Table 1. EHRA/HRS/APHRS/LAHRS 2022 Consensus Statement on genetic testing. Genes implicated in arrhythmogenic cardiomyopathy

Gene	Locus	Phenotype/syndrome	Protein (Cellular complex)	Frequency	ClinGen classification
PKP2	12p11.21	Classic ARVC. BiVACM and ALVC in a minority of cases.	Plakophilin 2 (desmosome)	20–45%	Definite
DSP	6p24.3	Frequent BiVACM and ALVC. Occasional hair and skin features. Rare homozygous variants—Carvajal Syndrome.	Desmoplakin (desmosome)	2–15%	Definite
DSG2	18q12.1	Frequent BiVACM and ALVC.	Desmoglein 2 (desmosome)	4–15%	Definite
DSC2	18q12.1	ARVC. Less frequent BiVACM and ALVC.	Desmocollin 2 (desmosome)	2–7%	Definite
FLNC	7q32.1	ALVC. Right ventricular involvement is rare	Filamin-C (cytoskeleton)	3%	Definite[a]
JUP	17q21.2	Naxos disease (cardioectodermal)	Plakoglobin (desmosome)	<1% (higher in Naxos, Greece)	Definite
TMEM43	3p25.1	ARVC and BiVACM	Transmembrane protein 43 (nuclear envelope)	<1% (higher in Newfoundland)	Definite
PLN	6q22.31	Frequent ALVC/DCM	Phospholamban (sarcoplasmic reticulum; calcium handling)	1% (10–15% in Netherlands)	Definite[a]
DES	2q35	Frequent ALVC. Right ventricular involvement is also possible. Conduction system abnormalities common. Skeletal myopathy possible.	Desmin (cytoskeleton)	1–2%	Moderate

ALVC, arrhythmogenic left ventricular cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy; BiVACM, bi-ventricular arrhythmogenic cardiomyopathy; DCM, dilated cardiomyopathy.
[a]Genes with a clear association with ALVC and included also in the ClinGen classification for DCM.

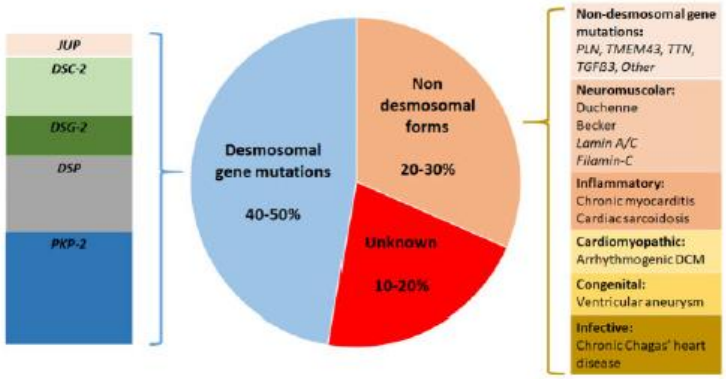


Figure 1. Aetiologic classification of arrhythmogenic cardiomyopathies. The most common cause of arrhythmogenic cardiomyopathy is a genetic defect of desmosomal genes, although there are other genetic and non-genetic causes.

Corrado D, et al. Arrhythmogenic right ventricular cardiomyopathy: evaluation of the current diagnostic criteria and differential diagnosis. *Eur Heart J*. 2020;41:1414-1429.

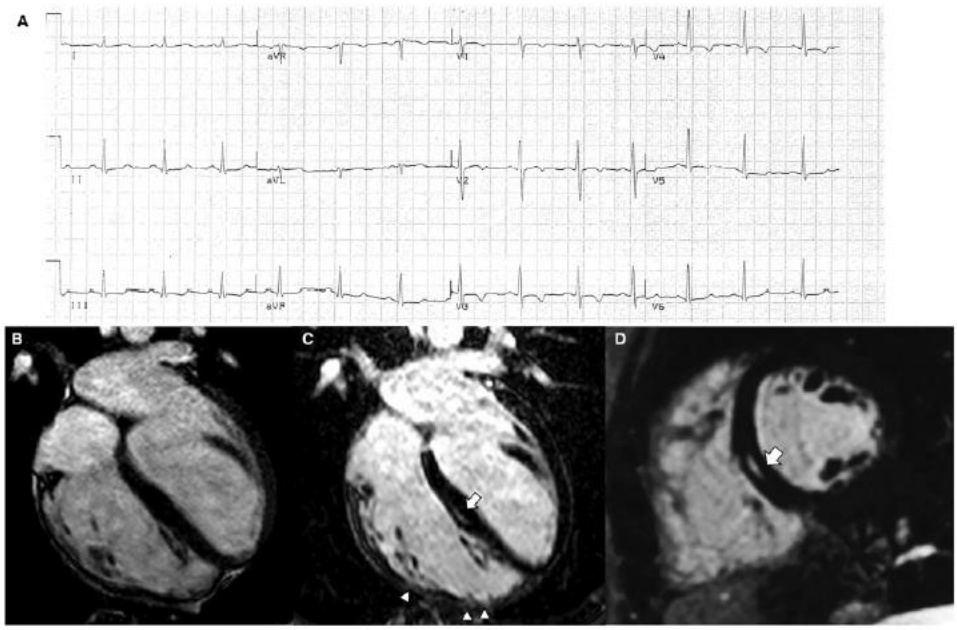


Figure 2. Electrocardiographic and cardiac magnetic resonance features of a representative case of right-dominant (classic) phenotypic variant of arrhythmogenic right ventricular cardiomyopathy.

(A) Basal electrocardiographic showing T-wave inversion in right precordial leads (V1–V4). (B) End-diastolic frame of cine cardiac magnetic resonance sequence in long-axis four-chamber view showing a dilated right ventricle (end-diastolic volume, 127 mL/m2) with a severely reduced ejection fraction (25%). The post-contrast orthogonal images in long-axis (C) and short-axis (D) views show late gadolinium enhancement as mid-wall stria in the mid-septum (white arrow). In C, late gadolinium enhancement is also visible in the anterolateral, mid, and apical regions of the right ventricular wall, with segmental transmural involvement (white arrowheads) associated with regional dyskinesia (not shown).

De Lazzari M, et al. Relationship between electrocardiographic findings and cardiac magnetic resonance phenotypes in arrhythmogenic cardiomyopathy. J Am Heart Assoc 2018;7:e009855.

