probability of BBR-VT as the underlying mechanism—an arrhythmia that is potentially curable with catheter ablation.[871,872]

SCD has been reported to occur in 0.2–0.4% of patients with MVP per year.[873,874] However, the total number of patients dying suddenly with this condition is most likely underestimated, considering that it is a common valve variant with an estimated prevalence of 2–3% in the general population.[875]

Using rigorous criteria for morphologic diagnosis (i.e. myxomatous mitral valve) at post-mortem, MVP has been associated with 7% of all cases of juvenile SCD in the Registry of the Veneto region of Italy.[228] Recent pathological and clinical studies on SCD victims with MVP or patients with MVP and major VAs have provided insights into the potential VA substrate.[130,228,876–880] In particular, myocardial fibrosis affecting both the infero-basal LV free wall and the papillary muscles has been recognized in pathological and LGE-CMR studies.[228] The scarring process has been related to mechanical stretch secondary to the excessive mobility of the mitral valve apparatus due to mitral valvular disjunction and posterior systolic curling.[876] This indicates a promising role of CMR for arrhythmic risk stratification beyond traditional electrophysiological markers.

Proposed criteria for an 'arrhythmic MVP syndrome' that have been associated with an increased risk for SCD include: young adults (most often women), QTc prolongation and/or negative T-wave in inferior ECG leads, mitral annular disjunction, bi-leaflet involvement on echocardiography, frequent PVCs, or non-sustained PVT on Holter monitoring and/or exercise testing.[130,228,876–880] Reduced LVEF and/or myocardial fibrosis on CMR may add to the risk profile. These data are mainly derived from small retrospective series of SCD survivors and post-mortem studies. Therefore, identification of the small subgroup of patients at risk of SCD remains challenging.[228,874] Robust data to support recommendations for risk stratification of SCD in patients with MVP are not available.

Recommendation Table 37 — Recommendations for sudden cardiac death prevention and treatment of ventricular arrhythmias in valvular heart disease

Recommendations	Class[a]	Level[b]
PES with standby catheter ablation is recommended in patients with aortic valve disease and SMVT to identify and ablate BBR-VT, especially if it occurs following a valve intervention.[871,872,881]	I	C

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In patients with valvular heart disease and persistent LV dysfunction after surgical correction, (if possible) it is recommended that ICD implantation for primary prevention follows DCM/HNDCM recommendations.[868]	I	C

BBR-VT, bundle branch re-entrant ventricular tachycardia; DCM, dilated cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; LV, left ventricular; PES, programmed electrical stimulation; SMVT, sustained monomorphic ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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7.1.6. Congenital heart disease

Advances in surgical repair and medical treatment have improved the long-term prognosis of children born with congenital heart disease (CHD). More than 90% now survive to adulthood,[882] and consequently the prevalence of adult CHD has steadily increased.[883] With fewer patients dying from peri-operative events and early heart failure, SCD has become a leading cause of death in adults with repaired CHD.[884] The combination of surgical incisions, myocardial scar and residual or new anatomical abnormalities form the substrate for VAs (*Figure 26*).

Risk stratification for SCD in CHD patients and no documented sustained VA remains difficult due to a mixed patient population, the absence of RCTs, and relatively small observational studies. In patients with biventricular physiology and a systemic LV, the standard criterion of an LVEF ≤35% is used for patient selection for primary prevention ICD implantation.[885,886] For patients with unexplained syncope, severe arrhythmia symptoms such as palpitations or pre-syncope and NSVT, PES should be considered.[887] In asymptomatic patients with tetralogy of Fallot (TOF) but other indicators for a VA substrate, electrophysiological evaluation may refine risk stratification.[888] The surgical era and the techniques used affect the VA substrate and occurrence of VAs and should be considered. The use of a transannular patch repair in TOF patients, for example, was found to be associated with a lower risk for VA.[889] The benefit of primary prevention ICD therapy in patients with single or systemic RVs is less well established and requires consideration of disease- and patient-specific factors.[890,891]

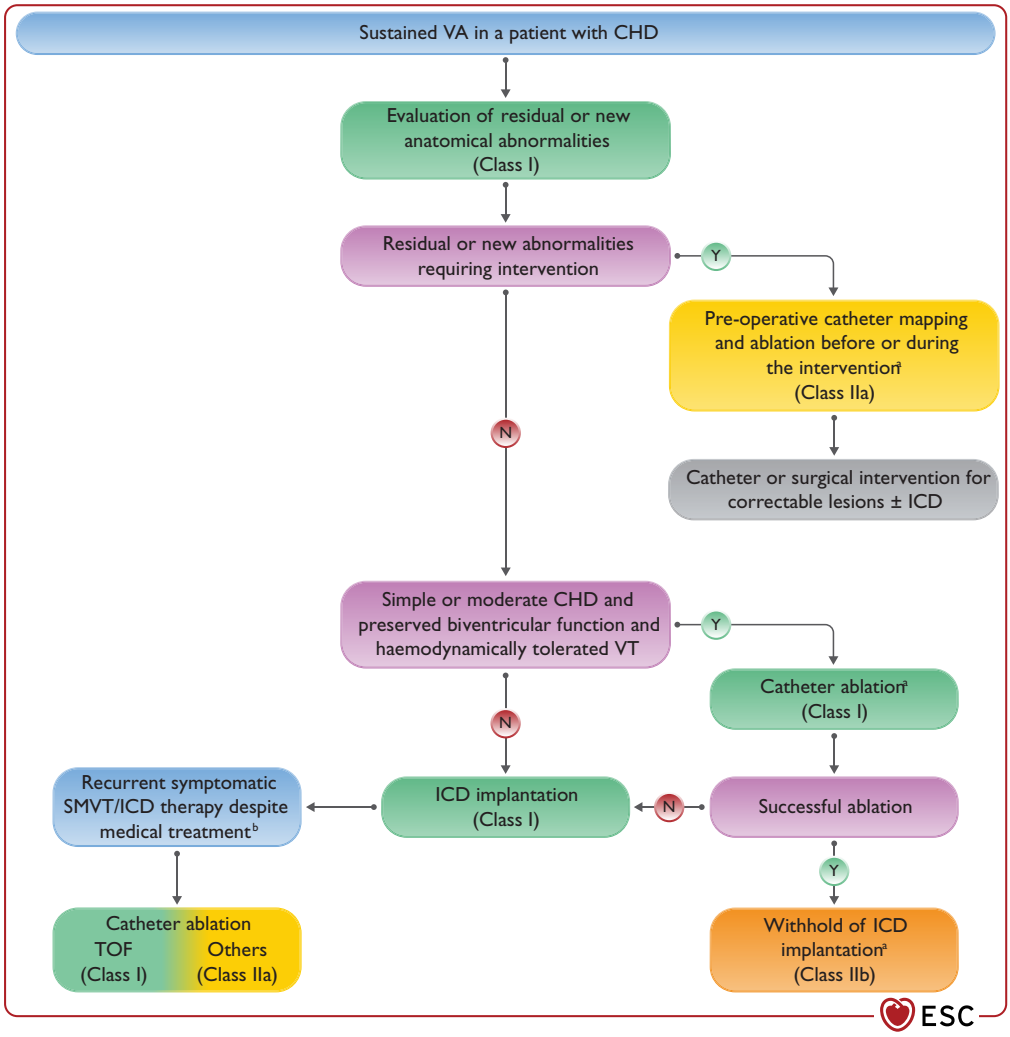

Figure 26 Algorithm for the management of sustained ventricular arrhythmia in patients with congenital heart disease. CHD, congenital heart disease; ICD, implantable cardioverter defibrillator; N, No; TOF, tetralogy of Fallot; VA, ventricular arrhythmia; VT, ventricular tachycardia; Y, Yes. [a]Data derived from patients with TOF and related lesions. [b]In TOF, anti-arrhythmic drug failure is not required.

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In CHD patients with sustained VA or CA survivors, a comprehensive evaluation of inciting factors, including cardiac imaging (particularly CMR) and haemodynamic assessment, is important (*Figure 26*).[892] If pre-existing or new anatomical abnormalities requiring intervention are detected, the treatment plan should consider pre- or intra-operative mapping and transection of the VT substrate, because accessibility might be impaired post-operatively.[888,893,894] Pre-operative evaluation and intervention are especially important in TOF patients undergoing surgical pulmonary re-valving. In selected patients with CHD (including those with atrial baffle repair for transposition of the great arteries, Fontan operation and Ebstein anomaly), evaluation and treatment of SVT (such as intra-atrial re-entrant tachycardias or AV re-entrant tachycardias) with rapid ventricular conduction should also be considered.[890,895,896]

In the absence of identifiable reversible factors, ICD implantation for secondary prevention of SCD is recommended.[349,350] While transvenous ICD systems have been most frequently used and have the advantage of anti-tachycardia and anti-bradycardia pacing, subcutaneous ICDs may be an alternative in selected patients with limited venous access to the ventricle or with intracardiac shunts.

In CHD patients, MVT most often arises from re-entrant tachycardias using anatomical isthmuses bounded by valves, patch material, and surgical incisions. Early mapping and ablation studies, particularly in TOF patients, identified critical anatomical isthmuses of reproducible anatomical location.[897,898] Following this concept, those anatomical isthmuses can be reconstructed and transected in sinus rhythm during catheter ablation procedures using electroanatomical mapping systems, achieving acute success rates of 80%.[888,899–901] The use of conduction block across anatomical isthmuses as a procedural endpoint, in addition to non-inducibility of VT, has further improved long-term ablation outcomes.[888,899] Accordingly, catheter ablation is recommended in particular in TOF patients with recurrent SMVT. Due to the complexity of CHD patients as well as the VT substrate, those procedures should be performed in centres with expertise in catheter ablation of CHD patients. Catheter ablation may be considered in lieu of ICD implantation in selected TOF patients with SMVT and preserved biventricular function, provided the combined procedural endpoint of non-inducibility and conduction block across the anatomical isthmus can be reached.[888,899]

Recommendation Table 38 — Recommendations for risk stratification and primary prevention of sudden cardiac death in congenital heart disease

Recommendations	Class[a]	Level[b]
Risk stratification and primary prevention of SCD		
All CHD patients		
In adults with CHD with biventricular physiology and a left systemic ventricle presenting with symptomatic heart failure (NYHA II/III) and EF ≤35% despite ≥3 months of OMT, ICD implantation is indicated.[885,886]	I	C
In patients with CHD with presumed arrhythmic syncope and with either at least moderate ventricular dysfunction or inducible SMVT on PES, ICD implantation should be considered.[887,889,902]	IIa	C
In patients with advanced single ventricle or systemic RV dysfunction with additional risk factors,[c] ICD implantation may be considered.[890,891]	IIb	C
Tetralogy of Fallot		
In patients after repair of TOF with arrhythmia symptoms and NSVT, electrophysiologic evaluation including PES should be considered.[889,903–905]	IIa	C
In patients after repair of TOF with arrhythmia symptoms and a positive PES, or a combination of other risk factors[d] and a positive PES, ICD implantation should be considered.	IIa	C
In patients after repair of TOF without arrhythmia symptoms, but with a combination of other risk factors,[d] electrophysiologic evaluation, including PES, may be considered.	IIb	C
In patients with repaired TOF undergoing surgical or transcutaneous pulmonary valve replacement, pre-operative catheter mapping and transection of VT-related anatomical isthmuses before or during the intervention may be considered.[894]	IIb	C

AV, atrioventricular; CHD, congenital heart disease; CMR, cardiac magnetic resonance; EF, ejection fraction; ICD, implantable cardioverter defibrillator; LV, left valve; NSVT, non-sustained monomorphic ventricular tachycarda; NYHA, New York Heart Association; OMT, optimal medical treatment; PES, programmed electrical stimulation; RV, right ventricular; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycarda; TOF, tetralogy of Fallot; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Data are sparse and risk factors may be lesion-specific, including non-sustained VT, NYHA II/III, severe AV valve regurgitation, and wide QRS ≥140 ms (transposition of the great arteries).
[d]Other risk factors include moderate RV or LV dysfunction, extensive RV scarring on CMR,[906,907] QRS duration ≥180 ms[886,908] and severe QRS fragmentation.[909,910]

Recommendation Table 39 — Recommendations for secondary prevention of sudden cardiac death and treatment of ventricular arrhythmia in congenital heart disease

Recommendations	Class[a]	Level[b]
Secondary prevention of SCD and treatment of VA		
All CHD patients		
In patients with CHD presenting with sustained VAs, evaluation for residual lesions or new structural abnormalities is recommended.[892,893]	I	B
In patients with CHD with not tolerated VT/aborted CA due to VF, ICD implantation is indicated after exclusion of reversible causes.[349,350]	I	C

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In patients with CHD and recurrent, symptomatic SMVT or ICD shocks for SMVT not manageable by medical therapy or ICD reprogramming, catheter ablation performed in specialized centres should be considered.[c] [899–901]	IIa	C
In selected patients with CHD (including atrial baffle repair for transposition of the great arteries, Fontan operation and Ebstein anomaly) presenting with CA, evaluation and treatment of SVT with rapid ventricular conduction should be considered.[890,895]	IIa	C
Tetralogy of Fallot		
In patients with repaired TOF who present with SMVT or recurrent, symptomatic appropriate ICD therapy for SMVT, catheter ablation performed in specialized centres is recommended.[899–901]	I	C
In patients with repaired TOF with SMVT who are undergoing surgical or transcutaneous pulmonary valve replacement, pre-operative catheter mapping and transection of VT-related anatomical isthmuses before or during the intervention should be considered.[888,893,894]	IIa	C
In patients with repaired TOF with a preserved biventricular function and symptomatic SMVT, catheter ablation or concomitant surgical ablation performed in specialized centres may be considered as an alternative to ICD therapy.[899,901]	IIb	C

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CA, cardiac arrest; CHD, congenital heart disease; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death; SMVT, sustained monomorphic ventricular tachycardia; SVT, supraventricular tachycardia; TOF, tetralogy of Fallot; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Specific recommendations for TOF (Class I-B).

7.2. Primary electrical disease

7.2.1. Idiopathic ventricular fibrillation

The diagnosis of idiopathic ventricular fibrillation (IVF) is made in SCA survivors, preferably with documented VF, after exclusion of structural, channelopathic, metabolic, or toxicological aetiologies.[135,222,911–913] Diagnostic tests include blood chemistry, ECG (including high lead), cardiac CT/coronary angiography, telemetry/Holter, exercise stress test, echocardiogram, sodium-channel blocker testing and CMR (see *Section 5.2.3*, scenario 3).[135,222,911] Genetic testing for channelopathy and cardiomyopathy genes may be considered with a mutation yield of 3–17%.[249,914,915] Clinical evaluation of first-degree family members may be considered, but the diagnostic yield is low. In particular the significance of detected early repolarization pattern (ERP) in asymptomatic relatives is uncertain.[182,916]

In IVF patients, ICD implantation reduces the risk of arrhythmic death by up to 68% compared to amiodarone[352,917–921] (*Figure 27*). In observational studies with a mean follow-up of 5–6 years, 21.0–29.6% of IVF patients experienced an arrhythmic recurrence, corresponding to an annual ICD shock rate of 3.6–5.7%, whereas 4.5–17.5% experienced inappropriate shocks.[919–921] Isoproterenol, verapamil, or quinidine have been employed for acute treatment of recurrent ICD discharges or electrical storm.[912,913,918,922–926] In several small studies, quinidine was highly effective in reducing or even preventing arrhythmia inducibility during programmed stimulation.[923,924,926] Moreover, a retrospective study in 46 patients showed a reduction of mean ICD shocks from 7.5 per patient over 2.9 years to 0.9 shocks per patient over 3.7 years, with a decrease in ventricular storms from 36 to 3 after quinidine initiation.[922] In patients with recurrent episodes of VF triggered by a similar PVC unresponsive to medical treatment, catheter ablation has shown success (*Figure 28*).[186,221,333,493,927–930] PVCs most commonly originate from the Purkinje system and can be eliminated with a high acute success rate of 87–100%.[186,221,333,493,927–930] Detailed electroanatomic mapping may also reveal localized structural alterations (62.5% in one study).[248]

Recommendation Table 40 — Recommendations for the management of patients with idiopathic ventricular fibrillation