Table 2. Revised (2010) International Task Force Criteria for Diagnosis of ARVC/D

Definitive diagnosis: 2 major or 1 major, and 2 minor criteria or 4 minor from different categories

Borderline: 1 major and 1 minor or 3 minor criteria from different categories

Possible: 1 major or 2 minor criteria from different categories

I. Global or regional dysfunction and structural alterations*

Major

By 2D echo:

Regional RV akinesia, dyskinesia, or aneurysm and one of the following (end diastole):

— PLAX RVOT ≥32 mm (corrected for body size [PLAX/BSA] ≥19 mm/m²)

— PSAX RVOT ≥ 36 mm (corrected for body size [PSAX/BSA] ≥21 mm/m²)

— or fractional area change ≤33%

By MRI:

Regional RV akinesia or dyskinesia or dyssynchronous RV contraction and one of the following:

— Ratio of RV end-diastolic volume to BSA ≥110 mL/m² (male) or ≥100 mL/m² (female)

— or RV ejection fraction ≤40%

By RV angiography:

Regional RV akinesia, dyskinesia, or aneurysm.

Minor

By 2D echo:

Regional RV akinesia or dyskinesia and 1 of the following (end diastole):

— PLAX RVOT ≥29 to <32 mm (corrected for body size [PLAX/BSA] ≥16 to <19 mm/m²)

— PSAX RVOT ≥32 to <36 mm (corrected for body size [PSAX/BSA] ≥18 to <21 mm/m²)

— or fractional area change >33% to ≤40%

By MRI:

Regional RV akinesia or dyskinesia or dyssynchronous RV contraction and one of the following:

— Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m² (male) or ≥90 to <100 mL/m² (female)

— or RV ejection fraction >40% to ≤45%

II. Tissue characterization of wall

Major

Residual myocytes <60% by morphometric analysis (or <50% if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty replacement of tissue on endomyocardial biopsy.

Minor

Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty replacement of tissue on endomyocardial biopsy.

III. Repolarization abnormalities

Major

Inverted T waves in right precordial leads (V1, V2, and V3) or beyond in individuals.

>14 years of age (in the absence of complete right bundle-branch block, QRS ≥120 ms).

Minor

Inverted T waves in leads V1 and V2 in individuals >14 years of age (in the absence of complete right bundle-branch block) or in V4, V5, or V6.

Inverted T waves in leads V1, V2, V3, and V4 in individuals >14 years of age in the presence of complete right bundle-branch block.

IV. Depolarization/conduction abnormalities

Major

Epsilon wave (reproducible low-amplitude signals between end of QRS complex to onset of the T wave) in the right precordial leads (V1 to V3).

Definitive diagnosis: 2 major or 1 major, and 2 minor criteria or 4 minor from different categories
Minor
Late potentials by SAECG in ≥1 of 3 parameters in the absence of a QRS duration of ≥110 ms on the standard ECG.
Filtered QRS duration (fQRS) ≥114 ms.
Duration of terminal QRS 40 mV (low-amplitude signal duration) ≥38 ms.
Root-mean-square voltage of terminal 40 ms ≤20 mV.
Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R′, in V1, V2, or V3, in the absence of complete right bundle-branch block.
V. Arrhythmias
Major
Nonsustained or sustained ventricular tachycardia of left bundle-branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and aVF and positive in lead aVL).
Minor
Nonsustained or sustained ventricular tachycardia of RV outflow configuration, LBBB morphology with inferior axis (positive QRS in leads II, III, and aVF and negative in lead aVL) or of unknown axis.
>500 ventricular extrasystoles per 24 hours (Holter).
VI. Family history
Major
ARVC/D confirmed in a first-degree relative who meets current Task Force criteria
ARVC/D confirmed pathologically at autopsy or surgery in a first-degree relative
Identification of a pathogenic mutation† categorized as associated or probably associated with ARVC/D in the patient under evaluation
Minor
History of ARVC/D in a first-degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force criteria
Premature sudden death (<35 years of age) due to suspected ARVC/D in a first-degree relative
ARVC/D confirmed pathologically or by current Task Force Criteria in second-degree relative

PLAX indicates parasternal long-axis view; RVOT, RV outflow tract; BSA, body surface area; PSAX, parasternal short-axis view; aVF, augmented voltage unipolar left foot lead; and aVL, augmented voltage unipolar left arm lead.
*Hypokinesis is not included in this or subsequent definitions of RV regional wall motion abnormalities for the proposed modified criteria.
†A pathogenic mutation is a DNA alteration associated with ARVC/D that alters or is expected to alter the encoded protein, is unobserved or rare in a large non-ARVC/D control population, and either alters or is predicted to alter the structure or function of the protein or has demonstrated linkage to the disease phenotype in a conclusive pedigree.
Marcus FI, *et al*. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. *Eur Heart J*. 2010;**31**:806–14 with permission from Oxford University Press.

Table 3. ESC 2023 GL on Cardiomyopathies. Recommendation for resting and ambulatory electrocardiogram monitoring in patients with arrhythmogenic right ventricular cardiomyopathy

Annual ambulatory ECG monitoring is recommended in patients with ARVC to aid in diagnosis, management, and risk stratification	I	C

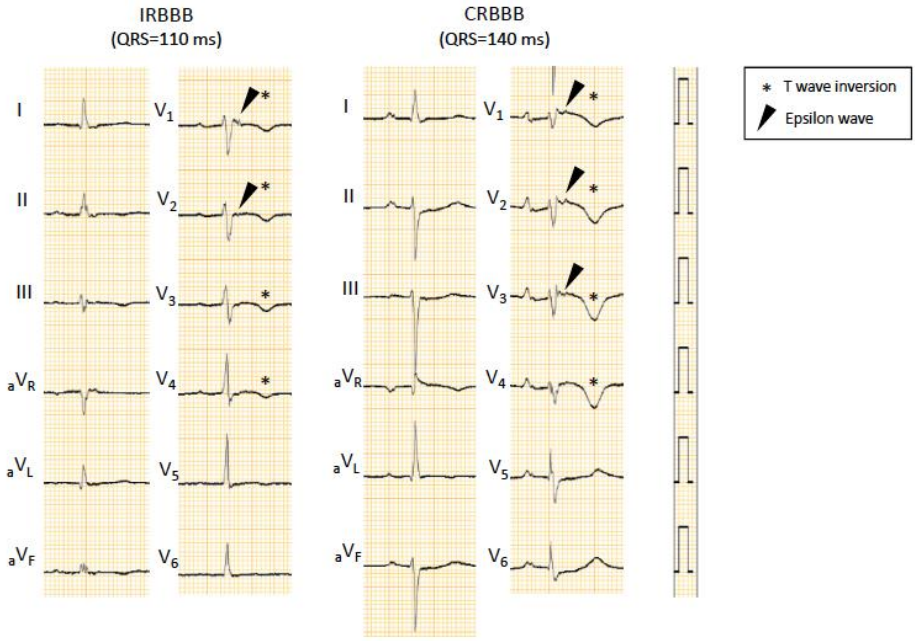


Figure 3. Representative 12-lead electrocardiogram (ECG) obtained from patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) with incomplete right bundle branch block (IRBBB) and complete right bundle branch block (CRBBB).
QRS duration of IRBBB and CRBBB was 110 ms and 140 ms, respectively. The closed arrow indicates an epsilon wave, which was defined as low-amplitude deflection located between the end of the QRS and the onset of the T wave in leads V1–V3. The asterisk indicates the T wave inversion recorded in V1–V4 in patients with ARVC and IRBBB or CRBBB.
Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm.* 2019.

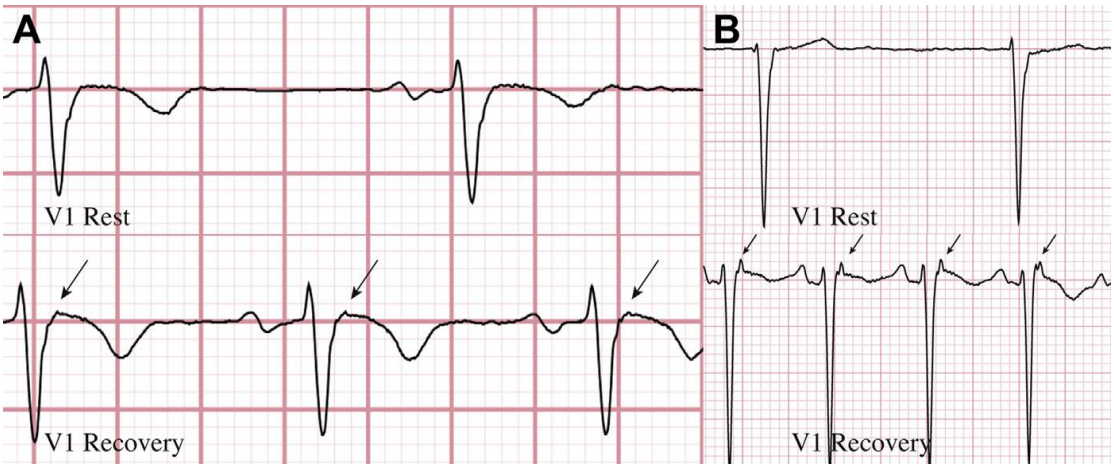


Figure 4. Epsilon Waves Appearing During Exercise.
(A) An epsilon wave appeared during early exercise and persisted during the recovery period (arrows). (B) A relatively large amplitude epsilon wave (arrows) was prominent late into the recovery period. Both asymptomatic subjects had normal results on rest electrocardiography and normal results on cardiac magnetic resonance imaging and harbored radical plakophilin 2 mutations.
Perrin MJ, et al. Exercise testing in asymptomatic gene carriers exposes a latent electrical substrate of arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol.* . 2013;62:1772-1779

Table 4. Differential diagnosis of arrhythmogenic right ventricular cardiomyopathy

Mimics of right-dominant ARVC
Primary arrhythmia conditions
Right ventricular outflow tract tachycardia
Brugada syndrome
Structural diseases
Congenital heart diseases (left to right shunt, Ebstein's anomaly, Uhl's anomaly)
Pulmonary artery hypertension
Athlete's heart
Chest deformity and pericardial absence
Mimics of left-dominant ARVC
Structural diseases
Dilated cardiomyopathy
Neuromuscular cardiomyopathies (muscular dystrophies and myofibrillar myopathies)
Myocarditis
Cardiac sarcoidosis
Congenital ventricular aneurysms
Chagas' heart disease

Dilated cardiomyopathy vs. left-dominant arrhythmogenic right ventricular cardiomyopathy.

	Dilated cardiomyopathy	Left-dominant ARVC
Inheritance	≤35% (AD)	>50% (AD, AR)
Predominant genetic background	Mutations of genes encoding for cytoskeleton, muscular sarcomere, and nuclear envelope proteins	Mutations of genes encoding for desmosomal proteins, PLN, or FLN-C
Main clinical manifestations	Heart failure, cardiac arrest, palpitations	Palpitations, syncope, cardiac arrest
ECG abnormalities	Left ventricular hypertrophy with a strain pattern of ST-segment; left bundle branch block	Low QRS voltages in limb leads; negative T waves in lateral leads; negative T waves in right precordial leads (biventricular form)
Echocardiography and cardiac magnetic resonance imaging findings	Dilated and hypokinetic LV with no or patchy non-ischaemic (mid-myocardial) LGE (septum) Regional wall motion abnormalities (uncommon). Systolic LV dysfunction unrelated to the global extent of LGE	Non-dilated and hypokinetic LV with large amount of non-ischemic (subepicardial) LGE (inferolateral LV wall) Regional wall motion abnormalities (common). Systolic LV dysfunction related to the global extent of LGE
EMB features	Non-specific myocardial abnormalities	Fibrofatty myocardial replacement
Types of ventricular arrhythmias	PVBs and NSVT (RBBB pattern); sustained VT(uncommon); VF	PVBs, NSVT, and monomorphic sustained VT (RBBB pattern; both LBBB and RBBB patterns in biventricular form); VF
Mechanism of VT	Scar-related or functional re-entry (branch to branch re-entry)	Scar-related re-entry
Most common site of VT origin	Intramural septum	Subepicardial infero-lateral LV free wall

AD, autosomal dominant; AR, autosomal recessive; EMB, endomyocardial biopsy; LBBB, left bundle branch block; LV, left ventricle; NSVT, non-sustained ventricular tachycardia; PVBs, premature ventricular beats; RBBB, right bundle branch block; RV, right ventricle; RVOT, right ventricular outflow tract; TWI, T-wave inversion; VF, ventricular fibrillation; VT, ventricular tachycardia.