Recommendations	Class[a]	Level[b]
Diagnostic evaluation		
It is recommended that idiopathic VF is diagnosed in a SCA survivor, preferably with documentation of VF, after exclusion of an underlying structural, channelopathic, metabolic, or toxicological aetiology.[222,911]	I	B
Clinical testing (history, ECG and high precordial lead ECG, exercise test, echocardiogram) of first-degree family members of idiopathic VF patients may be considered.[222,278,916]	IIb	B
In idiopathic VF patients, genetic testing of genes related to channelopathy and cardiomyopathy may be considered.[249,278,914,915]	IIb	B
Secondary prevention of SCD and treatment of VA		
ICD implantation is recommended in idiopathic VF.[352,917–919]	I	B
Isoproterenol infusion, verapamil, or quinidine for acute treatment of an electrical storm or recurrent ICD discharges should be considered in idiopathic VF.[912,913,918,922–924,926]	IIa	C
Quinidine should be considered for chronic therapy to suppress an electrical storm or recurrent ICD discharges in idiopathic VF.[923,924]	IIa	B
Catheter ablation by experienced electrophysiologists should be considered in idiopathic VF patients with recurrent episodes of VF triggered by a similar PVC non-responsive to medical treatment.[927–930]	IIa	C

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ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; PVC, premature ventricular complex; SCA, sudden cardiac arrest; SCD, sudden cardiac death; VA, ventricular arrhythmia; VF, ventricular fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

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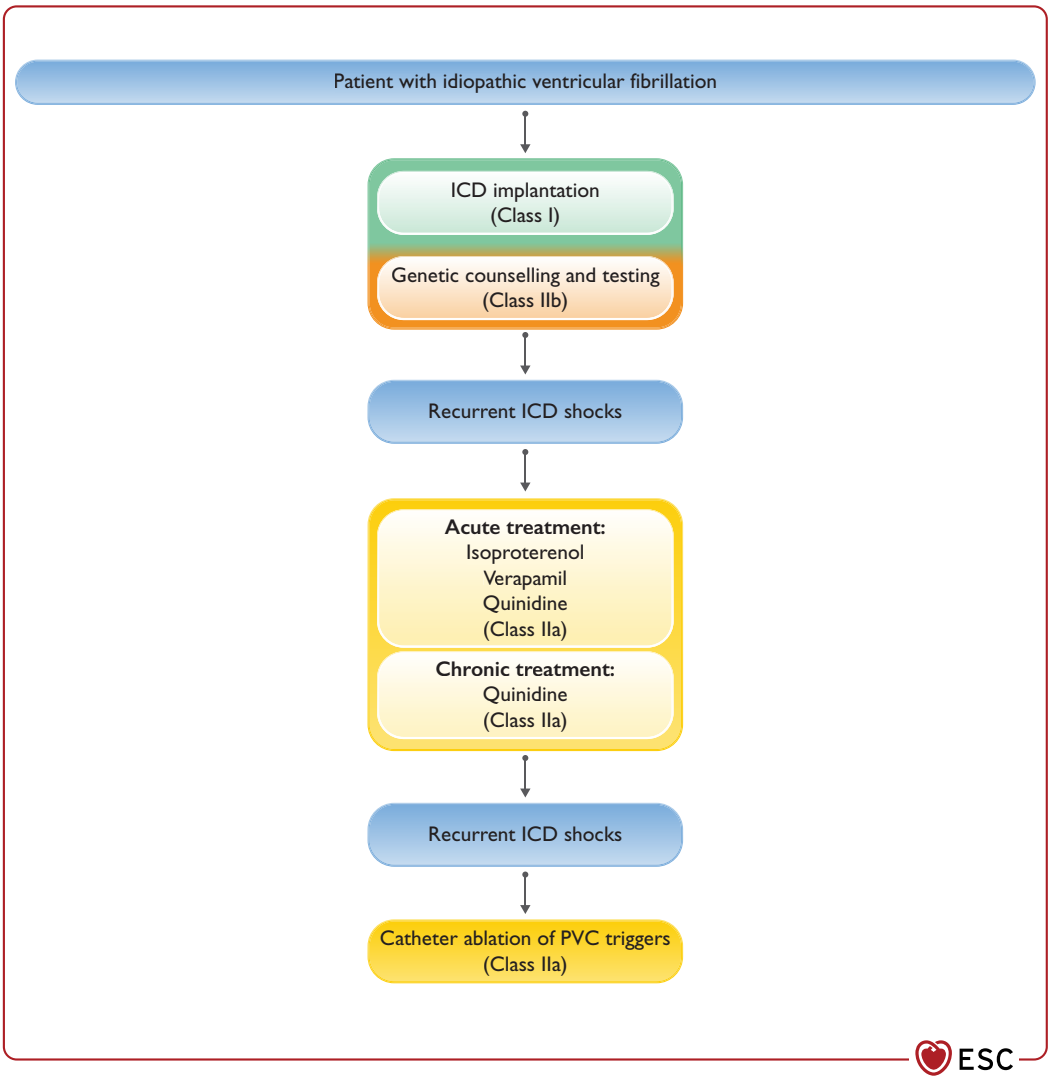

Figure 27 Algorithm for the management of patients with idiopathic ventricular fibrillation. ICD, implantable cardioverter defibrillator; PVC, premature ventricular complex.

7.2.2. Long QT syndrome (including acquired long QT syndrome)

LQTS is characterized by a prolonged QT interval and VAs mainly triggered by adrenergic activation. The mean age at presentation is 14 years. The annual rate of SCD in asymptomatic patients with untreated LQTS has been estimated to be less than 0.5%,[82] while it increases to around 5% in those with history of syncope.[931]

Rare variants in 17 genes[932] have been associated with LQTS. However, the causality for several of the identified genes has been questioned.[166] The undisputed genes are those causing LQT1, LQT2 and LQTS3: *KCNQ1*, *KCNH2* and *SCN5A*, respectively, with gene-specific triggers being exercise (LQTS1), emotional stress (LQTS2) and sleep (LQTS3). Genetic screening identifies a mutation in 75% of LQTS cases and three main genes account for 90% of positively genotyped cases.[178] The subtypes of LQTS may be grouped as follows:

(1) Autosomal-dominant LQTS (prevalence: 1 in 2500) without extra-cardiac manifestation.
(2) Autosomal-dominant LQTS with extra-cardiac manifestation, comprising:
   (a) Andersen–Tawil Syndrome (LQT7), increasingly considered its own entity.[933,934]
   (b) Timothy Syndrome (LQT8), characterized by prolonged QT, syndactyly, cardiac malformations, autism spectrum disorder and dysmorphism.[935]
(3) Autosomal-recessive LQTS (Jervell and Lange–Nielsen Syndrome), combining extreme QT prolongation with congenital deafness.[936]

This panel of experts has confirmed the diagnostic criteria proposed in the previous version of the guidelines: a QTc ≥480 ms or a LQTS risk score >3[937] (*Table 10*) for clinical diagnosis (*Figures 29* and *30*). In the presence of arrhythmic syncope or CA, a QTc ≥460 ms is sufficient to consider a diagnosis of LQTS. A challenge for the clinician is establishing the duration of the QT interval in patients with broad QRS complexes (e.g. in the presence of ventricular pacing or ventricular conduction defects). In this setting, a formula has been proposed that adjusts QT by QRS duration.[938] While measuring the QT, the patient moving briskly from recumbent to

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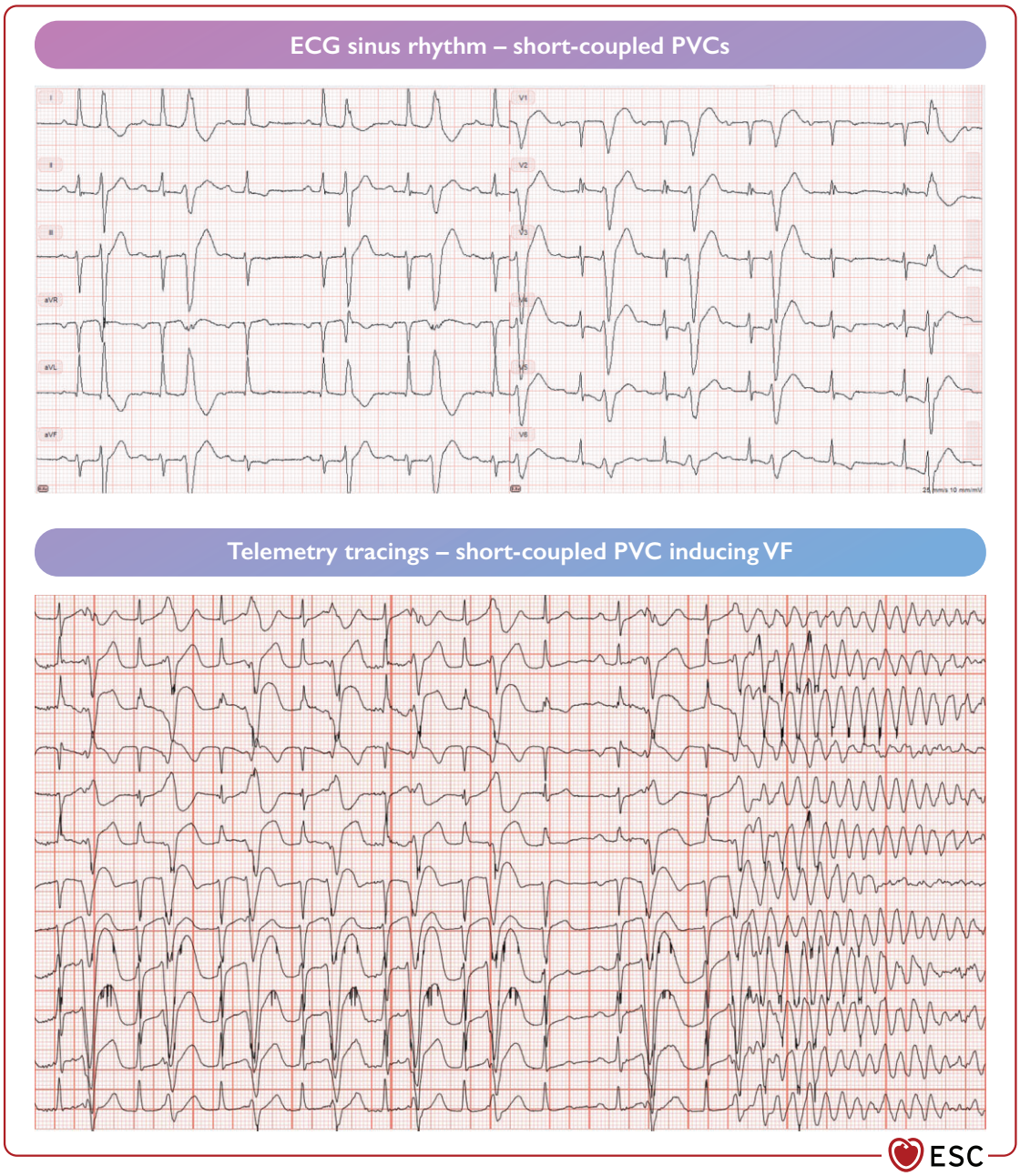

Figure 28 Idiopathic ventricular fibrillation triggered by short-coupled premature ventricular complexes. ECG, electrocardiogram; PVC, premature ventricular complex; VF, ventricular fibrillation.

orthostatic position may be helpful for the diagnosis of LQTS.[232,939] Epinephrine challenge is not recommended as a routine diagnostic tool, as reproducibility is modest.[137] Patients with a clinical diagnosis of LQTS are recommended to undergo genetic counselling and testing in specialized centres to receive genotype-specific management and permit identification of relatives at risk. Relatives with a mutation but without QT prolongation still receive a diagnosis of LQTS, as they are at risk of experiencing VA, although less frequently than phenotype-positive patients.[940]

All LQTS patients receive advice on avoidance of hypokalaemia, QT-prolonging medications and genotype-specific triggers.[941–943] Beta-blockers are also recommended in all LQTS patients. Non-selective beta-blockers nadolol and propranolol have greater efficacy in reducing arrhythmic risk.[940,944–946] Clinical, electrocardiographic and genetic parameters should be considered for the individual risk estimation.[82] Recently, risk stratification based on QT interval duration and genotype has been integrated in a LQTS calculator (the 1-2-3 LQTS Risk calculator).[947]

The utility of genetic testing is exemplified by the need to avoid genotype-specific risks and by the use of mexiletine as a genotype-specific treatment for LQT3, which reduces the length of QT interval and the number of arrhythmic events.[948] It should be noted that different mutations in *SCN5A* show different responses to mexiletine. For example, selected mutations identified in patients not responding to mexiletine showed a distinctive electrophysiological profile

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Table 10 Modified long QT syndrome diagnostic score[243]

Findings			Points
ECG	QTc	≥480 ms	3.5
		=460–479 ms	2
		=450–459 ms (in males)	1
		≥480 ms during 4th minute of recovery from exercise stress test	1
	Torsade de pointes		2
	T wave alternans		1
	Notched T wave in 3 leads		1
	Low heart rate for age		0.5
Clinical history	Syncope	With stress	2
		Without stress	1
Family history	Family member(s) with definite LQTS		1
	Unexplained SCD at age <30 years in first-degree family		0.5
Genetic finding	Pathogenic mutation		3.5

ECG, electrocardiogram; LQTS, long QT syndrome; SCD, sudden cardiac death.
Diagnosis of LQTS with a score >3.

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when studied *in vitro*.[949,950] Additionally, in the case of mutations that cause overlapping syndromes, mexiletine does not induce ST segment elevation, while flecainide has been reported to do so.[951]

Given the uncertain role of beta-blockers in LQT3, there are no indications on whether mexiletine should be administered as a stand-alone therapy or in combination with beta-blockers. Considering that some mutations may not respond to mexiletine, it is advisable to perform oral testing to verify that the QTc shortens 40 ms before prescribing chronic treatment.[948]

Survivors of a CA have a high risk of recurrences, even on beta-blockers (14% within 5 years on therapy), supporting the use of ICD in CA survivors.[952] Moreover, ICD implantation is indicated when a patient experiences syncope and/or VA despite optimal pharmacological therapy, as syncopal events are associated with increased risk of CA.[953,954] Women with LQTS, particularly LQT2, have an increased risk of arrhythmia both during pregnancy and especially first year post-partum.[955] Silent carriers of mutations present a low, but not negligible, risk of cardiac events, and the use of beta-blockers should be considered in this group of patients.[956]

Left cardiac sympathetic denervation (LCSD) is recommended for symptomatic patients despite beta-blockers when ICD is contraindicated or declined, or for an ICD carrier who experiences multiple shocks while on beta-blockers. This is supported by the evidence that LCSD, especially when performed with a video-assisted technique, is safe and effective,[957] well-tolerated by patients[958] and does not have a negative impact on cardiovascular performance.[959] However, because complications do occur and half of the patients experience breakthrough events after the procedure, LCSD is not an alternative to ICD for high-risk patients.[960] Prophylactic ICD

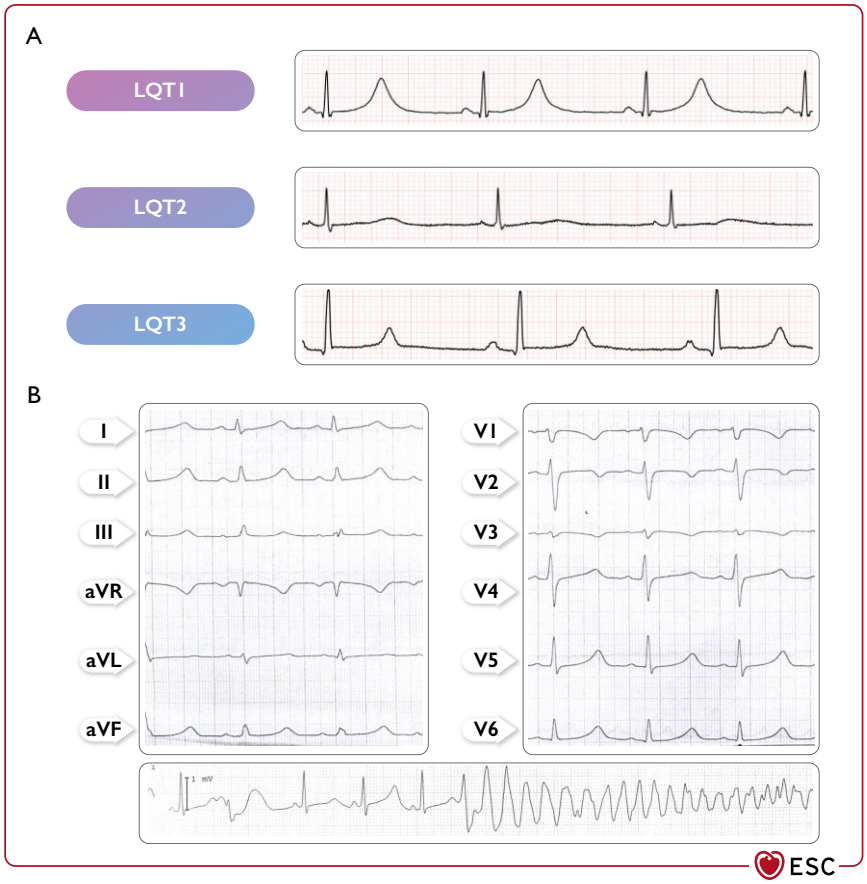

Figure 29 Long QT syndrome electrocardiograms and torsade-de-pointes ventricular tachycardia. *(A)* ECG characteristics in the three major LQTS phenotypes. *(B)* Example of Torsade-de-pointes in a male patient with a *SCN5A* (c.1238C>A, p.A413E) mutation. LQT, Long QT.