Brugada syndrome vs arrhythmogenic right ventricular cardiomyopathy

	Brugada syndrome	ARVC
Age of presentation (years)	30–40	15–30
Gender	M > F (8:1)	M > F (3:1)
Distribution	World-wide (predominantly Southeast Asia)	World-wide
Inheritance	AD	AD (AR)
Predominant pathogenetic genes	SCN5A gene	Desmosomal genes
Typical symptoms	Syncope, cardiac arrest Especially nocturnal	Palpitations, syncope, cardiac arrest
ECG repolarization	Right precordial ST elevation and TWI	Right precordial TWI
ECG depolarization	RBBB/LAD	Right precordial QRS prolongation, ϵ waves
AV conduction times	Prolonged PR/HV interval	Normal
Variability of ECG changes	Dynamic	Fixed
Imaging	Normal (or mild RVOT dilatation)	Structural RV (and LV) abnormalities with global and regional dilation and dysfunction
Biopsy	Normal	Fibrofatty replacement
Ventricular arrhythmias	Polymorphic VT, VF	Monomorphic VT, VF
Mechanism of VT	Phase 2 re-entry or local micro-reentry	Scar-related macro-reentry
Programmed ventricular stimulation	Inducibility of VF	Inducibility of monomorphic VT or VF
Natural history	Sudden death	Sudden death, heart failure

AD, autosomal dominant; AR, autosomal recessive; AV, atrioventricular; LAD, left axis deviation; LV, left ventricle; RBBB, right bundle branch block; RV, right ventricle; RVOT,
right ventricular outflow tract; TWI, T-wave inversion; VF, ventricular fibrillation; VT, ventricular tachycardia.

Corrado D, et al. Arrhythmogenic right ventricular cardiomyopathy: evaluation of the current diagnostic criteria and differential diagnosis. *Eur Heart J*. 2020;41:1414-1429.

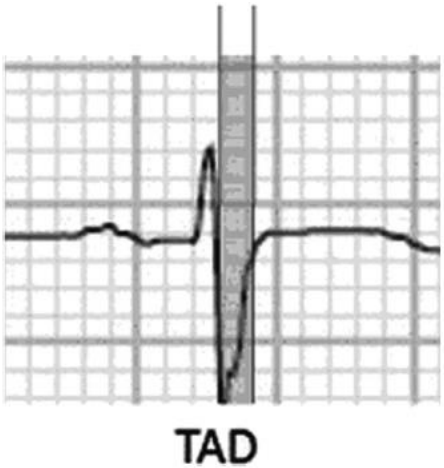


Figure 5. Terminal activation duration (TAD) is measured from the nadir of the S wave to the end of all depolarization deflections and is prolonged if >=55 ms in any of the V1–V3 leads in the absence of complete right bundle branch block.

Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm.* 2019.

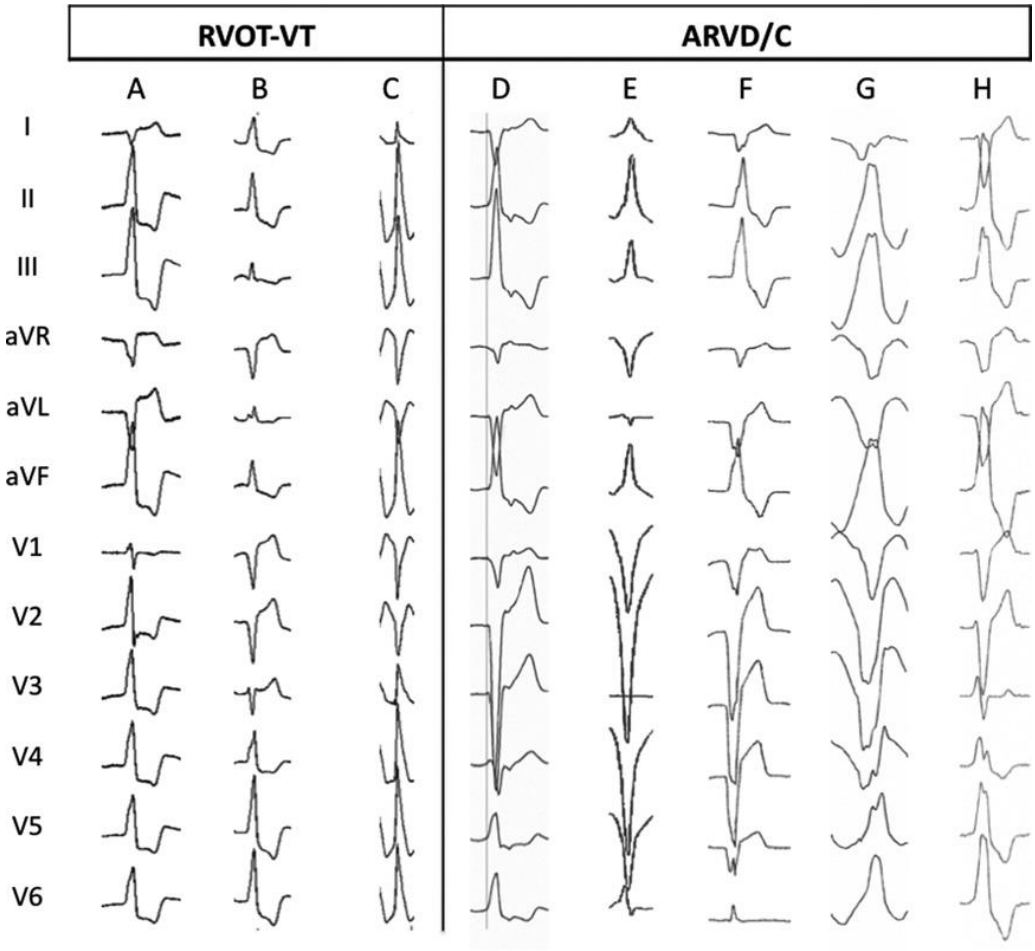


Figure 6. Differentiation between RVOT VT and ARVC.
Twelve-lead electrocardiograms from patients with right ventricular outflow tract tachycardia (RVOT-VT) **(A to C)** and arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC/C) **(D to H)** showing characteristic features. **(A)** RVOT-VT from an anterior-septal location showing precordial transition at V2 and narrow QRS duration in lead I (78 ms). **(B)** RVOT-VT originating superior to His bundle region showing precordial transition at V4, positive R-wave in aVL, and narrow QRS in lead I (86 ms). **(C)** RVOT-VT from a posterior-septal location showing precordial transition at V3 and narrow QRS duration in lead I (118 ms). **(D)** ARVC/C ventricular tachycardia (VT) showing late precordial transition V5, wide QRS duration in lead I (124 ms), and earliest onset QRS in V1 **(vertical line)**. **(E)** ARVC/C-VT shows very late precordial transition V6 and wide QRS duration in lead I (126 ms). **(F)** ARVC/C-VT shows very late precordial transition V6 and wide QRS duration in lead I (150 ms). **(G)** ARVC/C-VT shows late precordial transition V5, wide QRS duration in lead I (160 ms), and notching of the QRS (II, III, aVF, V4 to V6). **(H)** ARVC/C-VT shows wide QRS duration in lead I (128 ms) and notching of the QRS (II, III, aVF, V4 to V6).