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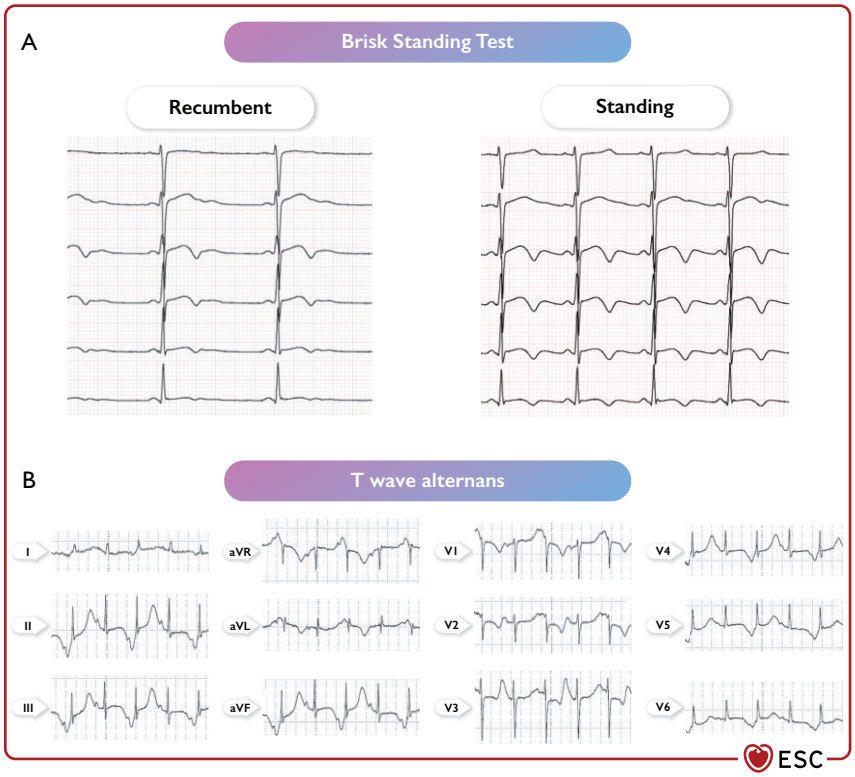

Figure 30 Brisk standing electrocardiogram changes and T wave alternans in Long QT syndrome patients. *(A)* ECG changes during brisk standing test in a male LQTS patient with *KCNH2* (p.S818L) mutation, increased heart rate is associated with less adaptation of QT interval. *(B)* T wave alternans in a male patient with *CACNA1C* (p.G406R) mutation.

therapy in addition to OMT may be considered in asymptomatic LQTS patients identified with high-risk according to the 1-2-3 LQTS Risk calculator.[947] PES is not useful for risk stratification in LQTS.[961]

Figure 31 illustrates the algorithm for the management of patients with long QT syndrome.

Recommendation Table 41 — Recommendations for the management of patients with long QT syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that LQTS is diagnosed with either QTc ≥480 ms in repeated 12-lead ECGs with or without symptoms or LQTS diagnostic score >3.	I	C
In patients with clinically diagnosed LQTS, genetic testing and genetic counselling are recommended.	I	C
It is recommended that LQTS is diagnosed in the presence of a pathogenic mutation, irrespective of the QT duration.	I	C
The LQTS diagnosis should be considered in the presence of a QTc ≥460 ms and <480 ms in repeated 12-lead ECGs in patients with an arrhythmic syncope in the absence of secondary causes for QT prolongation.[952,962,963]	IIa	C
Routine diagnostic testing with epinephrine challenge is not recommended in LQTS.[137]	III	C
General recommendations to prevent SCD		
The following is recommended in LQTS: • Avoid QT-prolonging drugs.[c] • Avoid and correct electrolyte abnormalities. • Avoid genotype-specific triggers for arrhythmias.[943]	I	C
Beta-blockers, ideally non-selective beta-blockers (nadolol or propranolol), are recommended in LQTS patients with documented QT interval prolongation, to reduce risk of arrhythmic events.[940,945,946]	I	B
Mexiletine is indicated in LQT3 patients with a prolonged QT interval.[948]	I	C
Beta-blockers should be considered in patients with a pathogenic mutation and a normal QTc interval.[82]	IIa	B
Risk stratification, prevention of SCD and treatment of VA		
ICD implantation in addition to beta-blockers is recommended in LQTS patients with CA.[952,953,962,963]	I	B
ICD implantation is recommended in patients with LQTS who are symptomatic[d] while receiving beta-blockers and genotype-specific therapies.	I	C

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LCSD is indicated in patients with symptomatic[d] LQTS when: (a) ICD therapy is contraindicated or declined; (b) patient is on beta-blockers and genotype-specific drugs with an ICD and experiences multiple shocks or syncope due to VA.[541,957–959]	I	C
Either ICD implantation or LCSD should be considered in patients with symptomatic[d] LQTS, when beta-blockers and genotype-specific therapies are not tolerated or contraindicated at the therapeutic dose.	IIa	C
In LQTS, it should be considered to calculate the arrhythmic risk before initiation of therapy based on the genotype and the duration of QTc interval.[940]	IIa	C
ICD implantation may be considered in asymptomatic LQTS patients with high-risk profile (according to the 1-2-3 LQTS Risk calculator) in addition to genotype-specific medical therapies (mexiletine in LQT3 patients).[82,940,947,948]	IIb	B
Invasive electrophysiologic study is not recommended in LQTS.[961]	III	C

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CA, cardiac arrest; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LCSD, left cardiac sympathetic denervation; LQTS, long QT syndrome; SCD, sudden cardiac death; VA, ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.
[c]http://www.crediblemeds.org
[d]Arrhythmic syncope or haemodynamically non-tolerated VA.

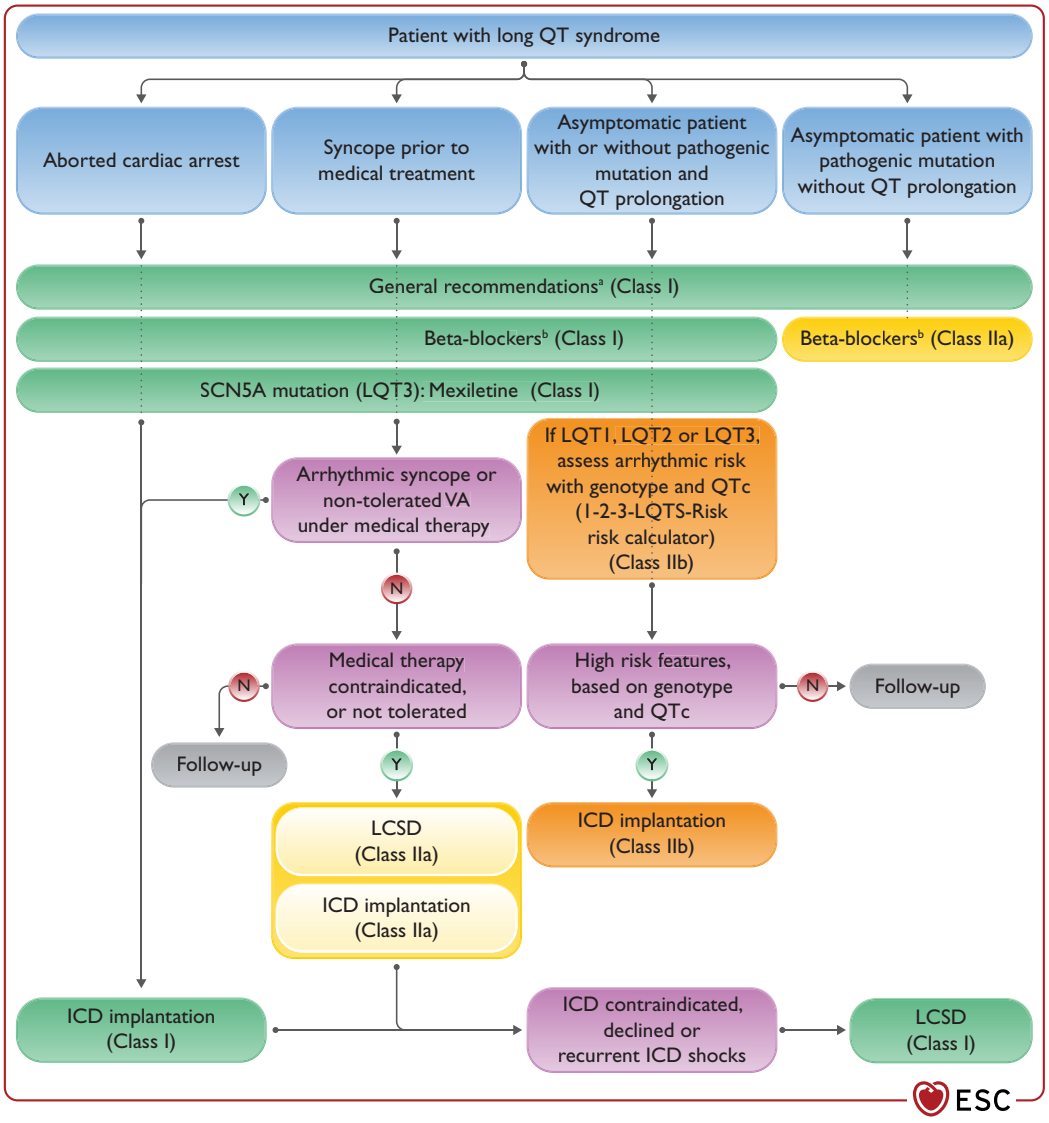

Figure 31 Algorithm for the management of patients with long QT syndrome. ICD, implantable cardioverter defibrillator; LCSD, left cardiac sympathetic denervation; LQT, long QT; N, No; VA, ventricular arrhythmia; Y, Yes. [a]General recommendations: avoidance of QT-prolonging drugs (http://www.crediblemeds.org), correction of electrolyte abnormalities (hypokalaemia, hypomagnesaemia, and hypocalcaemia), avoidance of genotype-specific triggers for arrhythmias (strenuous swimming in LQT1, exposure to loud noises in LQT2). [b]Preferred beta-blockers: nadolol and propranolol.

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7.2.3. Andersen–Tawil syndrome Type 1

Andersen–Tawil syndrome Type 1, also classified as LQT7, is a rare disease (1:1 000 000) characterized by three main symptoms: frequent VA (e.g. bidirectional VT), dysmorphologies and periodic paralysis.[964–967] The inward rectifier current (I_{K1}) decreased by *KCNJ2* loss of function mutation[968] causes an increase in U wave amplitude rather than QT prolongation.[964,967–970] Syncope or documented VT is associated with life-threatening VA, and a study found a 5-year probability of 7.9% of life-threatening VA.[967] In patients with sustained haemodynamically not-tolerated VT or CA, an ICD is recommended.[964,967] Flecainide and/or beta-blockers seem to reduce VA,[964,970,971] whereas amiodarone may be proarrhythmic and should only be used with an ICD.[967] In patients with syncope despite medical therapy, an ICD or ILR should be discussed.[967]

Recommendation Table 42 — Recommendations for management of patients with Andersen–Tawil syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
Genetic testing is recommended in patients with suspected Andersen–Tawil syndrome.[964,967]	I	C
Andersen–Tawil syndrome should be considered in patients without SHD who present with at least two of the following: • Prominent U waves with or without prolongation of the QT interval • Bidirectional and/or polymorphic PVCs/VT • Dysmorphic features • Periodic paralysis • *KCNJ2* pathogenic loss of function mutation.[964,965,967,968,972]	IIa	C
Risk stratification, prevention of SCD and treatment of VA		
ICD implantation is recommended in patients with Andersen–Tawil syndrome after aborted CA or not-tolerated sustained VT.[964,967]	I	C
Beta-blockers and/or flecainide with or without acetazolamide should be considered in patients with Andersen–Tawil syndrome to treat VA.[964,970]	IIa	C
An ILR should be considered in patients with Andersen–Tawil syndrome and unexplained syncope.	IIa	C
ICD implantation may be considered in patients with Andersen–Tawil syndrome who have a history of unexplained syncope or suffer from tolerated sustained VT.[967]	IIb	C

CA, cardiac arrest; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; PVCs, premature ventricular complexes; SCD, sudden cardiac death; SHD, structural heart disease; VA, ventricular arrhythmia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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7.2.4. Brugada syndrome

The type 1 Brugada ECG pattern is characterized by J point elevation of >2 mV with coved ST elevation and T wave inversion in at least one right precordial ECG lead, V1 or V2, positioned in the second, third or fourth intercostal spaces (*Figure 32*). It may occur either spontaneously or be induced by exposure to sodium channel-blocking drugs or fever.[135,231,973–978] It is mandatory to exclude other conditions that may explain the type 1 pattern, so-called phenocopies.[979]

BrS is diagnosed in patients without other heart disease and a spontaneous type 1 pattern, regardless of symptoms, due to its rarity in the general population and association with risk.[231,979,980] The type 1 pattern may also be induced by administration of a sodium channel-blocking drug as a diagnostic test in patients suspected to have concealed BrS but without a spontaneous type 1 ECG.[135,136,231,387,973,978,981–985] However, provocation with drug or fever is less specific than previously thought, with 2–4% prevalence in healthy subjects and higher prevalence in patients with AV nodal reentry tachycardia or an accessory pathway in one study.[977,978,986] In the opinion of this panel of experts, an induced type 1 ECG pattern therefore requires other clinical features, such as documented PVT/VF, arrhythmic syncope, or relevant family history.

The yield of genetic testing in BrS patients is approximately 20%, with the *SCN5A* gene the only gene with evidence of association for clinical testing purposes.[164,980] Phenotype and genotype mismatch is seen in *SCN5A* families, which is explained by variable effects of mutation severity and a polygenic risk score derived from genome-wide association studies.[170,979,987] Recent data also support a potential for prognostication.[988,989]

Psychotropic drugs, selected AADs, anaesthetic agents, cocaine, excessive alcohol intake and fever are potential triggers to exacerbate the type 1 pattern and trigger VF.[231,297] The risk of recurrent VF among patients presenting with CA is 48% at 10 years. ICD implantation is therefore indicated in symptomatic BrS patients who are survivors of CA or have documented spontaneous sustained VA (*Figure 33*).[980,990–994] Approximately one-third of BrS patients present with syncope.[995] The risk of arrhythmic events in BrS patients with unexplained syncope is 4 times higher than the risk in asymptomatic patients.[155,990–992,994,996] Detailed patient history, including absence of prodrome or specific triggers, is essential for distinguishing arrhythmic from non-arrhythmic syncope. Nonetheless, the aetiology of syncope is difficult to determine in up to 30% of BrS patients. In small studies, arrhythmia detected by ILR changed clinical management in 20–36% of the BrS patients with unexplained syncope.[997–999]

Asymptomatic patients represent a majority of newly diagnosed BrS patients with an incidence of arrhythmic events of 0.5% per year.[1000,1001] Their risk stratification remains challenging. A spontaneous type 1 ECG pattern, as well as other ECG markers such as early repolarization pattern and QRS fragmentation, have been associated with higher risk.[980,992,1002,1003] Some have been incorporated into risk scores, although their utility in intermediate-risk patients remains low.[1004,1005] Electrophysiological studies remain controversial. A multicentre pooled analysis showed that