Hoffmayer KS, Machado ON, Marcus GM, et al. Electrocardiographic comparison of ventricular arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract tachycardia. J Am Coll Cardiol. 2011;58:831-8.

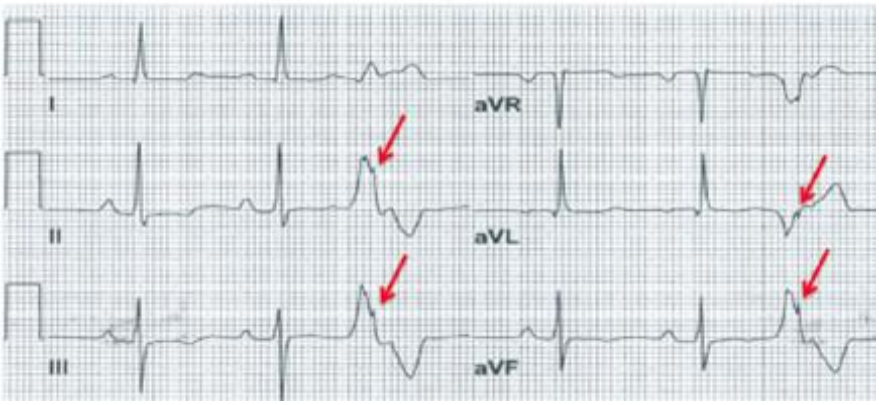


Figure 7. Example of QRS Notching.
Arrows show QRS notching in ectopic beats lead II, III, aVF, and aVL.
Hoffmayer KS, et al. An electrocardiographic scoring system for distinguishing right ventricular outflow tract arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy from idiopathic ventricular tachycardia. Heart Rhythm. 2013;10: 477-82.

Table 5. Idiopathic right ventricular outflow tract tachycardia vs ARVC-related ventricular tachycardia

	RVOT-VT	ARVC
Disease inheritance	No	Yes (AD)
Genetic defect	No	Desmosomal genes-mutations
Symptoms	Palpitations, pre-syncope	Palpitations, syncope, cardiac arrest
ECG abnormalities	Normal	Right precordial T-wave inversion, ϵ waves, right precordial QRS prolongation with delayed S-wave upstroke, and terminal activation delay (>55 ms), low QRS voltages
Imaging	Normal	Structural and functional RV abnormalities
Biopsy	Normal	Fibrofatty myocardial replacement
Morphology of VT	NSVT repetitive monomorphic; LBBB usually with inferior QRS axis	LBBB Usually with left deviation
Multiple VT morphologies	No	Yes
VT mechanism	Enhanced automaticity and triggered activity	Scar-related re-entry
Typical site of VT origin	Anteroseptal RVOT	Non-septal RVOT
RV EVM	Normal	Low-voltage areas
Programmed ventricular stimulation	Non-inducible VT	Inducible VT

AD, autosomal dominant; EVM, endocardial voltage mapping; LBBB, left bundle branch block; NSVT, non-sustained ventricular tachycardia; RV, right ventricle; RVOT, right ventricular outflow tract; TWI, T-wave inversion; VF, ventricular fibrillation; VT, ventricular tachycardia.

Corrado D, et al. Arrhythmogenic right ventricular cardiomyopathy: evaluation of the current diagnostic criteria and differential diagnosis. *Eur Heart J*. 2020;41:1414-1429.

Table 6. Electrocardiographic scoring system for distinguishing RVOT arrhythmias in patients with ARVC/D from idiopathic VT.

ECG characteristic	Points
Anterior T wave inversions (V_1–V_3) in sinus rhythm	3
VT/PVC:	
Lead I QRS duration ≥120 ms	2
QRS notching (multiple leads)	2
V_2 transition or later	1

Anterior T wave inversion is defined as T wave negativity in, at least, leads V_1, V_2, and V_3.
Lead I QRS duration ≥120 ms is defined as the duration from the initial deflection of the QRS complex to the end of the QRS complex in lead I.
QRS notching in multiple leads is defined as a QRS complex deflection on the upstroke or downstroke of >0.5 mV that did not cross the baseline occurring in, at least, two leads (Figure 39.4).
The precordial transition point is designated as the earliest precordial lead where the R wave amplitude exceeded the S wave amplitude.
Hoffmayer KS, *et al*. An electrocardiographic scoring system for distinguishing right ventricular outflow tract arrhythmias. *Heart Rhythm*. 2013;**10**: 477–82, with permission from Elsevier.

Table 7. Genetic Testing

ACC/AHA/HRS 2017 Guideline on VA/SCD

In first-degree relatives of patients with ARVC, clinical screening for the disease and genetic counseling and genetic testing, if the proband has a disease causing mutation.	I-B-NR

EHRA/HRS/APHRS/LAHRS 2022 Expert Consensus Statement. Arrhythmogenic Cardiomyopathy

Impact of genetic testing for the index case

Disease	Diagnostic	Prognostic	Therapeutic
ACM	+++	++	++

Recommendations

Should do

Comprehensive genetic testing is recommended for all patients with consistent phenotypic features of ACM, including those cases diagnosed post-mortem, whatever familial context.

Genetic testing of first tier definitive disease associated genes (currently PKP2, DSP, DSG2, DSC2, JUP, TMEM43, PLN, FLNC, DES, LMNA) is recommended.

Variant-specific genetic testing is recommended for family members and appropriate relatives following the identification of the disease-causative variant.

Predictive genetic testing in related children is recommended in those aged >10–12 years.

May do

Owing to the possibility of complex genotypes, in families with multiple affected members, the case with the more severe and/ or earlier phenotype may be considered the ‘genetic proband’ and be tested first.

In patients with a borderline ACM phenotype, comprehensive genetic testing may be considered. The identification of a LP/P genetic variant would be useful to confirm the diagnosis.

Predictive genetic testing in related children aged below 10–12 years may be considered, especially where there is a family history of early-onset disease.