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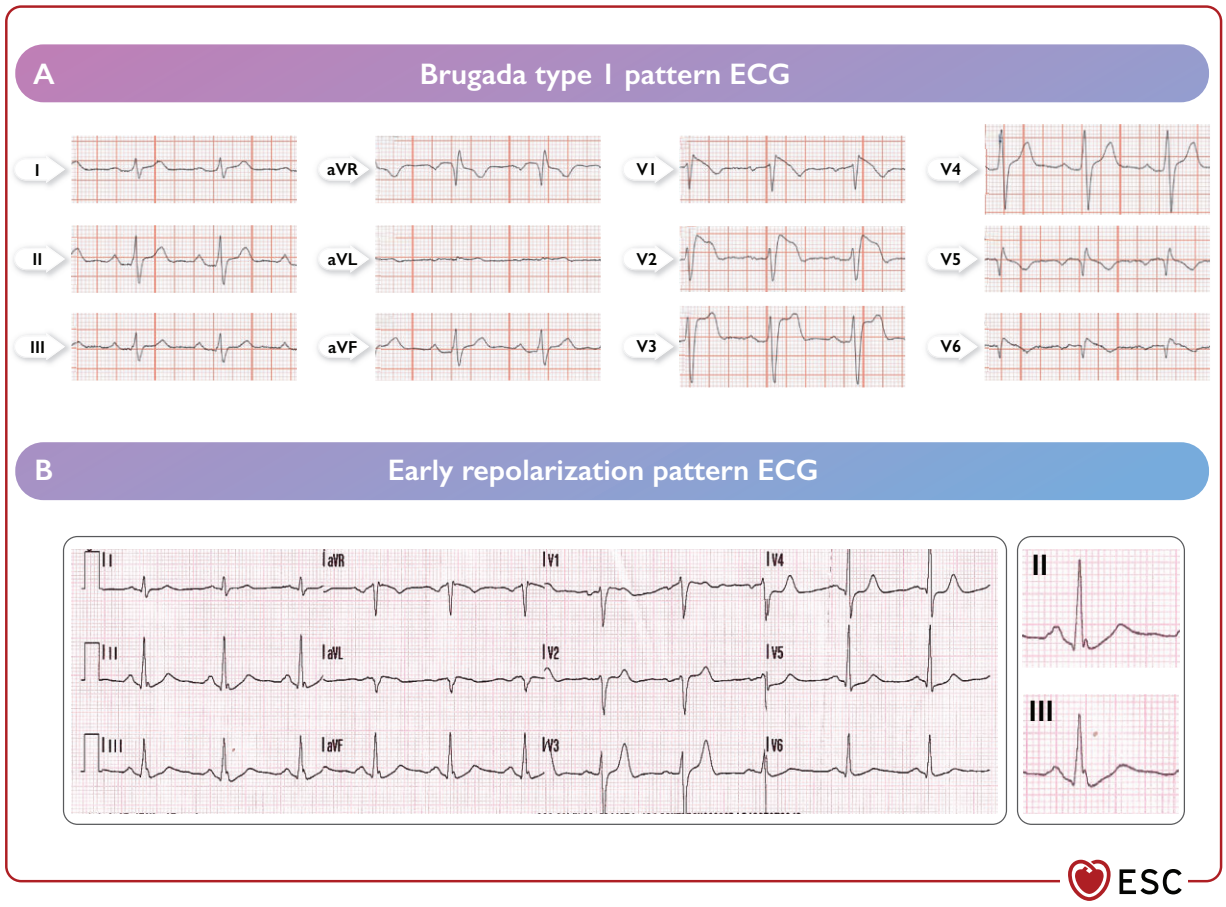

Figure 32 Typical examples of *(A)* Brugada type 1 electrocardiogram, and *(B)* early repolarization pattern electrocardiogram. ECG, Electrocardiogram.

induction of sustained VA during electrophysiological studies was associated with a higher future risk of VA.[155] Inducibility, however, was associated with a potentially clinically actionable result only in asymptomatic patients with a spontaneous type 1 Brugada pattern ECG.

In case of recurrent ICD shocks for VF, quinidine or catheter ablation have been successful in reducing shock frequency.[922,1006,1007] Isoproterenol infusion can suppress electrical storm.[1008] In several small studies, quinidine was effective in reducing or even preventing arrhythmia inducibility during programmed stimulation.[922,1006,1007] However, adverse effects of quinidine can occur in up to 37% of patients, and quinidine is inaccessible in many countries. Cilostazol (phosphodiesterase-3 inhibitor) can be an alternative to quinidine.[1008] Electrophysiological mapping data linked to histopathological studies suggest that an abnormal fibrotic arrhythmogenic substrate in the epicardial RVOT is responsible for the ST-segment elevation in the right precordial leads and VF occurrence in BrS patients.[1009] Ablation of these abnormal areas can markedly suppress recurrent VF and normalize the ECG in >75% of patients.[1009–1015] In patients with recurrent episodes of VF triggered by a similar PVC non-responsive to medical treatment, catheter ablation may target the PVC, which most commonly originates from the RVOT or Purkinje system.[1013] However, data regarding the long-term follow-up after ablation are limited, with neither trial data nor evidence for ablation in asymptomatic patients.

Recommendation Table 43 — Recommendations for management of patients with Brugada syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern.[974–976]	I	C
It is recommended that BrS is diagnosed in patients with no other heart disease who have survived a CA due to VF or PVT and exhibit a type 1 Brugada ECG induced by sodium channel blocker challenge or during fever.[135,136,975,981,982]	I	C
Genetic testing for *SCN5A* gene is recommended for probands with BrS.[164,1016]	I	C
BrS should be considered in patients with no other heart disease and induced type 1 Brugada pattern who have at least one of: • Arrhythmic syncope or nocturnal agonal respiration • A family history of BrS • A family history of SD (<45 years old) with a negative autopsy and circumstance suspicious for BrS.	IIa	C

Continued

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BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an induced type 1 Brugada ECG.[136,973,975,978,984,985]	IIb	C
Sodium channel blocker test is not recommended in patients with a prior type I Brugada pattern.	III	C
General recommendations		
The following is recommended in all patients with BrS: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org). (b) Avoidance of cocaine, cannabis, and excessive alcohol intake. (c) Treatment of fever with antipyretic drugs.	I	C
Risk stratification, prevention of SCD and treatment of VA		
ICD implantation is recommended in patients with BrS who: (a) Are survivors of an aborted CA and/or (b) Have documented spontaneous sustained VT.[980,990–992]	I	C
ICD implantation should be considered in patients with type 1 Brugada pattern and an arrhythmic syncope.[990,992,996]	IIa	C
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope.[997,999]	IIa	C
Quinidine should be considered in patients with BrS who qualify for an ICD but have a contraindication, decline, or have recurrent ICD shocks.[922,1006,1007]	IIa	C
Isoproterenol infusion should be considered in BrS patients suffering electrical storm.[1008]	IIa	C
Catheter ablation of triggering PVCs and/or RVOT epicardial substrate should be considered in BrS patients with recurrent appropriate ICD shocks refractory to drug therapy.[1010–1015]	IIa	C
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG.[155]	IIb	B
ICD implantation may be considered in selected asymptomatic BrS patients with inducible VF during PES using up to 2 extra stimuli.[155]	IIb	C
Catheter ablation in asymptomatic BrS patients is not recommended.	III	C

BrS, Brugada syndrome; CA, cardiac arrest; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; PES, programmed electrical stimulation; PVCs, premature ventricular complexes; PVT, polymorphic ventricular tachycardia; RVOT, right ventricular outflow tract; SCD, sudden cardiac death; SD, sudden death; VA, ventricular arrhythmia; VF, ventricular fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

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7.2.5. Early repolarization syndromes

Early repolarization syndrome (ERS) is diagnosed in a patient resuscitated from PVT or VF without any heart disease and the early repolarization pattern (ERP); J-point elevation ≥1 mm in ≥2 adjacent inferior and/or lateral ECG leads (*Figure 32*).[135,231,1017–1019] However, ERP is most often a benign finding and the prevalence of ERP has been reported as 5.8% in adults and is more common in young males and athletes.[135,231,1017–1021] Nonetheless, ERP is over-represented in relatives of SADS cases[282,1022] and of CA survivors.[182,916] The diagnostic yield and utility of genetic testing is low.[1023–1025] High-risk ECG features have been proposed to increase likelihood of ERS: prominent J-waves ≥2 mm, dynamic changes in J-point elevation (>0.1 mV) and J-waves associated with a horizontal or descending ST-segment (*Figure 34*).[231,1026,1027] ERP with a horizontal ST-segment was associated with arrhythmic risk in an elderly and IVF population.[1027] Nonetheless, ERS survivors and relatives of SADS cases also exhibit a higher prevalence of the ascending/upsloping ST segment than controls.[282,1018] At least 40% of ERS patients with VF have subsequent episodes, with 27% suffering multiple episodes.[231,1028,1029] Isoproterenol infusion is effective in acute suppression of recurrent ICD discharges and electrical storm.[1030–1032] AADs that block the transient outward potassium current can prevent VF.[922,1030,1033] A retrospective multicentre study showed a reduction of recurrent VF after initiation of quinidine.[1030] Phosphodiesterase-3 inhibitors such as cilostazol and milrinone also reduced the recurrence of VF.[1032] Ablation of a PVC trigger, usually from the Purkinje system, has an acute success rate of 87–100% and may be effective in preventing recurrence in patients with drug-refractory VF.[1010,1017] Detailed electroanatomic mapping may reveal localized structural alterations in 39% of ERS patients.[1010] Ablation of these areas successfully suppressed electrical storm and may be a therapeutic option in experienced centres. Whether catheter ablation improves long-term outcomes is currently unknown.

Data for risk stratification of patients with suspected ERS without prior CA are unavailable. In individuals with ERP and unexplained syncope, this panel has recommended that follow-up with an ILR should be considered. As the prognosis of asymptomatic subjects with ERP is good, ICD therapy is usually not indicated.[1034–1036] If, however, there is a high-risk ERP and a strong family history of unexplained juvenile SD, then ICD implantation or quinidine may be considered.

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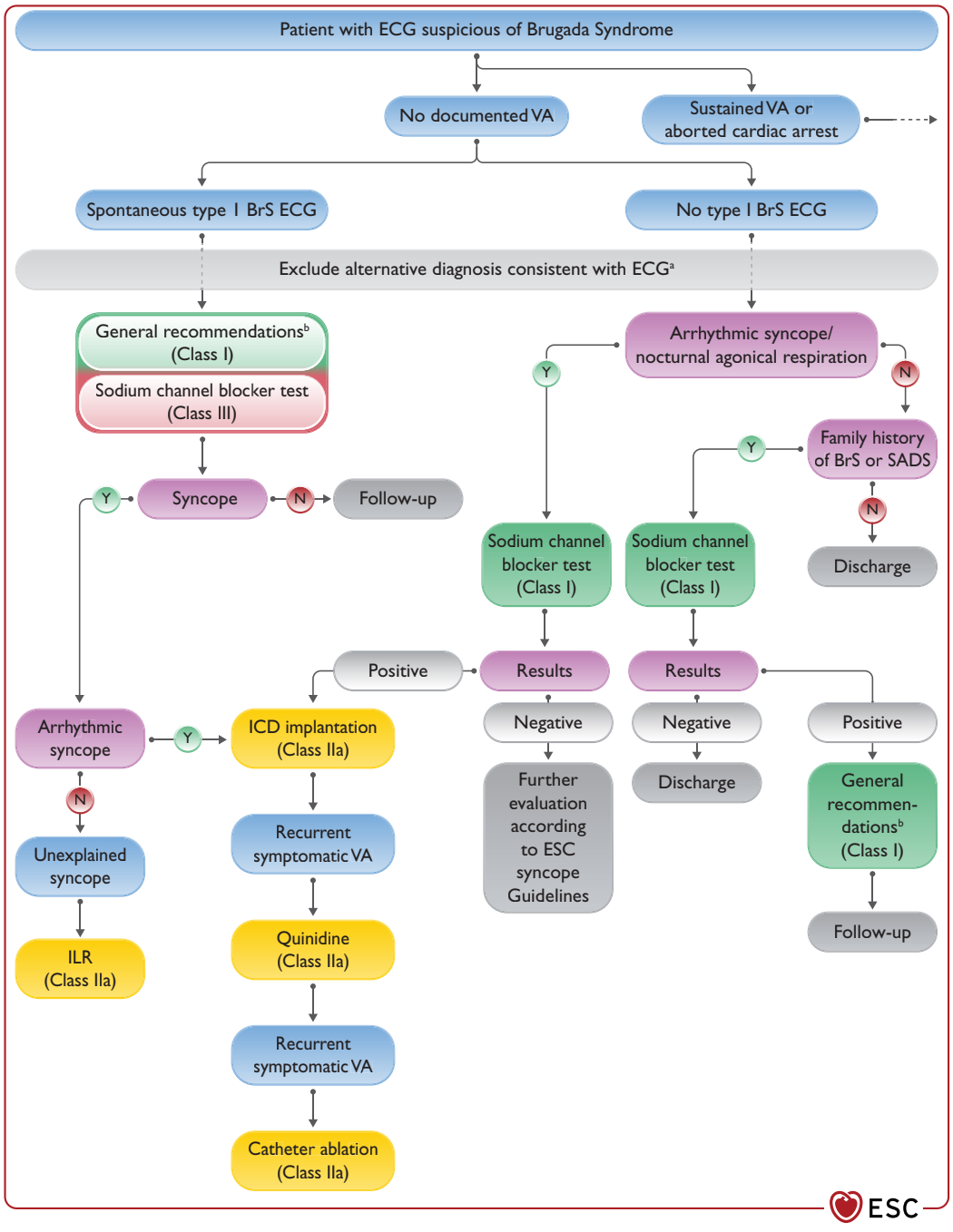

Figure 33 Part One. Algorithm for the management of patients with Brugada pattern electrocardiogram.

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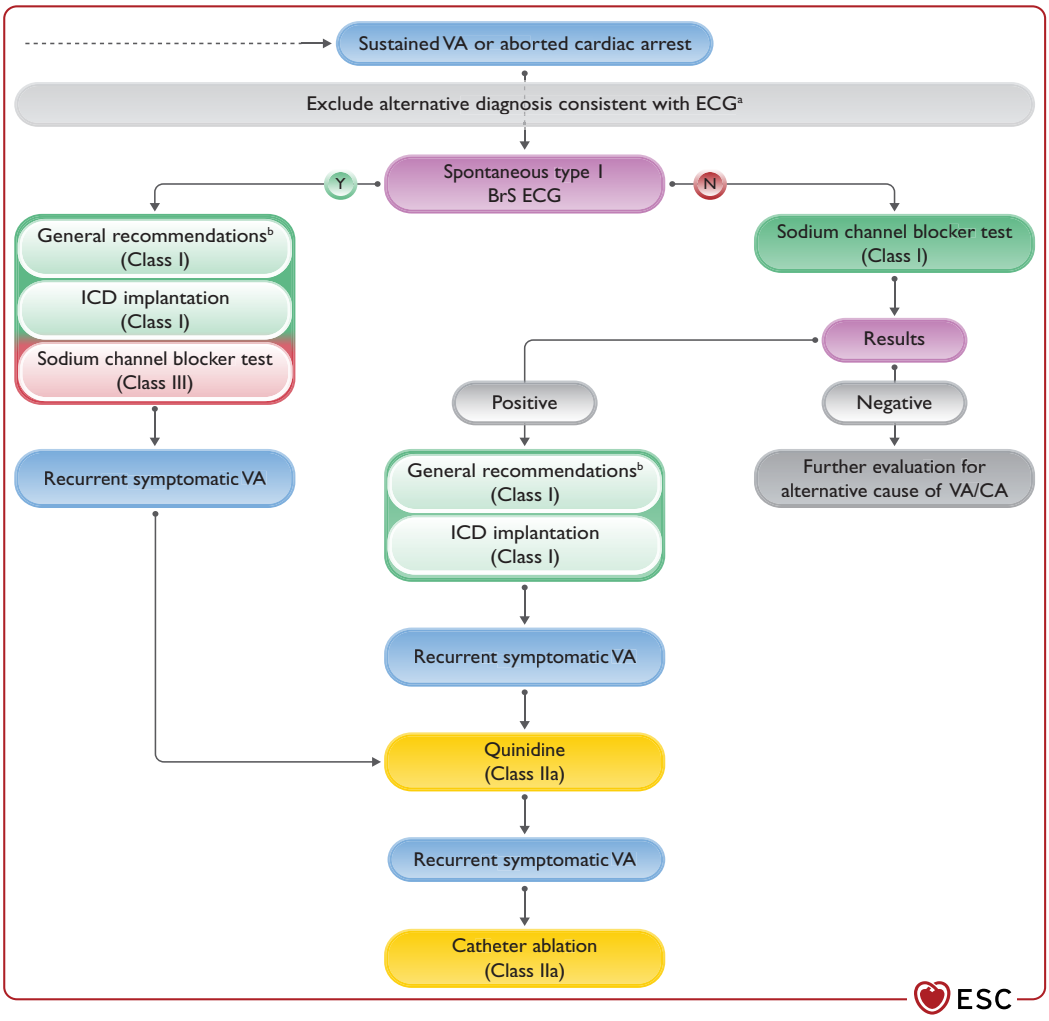

Figure 33 Part Two. Algorithm for the management of patients with Brugada pattern electrocardiogram. BrS, Brugada syndrome; CA, cardiac arrest; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; N, No; SADS, sudden arrhythmic death syndrome; VA, ventricular arrhythmia; Y, Yes. [a]Echo, CMR, cardiac CT, CAG indicated according to patient clinical presentation and risk factors. [b]General recommendations: avoidance of drugs that may induce ST-segmentation elevation in right precordial leads (http://www.brugadadrugs.org), avoidance of cocaine and excessive alcohol intake, treatment of fever with antipyretic drugs.