(EHRA)/HRS/APHRS/LAHRS Expert Consensus Statement on the state of genetic testing for cardiac diseases. Europace 2022

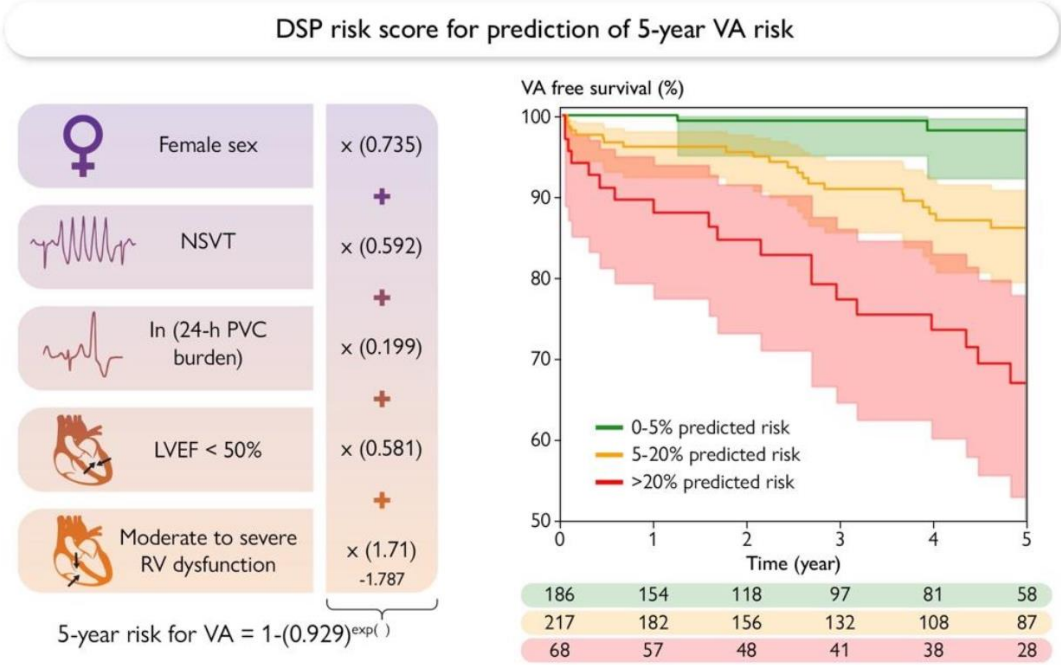


Figure 8. The desmoplakin risk score provides individualized predictions of 5-year ventricular arrhythmia risk in patients with pathogenic/likely pathogenic (P/LP) desmoplakin variants based on five readily available clinical risk factors (www.dsp-risk.com). The desmoplakin risk score demonstrated strong discrimination of ventricular arrhythmia risk (*c*-statistic .79 during external validation) and accurately stratifies patients into low- (0%–5% risk at 5 years), intermediate- (5%–20% risk at 5 years), and high-risk (>20% risk at 5 years) groups for the purposes of guiding primary prevention implantable cardiac defibrillator decision-making.

DSP, desmoplakin; LVEF, left ventricular ejection fraction; NSVT, non-sustained ventricular tachycardia; PVC, premature ventricular contraction; RV, right ventricular; VA, ventricular arrhythmia.

Carrick RT, et al. A novel tool for arrhythmic risk stratification in desmoplakin gene variant carriers. *Eur Heart J*. 2024;45:2968-2979.

Table 8. Risk stratification and therapy of ARVC/D

ESC 2023 GL on cardiomyopathies.

Recommendations for the antiarrhythmic management of patients with arrhythmogenic right ventricular cardiomyopathy

Beta-blocker therapy is recommended in ARVC patients with VE, NSVT, and VT.[920–922]	I	C
Amiodarone should be considered when regular beta-blocker therapy fails to control arrhythmia-related symptoms in patients with ARVC.[921,922]	IIa	C
Flecainide in addition to beta-blockers should be considered when single agent treatment has failed to control arrhythmia-related symptoms in patients with ARVC.[923,924]	IIa	C
Catheter ablation with availability for epicardial approach guided by 3D electroanatomical mapping of VT should be considered in ARVC patients with incessant VT or frequent appropriate ICD interventions for VT despite pharmacological therapy with beta-blockers.[925,929–934]	IIa	C

3D, three-dimensional; ARVC, arrhythmogenic right ventricular cardiomyopathy; ICD, implantable cardioverter defibrillator; NSVT, non-sustained ventricular tachycardia; VE, ventricular ectopic beats; VT, ventricular tachycardia.

Recommendations for sudden cardiac death prevention in patients with arrhythmogenic right ventricular cardiomyopathy

Secondary prevention		
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with ARVC who have survived a cardiac arrest or have recovered from a ventricular arrhythmia causing haemodynamic instability.[939,943,944,948,949]	I	A
An ICD should be considered in ARVC patients who have suffered a haemodynamically tolerated VT.[522,939,943–945,948–950]	IIa	B
Primary prevention		
High-risk features[c] should be considered to aid individualized decision-making for ICD implantation in patients with ARVC.[538,939]	IIa	B
The updated 2019 ARVC risk calculator should be considered to aid individualized decision-making for ICD implantation in patients with ARVC.[d,524,526,536–539]	IIa	B

ARVC, arrhythmogenic right ventricular cardiomyopathy; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NSVT, non-sustained ventricular tachycardia; PES, programmed electrical stimulation; RVEF, right ventricular ejection fraction; SMVT, sustained monomorphic ventricular tachycardia; VT, ventricular tachycardia.

c High-risk features: arrhythmic syncope, NSVT, RVEF <40%, LVEF <45%, SMVT at PES.

d See text for discussion of gene-specific differences in the performance of the updated 2019 ARVC risk calculator

ACC/AHA/HRS 2017 Guideline on VA/SCD. Arrhythmogenic Right Ventricular Cardiomyopathy

Cardiac MRI for establishing a diagnosis and for risk stratification in suspected ARVC and VA or electrocardiographic abnormalities.	I-B-NR
ICD* in ARVC and an additional marker of increased risk of SCD (resuscitated SCA, sustained VT, significant ventricular dysfunction with RVEF or LVEF ≤35%).	I-B-NR
A beta blocker in ARVC and VA.	I-B-NR
Avoiding intensive exercise by patients wityh a clinical diagnosis of ARVC is recommended.	I-B-NR
Genetic counseling and genetic testing for diagnosis and for gene-specific targeted family screening in patients with clinically diagnosed or suspected ARVC.	IIa-B-NR
ICD* in ARVC and syncope presumed due to VA	IIa-B-NR
A beta blocker in clinical evidence of ARVC but not VA	IIa-B-NR
Catheter ablation with availability of a combined endocardial/epicardial approach in ARVC and recurrent symptomatic sustained VT when a beta blocker is ineffective or not tolerated	IIa-B-NR
Signal averaged ECG for diagnosis and risk stratification in suspected ARVC	IIa-B-NR
Electrophysiological study for risk stratification in asymptomatic patients with clinical evidence of ARVC.	IIb-B-NR