Recommendation Table 44 — Recommendations for the management of patients with early repolarization pattern/syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that the ERP is diagnosed as J-point elevation of ≥1 mm in two adjacent inferior and/or lateral ECG leads.[1017,1018]	I	C
It is recommended that the ERS is diagnosed in a patient resuscitated from unexplained VF/PVT in the presence of ERP.[1017,1018]	I	C
In an SCD victim with a negative autopsy and medical chart review, and an ante-mortem ECG demonstrating the ERP, the diagnosis of ERS should be considered.[1017,1018]	IIa	C
First-degree relatives of ERS patients should be considered for clinical evaluation for ERP with additional high-risk features.[c,1022,1037]	IIa	B
Genetic testing in ERS patients may be considered.[1023,1025]	IIb	C
Clinical evaluation is not recommended routinely in asymptomatic subjects with ERP.[1038,1039]	III	C
Risk stratification, prevention of SCD and treatment of VA		
ICD implantation is recommended in patients with a diagnosis of ERS who have survived a CA.[1017]	I	B
Isoproterenol infusion should be considered for ERS patients with electrical storm.[1017,1030–1032]	IIa	B
Quinidine in addition to an ICD should be considered for recurrent VF in ERS patients.[922,1030,1033]	IIa	B
ILR should be considered in individuals with ERP and at least one risk feature[d] or arrhythmic syncope.[1020]	IIa	C
PVC ablation should be considered in ERS patients with recurrent VF episodes triggered by a similar PVC non-responsive to medical treatment.[1010]	IIa	C
ICD implantation or quinidine may be considered in individuals with ERP and arrhythmic syncope and additional risk features.[d,1030,1033]	IIb	C

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ICD implantation or quinidine may be considered in asymptomatic individuals who demonstrate a high-risk ERP[c] in the presence of a family history of unexplained juvenile SD.[1030,1033]	IIb	C
ICD implantation is not recommended in asymptomatic patients with an isolated ERP.[1034,1035,1040]	III	C

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CA, cardiac arrest; ECG, electrocardiogram; ERP, early repolarization pattern; ERS, early repolarization syndrome; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; PVC, premature ventricular complexes; PVT, ventricular tachycardia; SCD, sudden cardiac death; SD, sudden death; VA, ventricular arrhythmia; VF, ventricular fibrillation.
[a]Class of recommendation.
[b]Level of evidence.
[c]ERP high-risk features: J waves >2 mm, dynamic changes in J point and ST morphology.[1020,1041]
[d]High-risk ERP: family history of unexplained SD <40 years, family history of ERS.

7.2.6. Catecholaminergic polymorphic ventricular tachycardia

CPVT is a heritable disorder characterized by catecholamine-induced bidirectional VT and PVT in the absence of SHD or ischaemia. The disease has an estimated prevalence of 1 in 10 000 (*Figure 35*).[135]

There are two main genetic types: a dominant disorder due to mutations in the gene encoding for the cardiac ryanodine receptor (*RYR2*) and a recessive disorder caused by mutations in the cardiac calsequestrin gene (*CASQ2*).[135,178] Mutations in *TRDN* and *CALM1-3* have been identified in patients with atypical forms of catecholaminergic VAs.[1042] At the present time, however, it is unclear whether they are distinct arrhythmic entities.[1043] Patients with *KCNJ2* mutations causing Andersen–Tawil syndrome type 1 may sometimes exhibit bidirectional and PVT, but are distinguished by their syndromic associations.[1044]

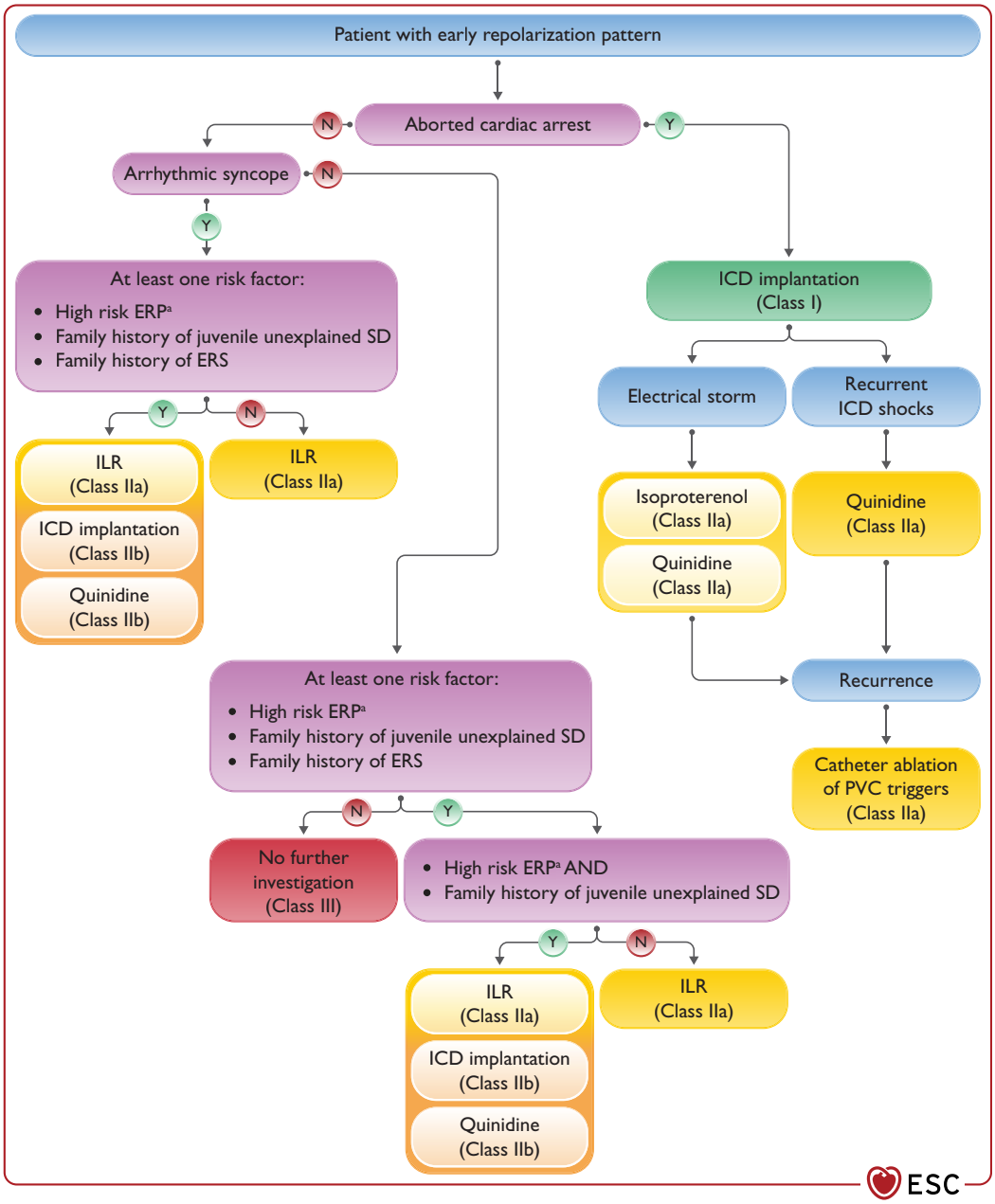

Figure 34 Management of patients with early repolarization pattern/syndrome. ERP, early repolarization pattern; ERS, early repolarization syndrome; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder; N, No; PVC, premature ventricular complex; SD, sudden death; Y, Yes. [a]ERP high risk features: J waves >2 mm, dynamic changes in ST morphology.

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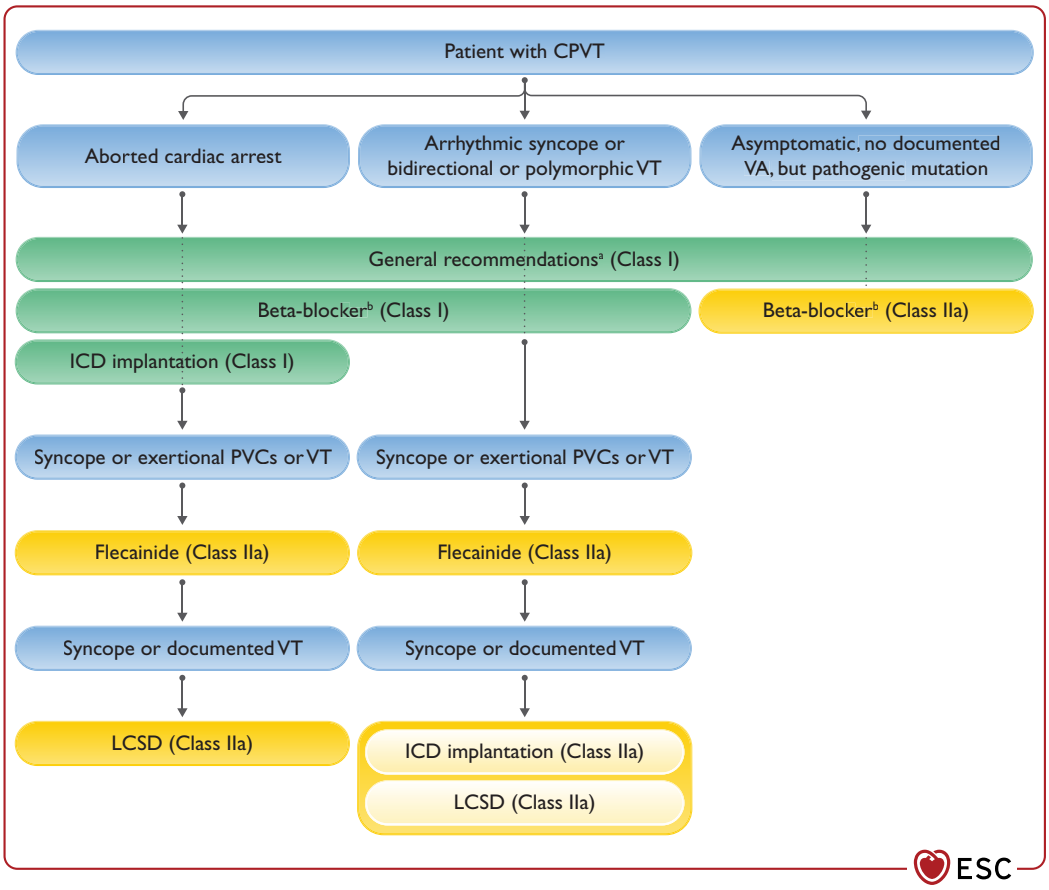

Figure 35 Management of patients with catecholaminergic polymorphic ventricular tachycardia. CPVT, catecholaminergic polymorphic ventricular tachycardia; ICD, implantable cardioverter defibrillator; LCSD, left cardiac sympathetic denervation; PVC, premature ventricular complex; VA, ventricular arrhythmia; VT, ventricular tachycardia. [a]General recommendations: avoidance of competitive sports, avoidance of strenuous exercise, avoidance of stressful environments. [b]Preferred beta-blockers: nadolol, propranolol.

The clinical manifestations of CPVT usually occur in the first decade of life prompted by physical activity or emotional stress.[1045] Most CPVT patients have normal ECG and echocardiogram. Nonetheless, some patients present mild ECG abnormalities, such as sinus bradycardia and prominent U waves. Exercise stress test is the most important diagnostic test, because it elicits the distinguishing bidirectional or PVT that establish the diagnosis (*Figure 36*).[135] A diagnosis can also be made in the presence of a mutation in genes associated with CPVT. Epinephrine or isoproterenol challenge may be considered when exercise stress testing is not feasible.[1046]

Diagnosis in childhood, the lack of beta-blocker therapy, and complex arrhythmias during the exercise stress test on a full dose of beta-blockers are independent predictors for arrhythmic events.[1047] Exercise restriction and beta-blockers without intrinsic sympathomimetic activity are the first-line therapy for CPVT patients.[135] Non-selective beta-blockers such as nadolol and propranolol are preferred.[1048,1049] This panel has confirmed the indication to treat genetically positive family members with beta-blockers, even in the absence of documented exercise- or stress-induced VAs.[1047,1050] Data suggest that flecainide significantly reduces the VA burden in CPVT patients and should be considered in addition to beta-blockers when control of arrhythmias is incomplete.[1051–1053] In selected patients who show intolerance to beta-blocker therapy, pharmacological therapy with flecainide alone is an option.[1054]

Maximal protection with beta-blockers, flecainide and ICD is indicated in survivors of a CA. An ICD should also be considered in CPVT patients with breakthrough VA on beta-blockers and flecainide.[135] The ICD should, however, be programmed with long delays and high rates before defibrillation, because initiating bidirectional VT responds less effectively to defibrillation than subsequent PVT/VF, and painful shocks can trigger further and incessant arrhythmias.[1055]

LCSD has been proposed as an additional therapy in patients in whom pharmacological treatment is not effective or feasible. Although LCSD reduces the recurrence of major cardiac events in previously symptomatic patients, one-third of patients still suffer recurrences of arrhythmia.[1056] Therefore, LCSD has not been considered to be a replacement for ICD therapy but a complementary therapy in symptomatic patients.

A recent systematic review of 53 studies including CPVT patients with an ICD concluded that secondary prevention patients managed with OMT, LCSD and exercise restriction could reduce ICD use.[1057] This observation was supported by a subsequent multicentric investigation showing that all the three SCD observed occurred in patients with an ICD.[1058] At present it seems premature, on the base of this evidence, to demote ICD implant in survivors of CA with CPVT.[1057]

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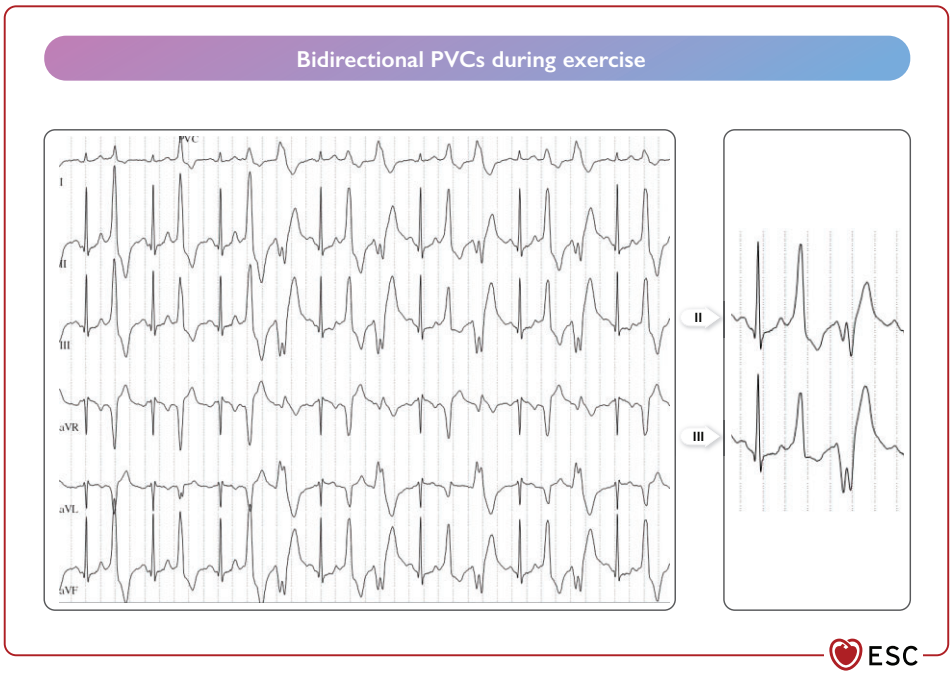

Figure 36 Exercise test of a patient with catecholaminergic polymorphic ventricular tachycardia. PVC, premature ventricular complex.