*: if meaningful survival greater than 1 year is expected

ACC/AHA/HRS 2017 Guideline on syncope

ICD in patients with ARVC who present with syncope and have a documented sustained ventricular arrhythmia	I-B-NR
ICD in patients with ARVC who present with syncope of suspected arrhythmic etiology.	IIa-B-NR

ESC 20022 GL on VA and SCD. Recommendations for diagnostic, risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy

Diagnostic evaluation and general recommendations	
CMR in patients with suspected ARVC.	I B
Genetic counselling and testing in patients with a suspected or definite diagnosis of ARVC.	I B

Avoidance of high-intensity exercise in patients with a definite diagnosis of ARVC.	I	B
Avoidance of high-intensity[a] exercise in carriers of ARVC-related pathogenic mutations and no phenotype.	IIb	C
Beta-blocker therapy in all patients with a definite diagnosis of ARVC.	IIb	C
Risk stratification and primary prevention of SCD		
ICD implantation in patients with definite ARVC and an arrhythmic syncope.	IIa	B
ICD implantation in patients with definite ARVC and severe RV or LV systolic dysfunction.	IIa	C
ICD implantation in symptomatic[b] patients with definite ARVC, moderate right or left ventricular dysfunction, and either NSVT or inducibility of SMVT at PES.	IIa	C
In patients with ARVC and symptoms highly suspicious for VA, PES for risk stratification.	IIb	C
Secondary prevention of SCD and treatment of Vas		
ICD implantation 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.	I	C
In patients with ARVC and recurrent, symptomatic SMVT or ICD shocks for SMVT despite beta-blockers, catheter ablation in specialized centres.	IIa	C
In ARVC patients with indication for ICDs, a device with the capability of ATP programming for SMVT up to high rates.	IIa	B
ICD implantation in ARVC patients with a haemodynamically tolerated SMVT.	IIa	C
In patients with ARVC and recurrent, symptomatic VT despite beta-blockers, AAD treatment.	IIa	C
Management of relatives of a patient with ARVC		
ECG and echocardiogram in a first-degree relative of a patient with ARVC.	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 The 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease.
b Presyncope or palpitations suggestive of VA.

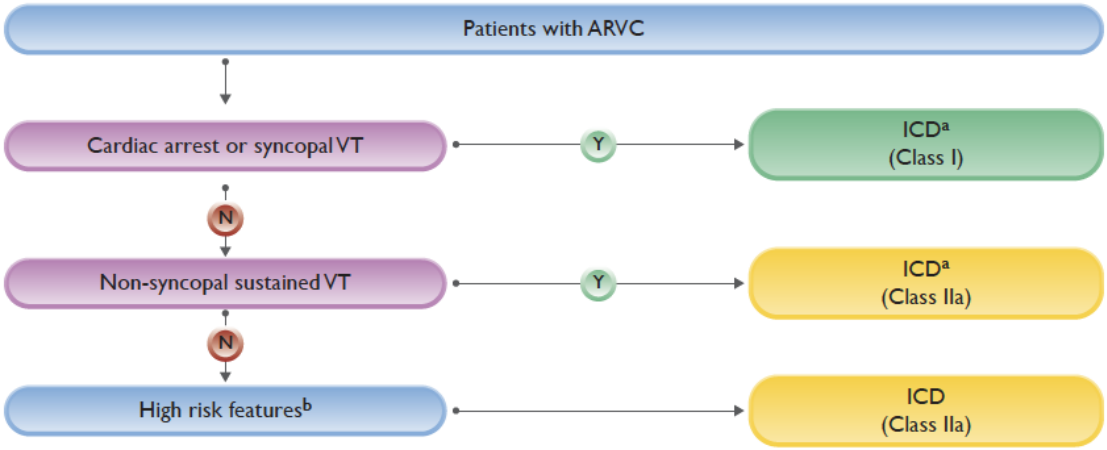


Figure 9. ESC 2023 GL on Cardiomyopathies Algorithm to approach implantable cardioverter defibrillator decision-making in patients with arrhythmogenic right ventricular cardiomyopathy.

ARVC, arrhythmogenic right ventricular cardiomyopathy; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NSVT, nonsustained
ventricular tachycardia; PES, programmed electrical stimulation; RVEF, right ventricular ejection fraction; SMVT, sustained monomorphic ventricular
tachycardia; VT, ventricular tachycardia.

a Clinicians should aim to control ventricular arrhythmia with pharmacological or invasive antiarrhythmic therapies in addition to offering an ICD.

b High-risk features are defined as either cardiac syncope, NSVT, RVEF <40%, LVEF <45%, SMVT at PES or as per the updated 2019 ARVC risk calculator.