Recommendation Table 45 — Recommendations for the management of patients with catecholaminergic polymorphic ventricular tachycardia

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that CPVT is diagnosed in the presence of a structurally normal heart, normal ECG, and exercise- or emotion-induced bidirectional, or PVT.	I	C
It is recommended that CPVT is diagnosed in patients who are carriers of a mutation in disease-causing genes.	I	C
Genetic testing and genetic counselling are indicated in patients with clinical suspicion or clinical diagnosis of CPVT.	I	C
Epinephrine or isoproterenol challenge may be considered for the diagnosis of CPVT when an exercise test is not possible.	IIb	C
General recommendations		
Avoidance of competitive sports, strenuous exercise, and exposure to stressful environments is recommended in all patients with CPVT.	I	C
Therapeutic interventions		
Beta-blockers, ideally non-selective (nadolol or propranolol) are recommended in all patients with a clinical diagnosis of CPVT.[1045,1048,1059]	I	C
ICD implantation combined with beta-blockers and flecainide is recommended in CPVT patients after aborted CA.[1045,1047,1060]	I	C
Therapy with beta-blockers should be considered for genetically positive CPVT patients without phenotype.[1047,1050]	IIa	C
LCSD should be considered in patients with diagnosis of CPVT when the combination of beta-blockers and flecainide at therapeutic dosage are either not effective, not tolerated, or contraindicated.[1056]	IIa	C
ICD implantation should be considered in patients with CPVT who experience arrhythmogenic syncope and/or documented bidirectional/PVT while on highest tolerated beta-blocker dose and on flecainide.[1047,1050]	IIa	C
Flecainide should be considered in patients with CPVT who experience recurrent syncope, polymorphic/bidirectional VT, or persistent exertional PVCs, while on beta-blockers at the highest tolerated dose.[1052,1053,1060]	IIa	C
PES is not recommended for stratification of SCD risk.	III	C

CA, cardiac arrest; CPVT, catecholaminergic ventricular tachycardia; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LCSD, left cardiac sympathetic denervation; PVT, polymorphic ventricular tachycardia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

7.2.7. Short QT syndrome

Short QT syndrome (SQTS) is a rare genetic disorder characterised by a short QT interval, premature AF and VF in the context of a structurally normal heart.[1061] It has been associated with gain of function mutations in *KCNH2*, *KCNQ1* and loss of

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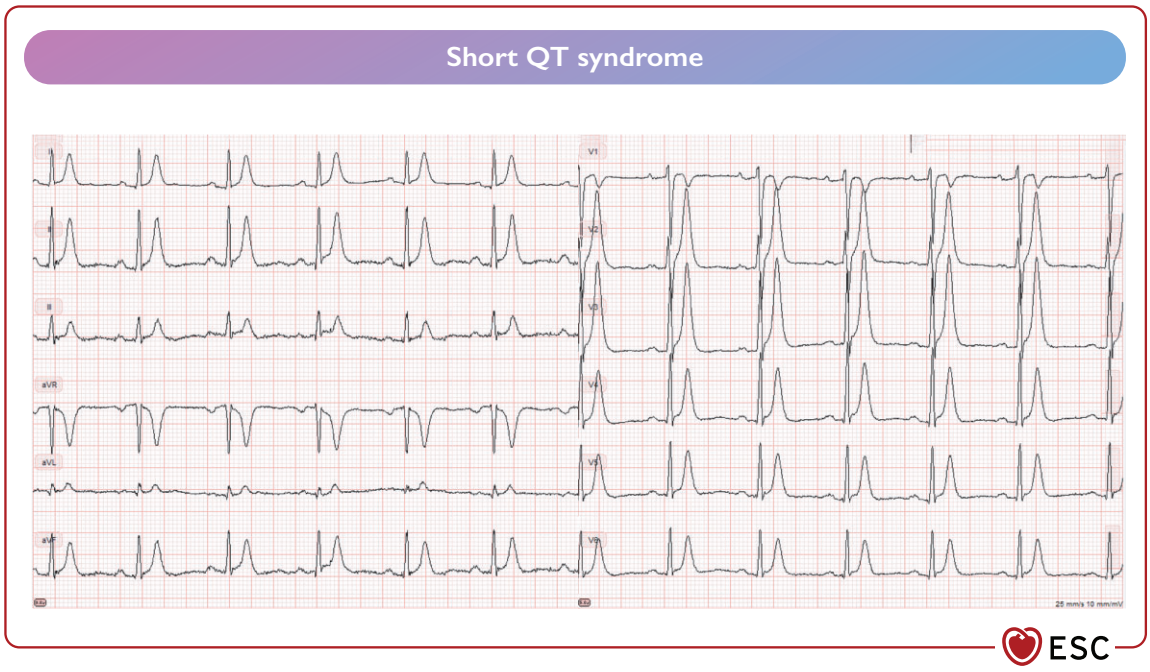

Figure 37 Short QT syndrome.

function in *SLC4A*.[1062,1063] This panel proposed two QTc cut-off threshold for diagnosis: A QTc ≤320 ms alone, or B a QTc ≤360 ms combined with a family history of SQTS, aborted CA in the absence of heart disease or pathogenic mutation[1064–1067] (*Figure 37*). The disease has high lethality in all age groups, including the first months of life.[1063,1068,1069] The probability of a first CA by the age of 40 years is >40%.[1068] While an ICD is used for secondary prevention,[1069] primary prevention remains contentious and is based upon prior symptoms and QTc interval.[1063,1068,1069] Quinidine is currently the best supported AAD, but should be monitored for excessive QT prolongation, while isoprenaline may be considered in electrical storm.[1070,1071] Drugs that shorten QT interval should be avoided, e.g. nicorandil.[1072] Loop recorder implantation should be considered in children and young asymptomatic SQTS patients.

Recommendation Table 46 — Recommendations for the management of patients with short QT syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that SQTS is diagnosed in the presence of a QTc ≤360 ms and one or more of the following: (a) a pathogenic mutation, (b) a family history of SQTS, (c) survival from a VT/VF episode in the absence of heart disease.[1061,1068]	I	C
Genetic testing is indicated in patients diagnosed with SQTS.[1063]	I	C
SQTS should be considered in the presence of a QTc ≤320 ms.[1064–1067,1073,1074]	IIa	C
SQTS should be considered in the presence of a QTc ≥320 ms and ≤360 ms and arrhythmic syncope.	IIa	C
SQTS may be considered in the presence of a QTc ≥320 ms and ≤360 ms and a family history of SD at age <40 years.	IIb	C
Risk stratification, SCD prevention and treatment of VA		
ICD implantation is recommended in patients with a diagnosis of SQTS who: (a) are survivors of an aborted CA and/or (b) have documented spontaneous sustained VT.[1063]	I	C
ILR should be considered in young SQTS patients.	IIa	C
ICD implantation should be considered in SQTS patients with arrhythmic syncope.	IIa	C
Quinidine may be considered in (a) SQTS patients who qualify for an ICD but present a contraindication to the ICD or refuse it, and (b) asymptomatic SQTS patients and a family history of SCD.[1069–1071]	IIb	C
Isoproterenol may be considered in SQTS patients with an electrical storm.[1075]	IIb	C
PES is not recommended for SCD risk stratification in SQTS patients.	III	C

CA, cardiac arrest; ICD, implantable cardioverter defibrillator; ILR, implantable loop recorder, SCD, sudden cardiac death; SD, sudden death; SQTS, short QT syndrome; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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8. Special aspects in selected populations

8.1. Pregnant patients and peri-partum cardiomyopathy

Pregnancy and the post-partum period contribute a significant risk in women with arrhythmic heart disease and is covered in the 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.[1076–1080] New-onset VT may present during pregnancy and risk of recurrent VT is higher in patients with previous VT and SHD.[1081] Peri-partum cardiomyopathy (PPCM) should be ruled out in the case of new-onset VT during the last 6 weeks of pregnancy or in the early post-partum period.[1082] A genetic contribution may be present in up to 20% of patients with PPCM (in particular titin-truncating variants)[1083] and future studies should reveal if genetic testing plays a role in PPCM patients with a positive family history.

8.1.1. Electrocardioversion and implantable cardioverter defibrillator therapy in pregnancy

Cardioversion seems safe in all phases of pregnancy and case reports show neither compromise in fetal blood flow nor initiation of preterm labour.[1084] Foetal heart rate should be routinely controlled after cardioversion.[1085] If an ICD is indicated, ICD implantation should be performed beyond 8 weeks of gestation with radiation protection by experienced operator teams.[1086] Echocardiographic guidance or a 3D mapping system may be helpful in ICD implantation to avoid radiation.[1087,1088] In pregnant patients with existing ICD, routine ICD interrogation is recommended prior to delivery. In patients with PPCM, thresholds for early ICD implantations are higher than in other conditions because of a high rate of spontaneous recovery after delivery.[1089] WCD have been suggested to temporarily prevent SCD during the first 3–6 months after diagnosis of PPCM with LVEF ≤35%, while awaiting recovery.[1090,1091]

8.1.2. Pharmacological treatment

Pharmacological treatment of arrhythmias and heart failure in pregnant women should follow treatment in non-pregnant patients with avoidance of drugs contraindicated in pregnancy, such as ACE inhibitors, ARB inhibitors/ARNI and renin inhibitors.[1080,1082,1092,1093] The first trimester is associated with the greatest teratogenic risk. Start of pharmacological therapy is advised to begin at the latest possible point in the pregnancy and with the lowest effective dose. Drug exposure in the second and third trimestera may confer adverse effects on foetal growth and development as well as increasing the risk of pro-arrhythmia.

It is recommended to check drugs and safety data before initiation of a new drug during pregnancy, according to the 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.[1080] From this list, AADs can be summarized as followed:

- **Well tolerated**: sotalol, oral verapamil
- **Use only if potential benefit outweighs potential risk**: bisoprolol, carvedilol, digoxin, diltiazem (possible teratogenic effects), disopyramide (uterine contractions), flecainide, lidocaine, metoprolol, nadolol, propranolol, verapamil IV, quinidine
- **Inadequate data:** Ivabradine, mexiletine, proprafenone, vernakalant
- **Contraindicated:** amiodarone, atenolol, dronedarone.

In LQTS (LQT2 in particular), risk of cardiac events increases substantially in the post-partum period (up to one year after delivery).[1094] Therefore, it is important to continue beta-blocker therapy throughout pregnancy and post-partum.[955,1094,1095] Continuation of beta-blocker treatment is recommended in LQTS and CPVT[1096] and should be considered in ARVC.[1097–1099] No additional risk by pregnancy is known in women with BrS[1100,1101] (ESC CardioMed chapter 53.6).[1102]

In patients with PPCM, use of bromocriptine as disease-specific therapy in addition to standard heart failure therapy has shown promising results in two clinical trials.[1103,1104]

8.1.3. Catheter ablation

In planned pregnancies, symptomatic tachyarrhythmia should be treated by catheter ablation before pregnancy. If catheter ablation is indicated in a pregnant patient, one should avoid the procedure in the first trimester, and electroanatomical mapping-guided procedures should be preferred.[1105,1106]

Recommendation Table 47 — Recommendations for the prevention of sudden cardiac death and management of ventricular arrhythmia during pregnancy

Recommendations	Class[a]	Level[b]
Acute management of VA		
During pregnancy, electrical cardioversion is recommended for sustained VT.[1084]	I	C
For acute conversion of haemodynamically tolerated SMVT during pregnancy, a beta-blocker, sotalol, flecainide, procainamide, or overdrive ventricular pacing should be considered.	IIa	C
Long-term management of VA		
If ICD implantation is indicated during pregnancy, implantation is recommended with optimal radiation protection.[1087,1107]	I	C
Continuation of beta-blockers is recommended during pregnancy and post-partum in women with LQTS or CPVT.[955,1094–1096]	I	C
Continuation of beta-blockers should be considered during pregnancy in women with ARVC.[1097–1099]	IIa	C
Oral metoprolol, propranolol, or verapamil should be considered for long-term management of idiopathic sustained VT during pregnancy.	IIa	C
Catheter ablation using non-fluoroscopic mapping systems should be considered, preferably after the first trimester, in women with highly symptomatic recurrent SMVT refractory or who are intolerant to AADs.[1105]	IIa	C

AAD, anti-arrhythmic drug; ARVC, arrhythmogenic right ventricular cardiomyopathy; CPVT, catecholaminergic polymorphic ventricular tachycardia; ICD, implantable cardioverter defibrillator; LQTS, long QT syndrome; SMVT, sustained monomorphic VT; VA, ventricular arrhythmia; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.

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8.2. Heart transplantation

Patients listed for HTX are exposed to an SCD risk and have a high incidence of VA. Data from large registries suggest a survival benefit from ICDs.[1108–1111] The only randomized study including patients listed for HTX was prematurely stopped because of low enrolment.[1112] There are no data regarding the role of WCD in patients listed for HTX. The median expected time on the waiting list, 8–16 months, needs to be considered.[1108,1110] However, this panel shares the opinion that a WCD may be an alternative for an ICD in selected patients waiting for HTX.[371,1113]

In post-HTX patients, SCD is responsible for around 10% of deaths.[1114,1115] Transplant rejection and allograft vasculopathy are associated with SCD[1114,1116,1117]; therefore, ICD implantation may be appropriate in selected high-risk patients.[1118]

Recommendation Table 48 — Recommendations for the prevention of sudden cardiac death before and after heart transplantation

Recommendations	Class[a]	Level[b]
Prior to heart transplant		
In patients awaiting heart transplantation, ICD implantation for primary prevention should be considered.[1108,1111,1112]	IIa	C
In patients awaiting heart transplantation, WCD may be considered.[1109,1113,1119]	IIb	C
Post heart transplant		
In selected transplanted patients with cardiac allograft vasculopathy or treated rejection, ICD implantation may be considered.[1114,1116]	IIb	C

ICD, implantable cardioverter defibrillator; WCD, wearable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

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8.3. Sudden cardiac death in athletes

The incidence of SCD in athletes increases with age.[4,1120] In apparently healthy athletes (>35 years), the estimated incidence of SCD ranges from 2 to 6.3 per 100 000 participant-years. In comparison, in young competitive athletes (≤35 years) the incidence of fatal events is significantly lower, 0.4–3 per 100 000 participant-years.[46,47,1120] Women athletes are at low risk of SCD; on average, 1 in 14 SCD in athletes occurs in women.[1121]

Pre-participation cardiovascular evaluation offers the potential to identify athletes at-risk for cardiovascular disease before onset of symptoms.[1122–1126] The evaluation protocol needs to be adapted to the age of the athlete to account for age-specific cardiovascular disease.[1125] Pre-participation evaluation, including medical history, physical examination, and ECG, appears effective in identifying cardiovascular disease in young athletes (≤35 years of age) by identification of relevant symptoms (e.g. exertional syncope) or ECG abnormalities consistent with inheritable cardiomyopathies or channelopathies.[1127–1130] Although echocardiography can increase the sensitivity of screening for SHD, it is unfeasible as a routine test in mass screening. More cardiovascular diseases are identified by serial (annual) evaluations of adolescent athletes.[1129,1131] The prevalence of false-positive results strongly depends on the criteria used to define an ECG as 'abnormal'.[1132,1133] Additional tests, such as echocardiography, 24-hour Holter monitoring, stress testing, and CMR, are requested for athletes who had positive findings at the initial evaluation. Athletes diagnosed with clinically relevant cardiovascular disease are managed according to available ESC Guidelines.[4,1134–1136]

In middle-aged/senior athletes, the most common cause of SCD is CAD.[1125,1137] Before engaging in a vigorous physical activity, asymptomatic middle-aged/senior athletes should be evaluated using risk score systems such as the ESC SCORE2.[4,65]

Excellent rates of survival with favourable neurological outcome after CA has been reported in sports centres equipped with AED.[1137,1138] This justifies the efforts for implementing emergency programs for SCD prevention, with distribution of AED in sports arenas and training of coaches and staff to perform CPR and defibrillation.[1139]

Recommendation Table 49 — Recommendations for risk stratification and prevention of sudden cardiac death in athletes

Recommendations	Class[a]	Level[b]
In athletes with positive medical history, abnormal physical examination, or ECG alterations, further investigations including echocardiography and/or CMR to confirm (or exclude) an underlying disease are recommended.[1123,1133,1135]	I	C
It is recommended that athletes diagnosed with a cardiovascular disease associated with SCD are managed according to current guidelines for sports eligibility.	I	C
It is recommended that staff at sporting facilities are trained in CPR and in the use of AED.[93,1137]	I	C
Pre-participation cardiovascular evaluation of competitive athletes should be considered.[46,1122,1123,1127]	IIa	C
It should be considered that cardiovascular evaluation of young (<35 years) competitive athletes includes history, physical examination, and 12-lead ECG.[1123,1126,1130,1140]	IIa	C
The cardiovascular risk of middle-aged and elderly individuals should be evaluated before engaging in strenuous sports through established scores such as the SCORE2 risk chart.[46,1141,1142]	IIa	C

AED, automated external defibrillator; CMR, cardiac magnetic resonance; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; SCD, sudden cardiac death.
[a]Class of recommendation.
[b]Level of evidence.

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8.4. Wolff–Parkinson–White syndrome

In patients with Wolff–Parkinson–White (WPW) syndrome, the most common arrhythmia is AV re-entry tachycardia (AVRT; 80%), followed by AF (20–30%). SCD secondary to pre-excited AF resulting in VF is the most feared manifestation of WPW syndrome. The risk of CA/VF in untreated WPW patients has been estimated at 0.9–2.4 per 1000 person-year.[1143,1144] The management of WPW patients has recently been reviewed in the 2019 ESC Guidelines for the management of patients with SVT[302] and updated with a particular focus on athletes in 2020.[1145] In patients with ventricular pre-excitation and symptomatic AVRT, catheter ablation is recommended (class I). In asymptomatic patients with ventricular pre-excitation, both invasive (class IIa) and non-invasive (class IIb) assessment are options for risk stratification for SCD. While catheter ablation is recommended for asymptomatic accessory pathways with high-risk features (class I), clinical follow-up (class IIa), or catheter ablations (class IIb) are options based on informed patient choice. This decision should take into account the location of the accessory pathway, the local ablation experience and the fact that symptomatic arrhythmias will frequently develop during follow-up.[1146] For the paediatric population, SVT due to WPW can usually be managed pharmacologically, and accessory pathways often lose antegrade conduction in the first years of life.[1147] In children with asymptomatic accessory pathways, risk stratification is not recommend before the age of 8 years.[1148]

8.5. Prevention of sudden cardiac death in the elderly

Age is a strong risk factor for death. In several studies, advanced age was one of the factors associated with a reduced expected benefit from ICD treatment. In patients with ischaemic cardiomyopathy enrolled in MADIT-II trial, a risk scheme composed of 5 clinical factors including age >70 years was predictive of the absence of long-term benefit conferred by the ICD.[1149] In a recent analysis of ICD patients enrolled in four MADIT studies, age <75 years was a predictor of VT/VF whereas age ≥75 years was a predictor of non-arrhythmic mortality.[365] Consistently, in the recent randomized DANISH trial in patients with non-ischaemic heart failure, the association between the ICD and survival decreased linearly with increasing age, while an age cut-off at ≤70 years yielded the highest survival.[647] Contemporary non-randomized data corroborate these findings. In the EU-CERT-ICD prospective cohort study in patients with CAD or cardiomyopathies with indication for primary prevention ICD implantation, no ICD benefit was observed in patients aged ≥75 years.[357] In contrast, there was a significant survival benefit in patients aged <75 years. Further retrospective data are in line with this observation.[1150]

Biological age may vary in part according to comorbidities. Indeed, comorbidities significantly influence survival of ICD recipients and a high comorbidity index is associated with less survival gain in primary or secondary prevention ICD patients.[1149,1151] Therefore, a simple age cut-off cannot guide the decision on ICD implantation adequately and the ICD indication in elderly patients should be based on a personalized assessment considering the overall condition and comorbidities.

Recommendation Table 50 — Recommendations for implantable cardioverter defibrillator implantation in the elderly

Recommendations	Class[a]	Level[b]
In elderly patients in whom a benefit from the defibrillator is not expected due to the patient's age and comorbidities, omission of ICD implantation for primary prevention may be considered.[647,1150,1152]	IIb	B

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ICD, implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.

9. Key messages

9.1. General aspects

- Increased availability of public access defibrillators and community training in basic life support are key elements to improve survival of out-of-hospital cardiac arrest victims.
- Risk calculators for SCD and VA implemented in clinical practice need to meet agreed high standards for the development, external validation, and reporting of prediction models.
- Patients with genetic cardiomyopathies and arrhythmia syndromes require genetic testing as a routine part of their care.
- Genetic testing and counselling require access to an expert multidisciplinary team.
- A systematic workup of cardiac arrest survivors requires a multimodal approach.
- A comprehensive autopsy is recommended in all cases of sudden death under 50 years and is desirable in all sudden death victims.
- Clinical and genetic evaluation of SADS decedents and their families leads to a diagnosis of genetic heart disease in a substantial proportion of families.
- An electrical storm refractory to drug treatment requires the availability of advanced catheter ablation techniques, mechanical circulatory support, and autonomic modulation.
- When considering ICD therapy benefit, competing risk factors for non-arrhythmic death and the patient's wishes and quality of life need to be taken into account.

9.2. Structural heart disease

- Catheter ablation is recommended in CAD patients with recurrent symptomatic SMVT despite chronic amiodarone therapy.
- Catheter ablation is the first-line treatment for PVC-induced cardiomyopathy.
- In HNDCM/DCM patients, indication for primary prevention ICD implantation should not be restricted to an LVEF ≤35%. Additional risk factors (e.g. CMR and genetics) are important to consider.
- Patients with an *LMNA* mutation require specific risk stratification for SCD.
- ARVC patients have a high rate of appropriate ICD interventions which may not necessarily be classified as lifesaving.

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- A validated risk calculator (HCM Risk-Kids score) is useful to assess the risk for SCD in HCM patients younger than 16 years.
- Myotonic dystrophy patients with palpitations suspected of arrhythmia, syncope or aborted sudden death need to be evaluated by invasive electrophysiological study.
- In patients with repaired tetralogy of Fallot and monomorphic VT, catheter ablation is the preferred treatment.

9.3. Primary electrical disease

- Nadolol or propranolol are the preferred beta-blockers in LQTS and CPVT patients.
- In asymptomatic LQTS patients the arrhythmic risk (1-2-3 Risk calculator) may be useful to calculate.
- A type 1 Brugada ECG pattern provoked by sodium channel blocker test in the absence of other findings does not diagnose the BrS.
- SCD risk stratification in asymptomatic BrS patients with a spontaneous type 1 pattern remains controversial.
- Routine catheter ablation is not recommended in asymptomatic BrS patients.
- The diagnosis of idiopathic VF requires exclusion of an underlying structural, channelopathic, or metabolic aetiology.
- ERP can be a benign finding and is distinct from ERS.
- Left cardiac denervation plays an important role in the management of CPVT and LQTS patients.

10. Gaps in evidence

10.1. General aspects

- Accurate screening tests to detect heart conditions associated with SCD in asymptomatic individuals in the general population are required.
- In patients with SHD, the optimal time interval between repeated non-invasive and invasive prognostic tests, in case of a negative test, is unknown.
- Improved assessment of genetic variants of uncertain significance and likely pathogenic variants is needed.
- The utility of polygenic risk scores in patients at risk of SCD requires investigation.

10.2. Structural heart disease—general

- The long-term safety and efficacy of S-ICDs is unknown.
- The role of primary preventive ICD therapy in patients with SHD and mildly reduced or preserved ejection fraction has not been studied systematically.
- The optimal techniques to undertake VT substrate mapping and ablation in SHD remain to be determined.
- The role of ICD implantation in end-stage heart failure patients supported by current-generation, continuous-flow LVADs is unclear.

10.3. Idiopathic premature ventricular complexes/ventricular tachycardia

- The beneficial role of catheter ablation or anti-arrhythmic drug treatment in patients with asymptomatic, frequent PVCs and preserved cardiac function needs to be determined.

10.4. Coronary artery disease

- It is unknown which patients with chronic CAD and severely impaired LVEF are at low risk for SCD.
- The role of LGE-CMR for risk stratification for SCD in chronic CAD is unclear.
- RCTs are needed to determine the role of ICDs after successful VT ablation in chronic CAD with mildly reduced or preserved LVEF.

10.5. Cardiomyopathies

- It is unknown if PVC-induced cardiomyopathy is a diagnosis on its own or if an underlying predisposition is needed.
- The predictive value of LGE-CMR findings (e.g. pattern and amount of LGE) for *individual* risk stratification for SCD in patients with cardiac sarcoidosis, HCM, and DCM/HNDC is unclear.
- Studies are needed to determine the role of PES in patients with cardiac sarcoidosis and DCM/HNDC who have a mildly reduced or preserved cardiac function and LGE on CMR.
- Prospective data on the association between intensity and duration of exercise and manifestation and severity of the phenotype in healthy ARVC mutation carriers are lacking.
- The beneficial role of ICDs after successful ablation in ARVC patients who present with haemodynamically tolerated VT needs to be studied.
- Data on clinical outcome, predictors for arrhythmic events, and indication for treatment, including ICD therapy, in patients with biventricular and left-dominant arrhythmogenic cardiomyopathy are required.

10.6. Valvular heart disease

- There is a lack of knowledge to identify patients with MVP at risk for VA and SCD.

10.7. Congenital heart disease

- There is a lack of knowledge regarding the absolute risk for VA and SCD in CHD that have undergone repair with contemporary surgical approaches.

10.8. Primary electrical disease

- Robust evidence is required to support the prophylactic use of the ICD on top of medical therapy with beta-blockers and gene-specific therapy in LQTS patients.
- More data are required to determine the role of LCSD and ICD in high-risk LQTS patients who do not tolerate medical therapy.

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- Improved diagnostic and risk stratification tools for asymptomatic Brugada patients and suspected early repolarization syndrome are needed.
- The role of endo-epicardial mapping to identify localized structural alterations potentially related to IVF and targeted catheter ablation needs to be further studied.
- Long-term data are required on the efficacy of the ICD vs. no ICD in CPVT survivors of cardiac arrest.
- It is poorly understood why women are at low risk of sport-related SCD.

11. 'What to do' and 'what not to do' messages from the Guidelines

Recommendations	Class[a]	Level[b]
Recommendations for public basic life support and access to automated external defibrillator		
It is recommended that public access defibrillation be available at sites where cardiac arrest is more likely to occur.[c]	I	B
Prompt CPR by bystanders is recommended at OHCA.	I	B
It is recommended to promote community training in basic life support to increase bystander CPR rate and AED use.	I	B
Recommendations for genetic testing		
Genetic testing is recommended when a condition is diagnosed in a living or deceased individual with a likely genetic basis and a risk of VA and SCD.	I	B
When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.	I	C
When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I	C
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.	I	C
It is recommended that Class III variants (of uncertain significance) and Class IV variants should be evaluated for segregation in families where possible, and the variant re-evaluated periodically.	I	C
It is not recommended to undertake genetic testing in index patients with insufficient evidence of a genetic disease.	III	C
Recommendations for evaluation of patients presenting with newly documented ventricular arrhythmia		
In patients with newly documented VA (frequent PVCs, NSVT, SMVT), a baseline 12-lead ECG, recording of the VA on 12-lead ECG, whenever possible, and an echocardiogram are recommended as first-line evaluation.	I	C
Recommendations for evaluation of sudden cardiac arrest survivors		
The investigation of a SCA survivor without obvious extra-cardiac cause is recommended to be overseen by a multidisciplinary team.	I	B
In electrically unstable patients after SCA, with suspicion of ongoing myocardial ischaemia, a coronary angiogram is indicated.	I	C
In SCA survivors, collection of blood samples at presentation is recommended for potential toxicology and genetic testing.	I	B
Retrieval of recordings from CIEDs and wearable monitors is recommended for all SCA survivors.	I	B
In SCA survivors, repeated 12-lead ECGs during stable rhythm (including high precordial lead ECG) as well as continuous cardiac monitoring are recommended.	I	B
Echocardiography is recommended for evaluation of cardiac structure and function in all SCA survivors.	I	C
Coronary imaging and CMR with LGE are recommended for evaluation of cardiac structure and function in all SCA survivors without a clear underlying cause.	I	B
Sodium channel blocker test and exercise testing is recommended in SCA survivors without a clear underlying cause.	I	B

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Recommendations for evaluation of sudden death victims		
Investigation of unexpected SD, especially in case of suspicion of inherited disease, should be made a public health priority.	I	B
In cases of SD, it is recommended to collect a detailed description of circumstances of death, symptoms prior to death, the family history, and to review prior medical files.	I	B
A comprehensive autopsy is recommended, ideally, in all cases of unexpected SD, and always in those under 50 years of age.	I	B
In cases of SCD, it is recommended to retain samples suitable for DNA extraction and consult a cardiac pathologist when an inherited cause is suspected or the cause of death unexplained.	I	B
Toxicology screens are recommended in SD cases with uncertain cause of death.	I	B
For SCD where the cause is known or suspected to be heritable, genetic testing targeted to the cause is recommended.	I	B
Following SADS, post-mortem genetic testing targeted to primary electrical disease is recommended when the decedent is young (<50 years of age) and/or the circumstances and/or family history support a primary electrical disease.	I	B
When an autopsy diagnoses possible heritable cardiac disease, it is recommended to refer first-degree relatives for cardiac assessment in a specialized clinic.	I	B
In non-autopsied cases of SD where inherited cardiac disease is suspected, it is recommended to refer first-degree relatives for cardiac assessment in a specialized clinic.	I	B
Recommendations for evaluation of relatives of sudden arrhythmic death syndrome decedents		
Following SADS, hypothesis-free post-mortem genetic testing using exome or genome sequencing is not recommended.	III	B
Familial evaluation of SADS decedents is recommended: • for first-degree relatives • for relatives who must carry a mutation based on analysis of the family history • for relatives with suspicious symptoms • when the decedent's age is <50 years or if there are other circumstantial data or family history to suggest heritable disease.	I	B
Familial evaluation of SADS decedents is recommended to include genetic testing when post-mortem genetic testing in a SADS decedent detects a pathogenic mutation.	I	B
Baseline familial evaluation of SADS decedents is recommended to include taking a medical history and performing physical examination, standard- and high-precordial lead ECG, echocardiography, and exercise testing.	I	B
In SADS families without a diagnosis after clinical evaluation, follow-up is recommended for children of decedents until they reach adulthood.	I	C
In SADS families without a diagnosis after clinical evaluation, follow-up is not recommended for asymptomatic adults who can be discharged with advice to return if they develop symptoms or if the family history changes.	III	C
Recommendations for treatment of reversible conditions		
Withdrawal of offending agents is recommended whenever drug-induced VA are suspected.	I	B
Investigation for reversible causes (e.g. electrolyte imbalances, ischaemia, hypoxaemia, fever)[d] is recommended in patients with VA.	I	C
Recommendations for the acute treatment of sustained ventricular tachycardia and electrical storm		
DC cardioversion is recommended as the first-line treatment for patients with haemodynamically not-tolerated SMVT.	I	B
DC cardioversion is recommended as the first-line treatment for patients presenting with tolerated SMVT provided that the anaesthetic/sedation risk is low.	I	C
In patients presenting with a haemodynamically tolerated idiopathic VT, treatment with intravenous beta-blocker (RVOT VT) or verapamil (fascicular VT) is recommended.	I	C
Intravenous verapamil is not recommended in broad QRS complex tachycardia of unknown mechanism.	III	B
Mild to moderate sedation is recommended in patients with electrical storm to alleviate psychological distress and reduce sympathetic tone.	I	C
Antiarrhythmic therapy with beta-blockers (non-selective preferred) in combination with intravenous amiodarone is recommended in patients with SHD and electrical storm unless contraindicated.	I	B

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Intravenous magnesium with supplementation of potassium is recommended in patients with TdP.	I	C
Isoproterenol or transvenous pacing to increase heart rate is recommended in patients with acquired LQT syndrome and recurrent TdP despite correction of precipitating conditions and magnesium.	I	C
Catheter ablation is recommended in patients presenting with incessant VT or electrical storm due to SMVT refractory to AADs.	I	B
Recommendations for treatment with heart failure medication		
Optimal medical treatment including ACE-I/ARB/ARNIs, MRAs, beta-blockers, and SGLT2 inhibitors is indicated in all heart failure patients with reduced EF.	I	A
Recommendations for implantable cardioverter defibrillation implantation (general aspects)		
Implantation of a cardioverter defibrillator is only recommended in patients who have an expectation of good quality survival >1 year.	I	C
It is not recommended to implant an ICD in patients with incessant VAs until the VA is controlled.	III	C
Recommendations for secondary prevention of sudden cardiac death		
ICD implantation is recommended in patients with documented VF or haemodynamically not-tolerated VT in the absence of reversible causes.	I	A
Recommendations for adding cardiac resynchronization therapy to implantable cardioverter defibrillator		
When an ICD is indicated, it is recommended to evaluate whether the patient could benefit from CRT-defibrillator.	I	C
Recommendations for optimization of device programming		
Optimization of ICD programming is indicated to avoid inappropriate and unnecessary therapies and to reduce mortality.	I	A
In single- or dual-chamber ICD patients without bradycardia pacing indications, it is recommended to minimize ventricular pacing.	I	A
Programming of prolonged detection settings is indicated (duration criteria of at least 6–12 s or 30 intervals).	I	A
It is recommended to program the slowest tachycardia therapy zone limit ≥188 b.p.m. in primary prevention ICD patients.	I	A
In patients with SHD, programming of at least one ATP therapy is recommended in all tachyarrhythmias zones.	I	A
It is recommended to program algorithms for SVT vs. VT discrimination for tachycardias with rates up to 230 b.p.m.	I	B
It is recommended to activate lead failure alerts.	I	B
Remote monitoring is recommended to reduce the incidence of inappropriate shocks.	I	B
Programming of burst ATP as a first attempt is recommended over ramp ATP.	I	B
For S-ICDs, a dual detection zone configuration is recommended with activation of discrimination algorithm in the lower conditional shock zone	I	B
Recommendations for concomitant treatment to avoid inappropriate implantable cardioverter defibrillator therapy		
Catheter ablation is recommended for ICD patients with recurrent SVT resulting in inappropriate ICD therapies.	I	C
Pharmacological treatment or catheter ablation is recommended in patients with AF-related inappropriate ICD therapies despite optimal ICD programming.	I	C
Recommendation for psychosocial management after implantable cardioverter defibrillator implantation		
Assessment of psychological status and treatment of distress is recommended in ICD patients.	I	C
Communication between patient and physician/healthcare professional is recommended to address ICD-related concerns and to discuss quality-of-life issues before ICD implantation and during disease progression.	I	C

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Recommendations for prevention of implantable cardioverter defibrillator complications		
Single-chamber ICD is recommended over dual-chamber ICD in primary prevention patients without current or expected indication for atrial or AV sequential pacing due to a lower risk of device-related complications.	I	A
Recommendations for end-of-life issues in implantable cardioverter defibrillator carriers		
Informed discussion with patient and family about ICD deactivation options and shared decision-making is indicated prior to implantation and in case of significant health status deterioration.	I	C
Recommendations for treatment of ventricular arrhythmia in acute coronary syndrome and vasospasm		
Intravenous beta-blocker treatment is indicated for patients with recurrent PVT/VF during STEMI unless contraindicated.	I	B
Prophylactic treatment with AADs (other than beta-blockers) is not recommended in ACS.	III	B
Recommendations for risk stratification and treatment of ventricular arrhythmia early after myocardial infarction		
Early (before discharge) assessment of LVEF is recommended in all patients with acute MI.	I	B
In patients with pre-discharge LVEF ≤40%, re-evaluation of LVEF 6–12 weeks after MI is recommended to assess the potential need for primary prevention ICD implantation.	I	C
Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in chronic coronary artery disease		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.	I	C
ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.	I	A
In patients with CAD, prophylactic treatment with AADs other than beta-blockers is not recommended.	III	A
ICD implantation is recommended in patients without ongoing ischaemia with documented VF or haemodynamically not-tolerated VT occurring later than 48 h after MI.	I	A
In patients with CAD and recurrent, symptomatic SMVT or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy.	I	B
Recommendations for sudden cardiac death prevention in patients with coronary anomalies		
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test in patients with anomalous aortic origin of a coronary artery with an interarterial course to confirm/exclude myocardial ischaemia.	I	C
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test after surgery in patients with anomalous aortic origin of a coronary artery with a history of aborted CA.	I	C
Surgery is recommended in patients with anomalous aortic origin of a coronary artery with CA, syncope suspected to be due to VAs or angina when other causes have been excluded.	I	C
Recommendations for the management of patients with idiopathic premature ventricular complexes/ventricular tachycardia		
Regular assessment of ventricular function of patients with PVC burden >10% and normal ventricular function is indicated.	I	C
Catheter ablation as first-line treatment is recommended for symptomatic idiopathic VT/PVCs from the RVOT or the left fascicles.[e]	I	B
Beta-blockers or non-dihydropyridine CCB are indicated in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.	I	C
Catheter ablation is not recommended in children <5 years of age or <10 kg weight except when previous medical therapy fails or when VT is not haemodynamically tolerated.	III	C
Amiodarone as a first-line treatment is not recommended in patients with idiopathic VTs/PVCs.	III	C
Verapamil is not recommended in children <1 year of age with PVC/VT, particularly if they have signs of heart failure or concurrent use of other AADs.	III	C
Recommendations for the management of patients with premature ventricular complex-induced or aggravated cardiomyopathy		
In patients with a cardiomyopathy suspected to be caused by frequent and predominately monomorphic PVCs, catheter ablation is recommended.	I	C

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Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in dilated cardiomyopathy/hypokinetic non-dilated cardiomyopathy		
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) is recommended in patients with DCM/HNDCM and AV conduction delay at <50 years, or who have a family history of DCM/HNDCM or SCD in a first-degree relative (at age <50 years).	I	B
Participation in high-intensity exercise including competitive sports is not recommended for individuals with DCM/HNDCM and a *LMNA* mutation.	III	C
ICD implantation is recommended in patients with DCM/HNDCM, who survive SCA due to VT/VF or experience haemodynamically not-tolerated SMVT.	I	B
In a first-degree relative of a DCM/HNDCM patient, an ECG, and an echocardiogram are recommended if: • the index patient was diagnosed <50 years of age or has clinical features suggestive of an inherited cause, or • there is family history of DCM/HNDCM, or premature unexpected SD.	I	C
Recommendations for diagnostic, risk stratification, sudden cardiac death prevention and treatment of ventricular arrhythmia in arrhythmogenic right ventricular cardiomyopathy		
In patients with suspected ARVC, CMR is recommended.	I	B
In patients with a suspected or definite diagnosis of ARVC, genetic counselling and testing are recommended.	I	B
Avoidance of high-intensity exercise is recommended in patients with a definite diagnosis of ARVC.	I	B
ICD implantation is recommended in ARVC patients with haemodynamically not-tolerated VT or VF.	I	C
In patients with ARVC and non-sustained or sustained VAs, beta-blocker therapy is recommended.	I	C
In a first-degree relative of a patient with ARVC, ECG, and echocardiogram are recommended.	I	C
Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in hypertrophic cardiomyopathy		
CMR with LGE is recommended in HCM patients for diagnostic work-up.	I	B
Genetic counselling and testing are recommended in HCM patients.	I	B
It is recommended that the 5-year risk of SCD is assessed at first evaluation and at 1–3-year intervals or when there is a change in clinical status.	I	C
ICD implantation is recommended in HCM patients with haemodynamically not-tolerated VT or VF.	I	B
In a first-degree relative of a patient with HCM, ECG, and echocardiogram are recommended.	I	C
Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in neuromuscular diseases		
Annual follow-up with at least a 12-lead ECG is recommended in patients with muscular dystrophies, even in the concealed phase of the disease.	I	C
It is recommended that patients with neuromuscular disorders who have VAs or ventricular dysfunction are treated in the same way for arrhythmia as patients without neuromuscular disorders.	I	C
Invasive electrophysiological evaluation is recommended in patients with myotonic dystrophy and palpitations or syncope suggestive of VA, VT, or surviving a CA.	I	C
ICD implantation is recommended in patients with myotonic dystrophy and SMVT or aborted CA not caused by BBR-VT.	I	C
In myotonic dystrophy patients, serial electrophysiological evaluation of AV conduction and arrhythmia induction is not recommended without arrhythmia suspicion or progression of ECG conduction disorders.	III	C
In symptomatic patients with BBR-VT, catheter ablation is recommended.	I	C
In patients with myotonic dystrophy undergoing ablation for BBR-VT, pacemaker/ICD implantation is recommended.	I	C

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Recommendations for sudden cardiac death prevention, and treatment of ventricular arrhythmia in myocarditis		
In confirmed or clinically suspected acute myocarditis, it is recommended that patients who present with life-threatening VA are referred to a specialized centre.	I	C
In patients with haemodynamically not-tolerated SMVT occurring in the chronic phase of myocarditis, an ICD implantation is recommended.	I	C
Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmia in cardiac sarcoidosis		
ICD implantation is recommended in patients with cardiac sarcoidosis who have an LVEF ≤35%.	I	B
ICD implantation is recommended in patients with cardiac sarcoidosis who (a) have documented sustained VT, or (2) aborted CA.	I	B
Recommendations for sudden cardiac death prevention, and treatment of ventricular arrhythmia in valvular heart disease		
PES with standby catheter ablation is recommended in patients with aortic valve disease and SMVT to identify and ablate BBR-VT, especially if it occurs following a valve intervention.	I	C
In patients with valvular heart disease and persistent LV dysfunction after surgical correction (if possible) it is recommended that ICD implantation for primary prevention follows DCM/HNDCM recommendations.	I	C
Recommendations for sudden cardiac death prevention, and treatment of ventricular arrhythmia in congenital heart disease		
In adults with CHD with biventricular physiology and a left systemic ventricle presenting with symptomatic heart failure (NYHA II/III) and EF ≤35% despite ≥3 months of OMT, ICD implantation is indicated.	I	C
In patients with CHD presenting with sustained VAs, evaluation for residual or new anatomical abnormalities is recommended.	I	B
In patients with CHD with not-tolerated VT/aborted CA due to VF, ICD implantation is indicated after exclusion of reversible causes.	I	C
In patients with repaired TOF who present with SMVT or recurrent, symptomatic appropriate ICD therapy for SMVT, catheter ablation performed in specialized centres is recommended.	I	C
Recommendations for management of patients with idiopathic ventricular fibrillation		
It is recommended that idiopathic VF is diagnosed in a SCA survivor, preferably with documentation of VF, after exclusion of an underlying structural, channelopathic, metabolic, or toxicological aetiology.	I	B
ICD implantation is recommended in idiopathic VF.	I	B
Recommendations for management of patients with long QT syndrome		
It is recommended that LQTS is diagnosed with either QTc ≥ 480 ms in repeated 12-lead ECGs with or without symptoms or LQTS diagnostic score >3.	I	C
In patients with clinically diagnosed long QT syndrome, genetic testing, and genetic counselling are recommended.	I	C
It is recommended that LQTS is diagnosed in the presence of a pathogenic mutation, irrespective of the QT duration.	I	C
Routine diagnostic testing with epinephrine challenge is not recommended in LQTS.	III	C
The following is recommended in LQTS: • Avoid QT-prolonging drugs.[f] • Avoid and correct electrolyte abnormalities. • Avoid genotype-specific triggers for arrhythmias.	I	C
Beta-blockers, ideally non-selective beta-blockers (nadolol or propranolol), are recommended in LQTS patients with documented QT interval prolongation, to reduce risk of arrhythmic events.	I	B
Mexiletine is indicated in LQT3 patients with a prolonged QT interval.	I	C
ICD implantation in addition to beta-blockers is recommended in LQTS patients with CA.	I	B
ICD implantation is recommended in patients with LQTS who are symptomatic[g] while receiving beta-blockers and genotype-specific therapies.	I	C

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LCSD is indicated in patients with symptomatic[g] LQTS when: (a) ICD therapy is contraindicated or declined; (b) patient is on beta-blockers and genotype-specific therapies with an ICD and experiences multiple shocks or syncope due to VA.	I	C
Invasive electrophysiologic study is not recommended in LQTS.	III	C
Recommendations for management of patients with Andersen–Tawil syndrome		
Genetic testing is recommended in patients with suspected Andersen–Tawil syndrome.	I	C
ICD implantation is recommended in patients with Andersen–Tawil syndrome after aborted CA not tolerated sustained VT.	I	C
Recommendations for management of patients with Brugada syndrome		
It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern.	I	C
It is recommended that BrS is diagnosed in patients with no other heart disease who have survived a CA due to VF or PVT and exhibit a *type 1 Brugada ECG induced* by sodium channel blocker challenge or during fever.	I	C
Genetic testing for *SCN5A* gene is recommended for probands with BrS.	I	C
Sodium channel blocker test is not recommended in patients with a prior type I Brugada pattern.	III	C
The following is recommended in all patients with BrS: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org). (b) Avoidance of cocaine, cannabis, and excessive alcohol intake. (c) Treatment of fever with antipyretic drugs.	I	C
ICD implantation is recommended in patients with BrS who: (a) Are survivors of an aborted CA, and/or (b) Have documented spontaneous sustained VT.	I	C
Catheter ablation in asymptomatic BrS patients is not recommended.	III	C
Recommendations for management of patients with early repolarizaton pattern/syndrome		
It is recommended that the ERP is diagnosed as J-point elevation of ≥1 mm in two adjacent inferior and/or lateral ECG leads.	I	C
It is recommended that the ERS is diagnosed in a patient resuscitated from unexplained VF/PVT in the presence of ERP.	I	C
Clinical evaluation is not recommended routinely in asymptomatic subjects with ERP.	III	C
ICD implantation is recommended in patients with a diagnosis of ERS who have survived a CA.	I	B
ICD implantation is not recommended in asymptomatic patients with an isolated ERP.	III	C
Recommendations for management of patients with catecholaminergic polymorphic ventricular tachycardia		
It is recommended that CPVT is diagnosed in the presence of a structurally normal heart, normal ECG, and exercise- or emotion-induced bidirectional or PVT.	I	C
It is recommended that CPVT is diagnosed in patients who are carriers of a mutation in disease-causing genes.	I	C
Genetic testing and genetic counselling are indicated in patients with clinical suspicion or clinical diagnosis of CPVT.	I	C
Avoidance of competitive sports, strenuous exercise, and exposure to stressful environments is recommended in all patients with CPVT.	I	C
Beta-blockers, ideally non-selective (nadolol or propranolol), are recommended in all patients with a clinical diagnosis of CPVT.	I	C
ICD implantation combined with beta-blockers and flecainide is recommended in CPVT patients after aborted CA.	I	C
PES is not recommended for stratification of SCD risk.	III	C

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Recommendations for management of patients with short QT syndrome		
It is recommended that SQTS is diagnosed in the presence of a QTc ≤360 ms and one or more of the following: (a) a pathogenic mutation, (b) a family history of SQTS, (c) survival from a VT/VF episode in the absence of heart disease.	I	C
Genetic testing is indicated in patients diagnosed with SQTS.	I	C
ICD implantation is recommended in patients with a diagnosis of SQTS who: (a) are survivors of an aborted CA, and/or (b) have documented spontaneous sustained VT.	I	C
PES is not recommended for SCD risk stratification in SQTS patients.	III	C
Recommendations for the prevention of sudden cardiac death and management of ventricular arrhythmia during pregnancy		
During pregnancy, electrical cardioversion is recommended for sustained VT.	I	C
If ICD implantation is indicated during pregnancy, implantation is recommended with optimal radiation protection.	I	C
Continuation of beta-blockers is recommended during pregnancy and post-partum in patients with LQTS or CPVT.	I	C
Recommendations for risk stratification and prevention of sudden cardiac death in athletes		
In athletes with positive medical history, abnormal physical examination, or ECG alterations, further investigations including echocardiography and/or CMR to confirm (or exclude) an underlying disease are recommended.	I	C
It is recommended that athletes diagnosed with a cardiovascular disease associated with SCD are managed according to current guidelines for sports eligibility.	I	C
It is recommended that staff at sporting facilities are trained in CPR and in the use of AED.	I	C

AAD, anti-arrhythmic drug; ACE-I, angiotensin-converting-enzyme inhibitor; AED, automated external defibrillator; ARB, angiotensin receptor blockers; ARNIs, angiotensin receptor neprilysin inhibitor; ARVC, arrhythmogenic right ventricular cardiomyopathy; ATP, anti-tachycardia pacing; AV, atrioventricular; BBR-VT, bundle branch re-entry; BrS, Brugada syndrome; CA, cardiac arrest; CAD, coronary artery disease; CCB, calcium channel blocker; CHD, congenital heart disease; CIED, cardiac implantable electronic devices; CMR, cardiac magnetic resonance; CPR, cardiopulmonary resuscitation; CPVT, catecholaminergic polymorphic ventricular tachycardia; CRT, cardiac resynchronization therapy; DC, direct current; DCM, dilated cardiomyopathy; ECG, electrocardiogram; EF, ejection fraction; ERP, early repolarization pattern; ERS, early repolarization syndrome; HCM, hypertrophic cardiomyopathy; HNDCM, hypokinetic non-dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; CAD, coronary artery disease; ILR, implantable loop recorder; LCSD, left cardiac sympathetic denervation; LGE, late gadolinium enhancement; LQTS, long QT syndrome; LV, left ventricular; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; OHCA, out-of-hospital cardiac arrest; OMT, optimal medical therapy; PES, programmed electrical stimulation; PVC, premature ventricular complex; PVT, polymorphic ventricular tachycardia; RVOT, right ventricular outflow tract; SADS, sudden arrhythmic death syndrome; SCA, sudden cardiac arrest; SCD, sudden cardiac death; SD, sudden death; SGLT2, sodium–glucose co-transporter 2; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; SQT, short QT syndrome; STEMI, ST-elevation myocardial infarction; SVT, supraventricular tachycardia; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.

[a]Class of recommendation.

[b]Level of evidence.

[c]Shopping malls, stadiums, public transport stations, casinos.

[d]List not exhaustive.

[e]LOE C for VT/PVCs from left fascicles.

[f]http://www.crediblemeds.org

[g]Arrhythmic syncope or haemodynamically non-tolerated VA

12. Quality indicators

Quality indicators (QIs) are tools that may be used to evaluate care quality, including structural aspects, process, and outcomes of care.[1153] They serve as a mechanism for enhancing adherence to guideline recommendations, through associated quality improvement initiatives and the benchmarking of care providers.[1154,1155] As such, the role of QIs in improving care and outcomes is increasingly recognized by healthcare authorities, professional organizations, payers, and the public.[1153]

The ESC understands the need for measuring and reporting quality and outcomes of cardiovascular care, and has established methods for the development of the ESC QIs for the quantification of care and outcomes for cardiovascular disease.[1153] In parallel with the writing of this Clinical Practice Guideline document, a process has been initiated to develop QIs for patients with, or at risk of, VA or SCD using the ESC methodology and through the collaboration with domain experts and the European Heart Rhythm Association. These QIs, alongside their specifications and development process, will be published separately.

13. Supplementary data

Supplementary data is available at *European Heart Journal online*.

14. Data availability statement

No new data were generated or analysed in support of this research.

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