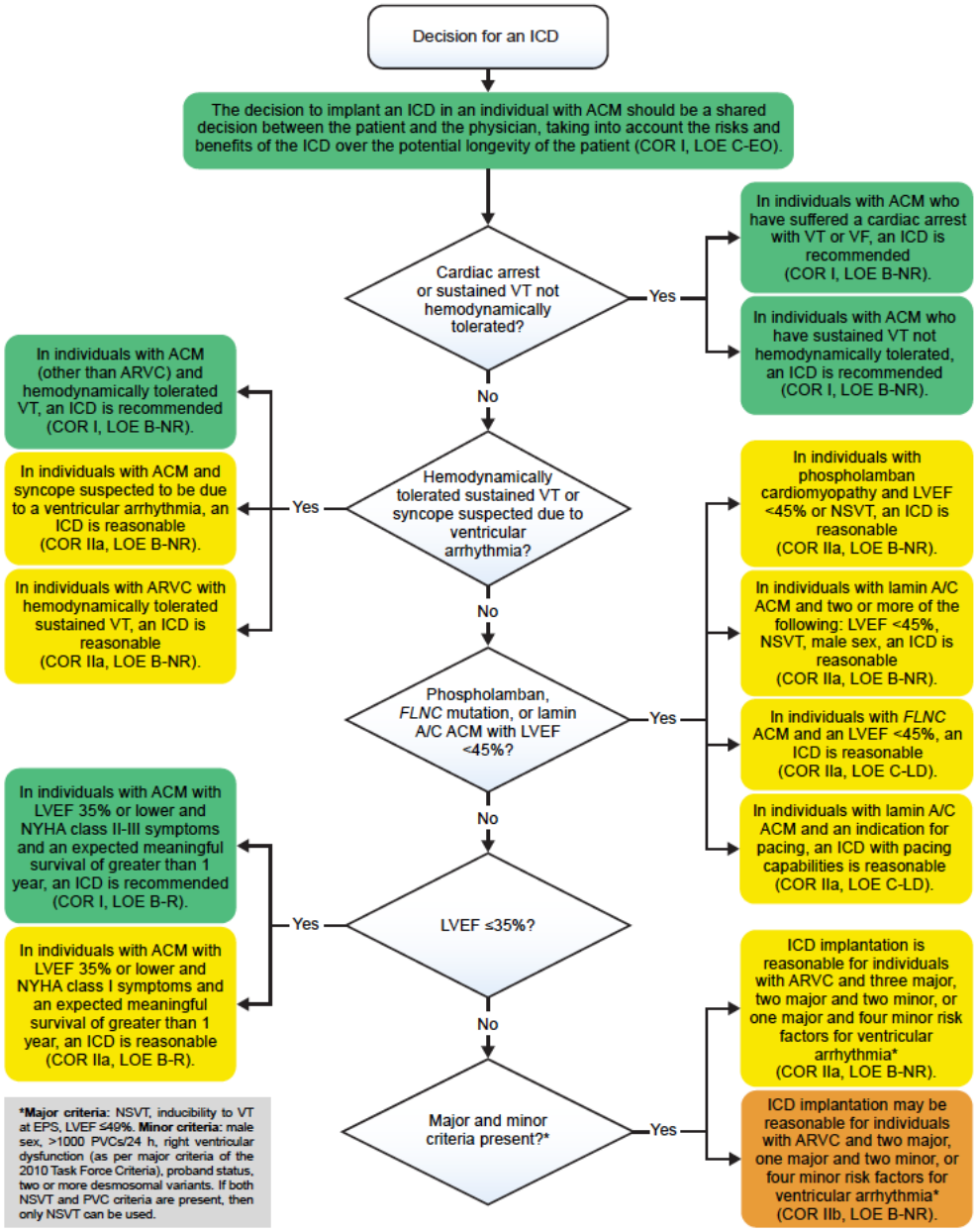


Figure 10. Implantable cardioverter defibrillator (ICD) recommendations.

ACM = arrhythmogenic cardiomyopathy; ARVC = arrhythmogenic right ventricular cardiomyopathy; COR = Class of Recommendation; FLNC= filamin-C; LOE = Level of Evidence; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; NYHA = New York Heart Association; PVC = premature ventricular contraction; VF = ventricular fibrillation; VT = ventricular tachycardia

Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019.

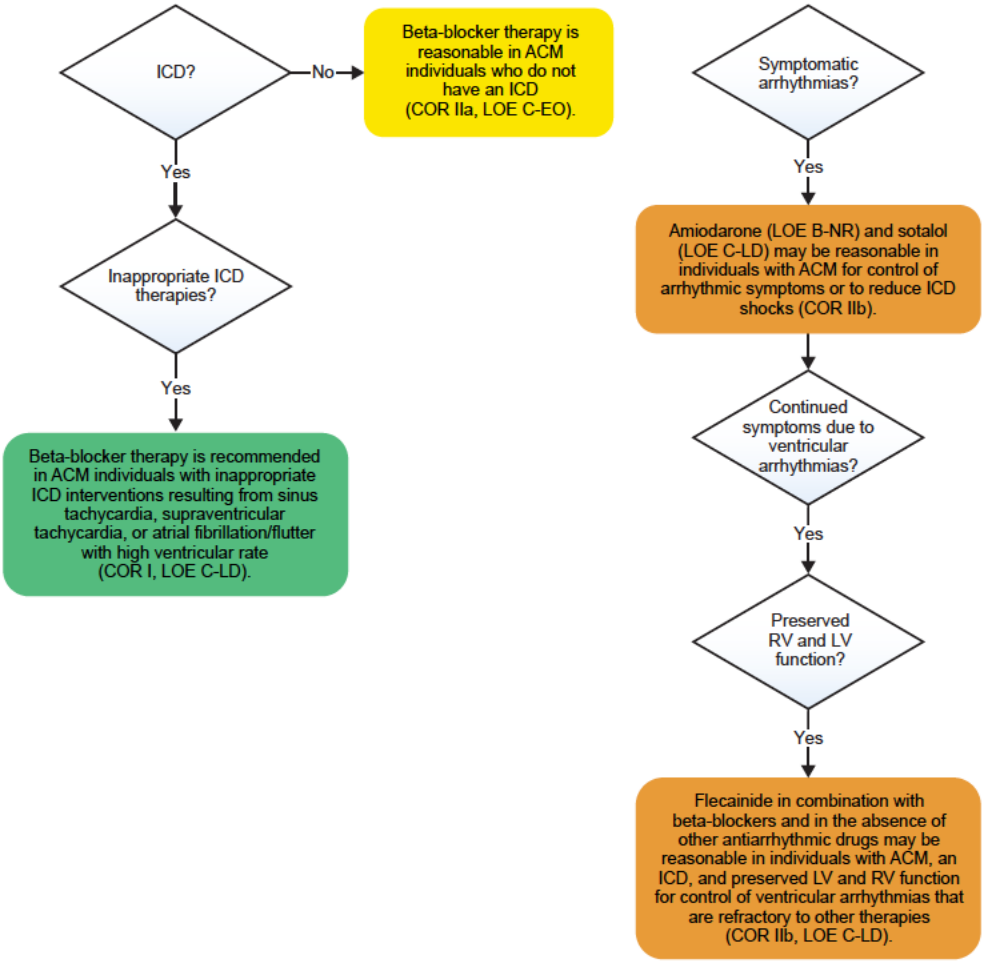


Figure 11. Medical therapy recommendations for arrhythmias.

ACM=arrhythmogenic cardiomyopathy; COR=Class of Recommendation; ICD=implantable cardioverter defibrillator; LOE = Level of Evidence; LV = left ventricular; RV = right ventricular

Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019.

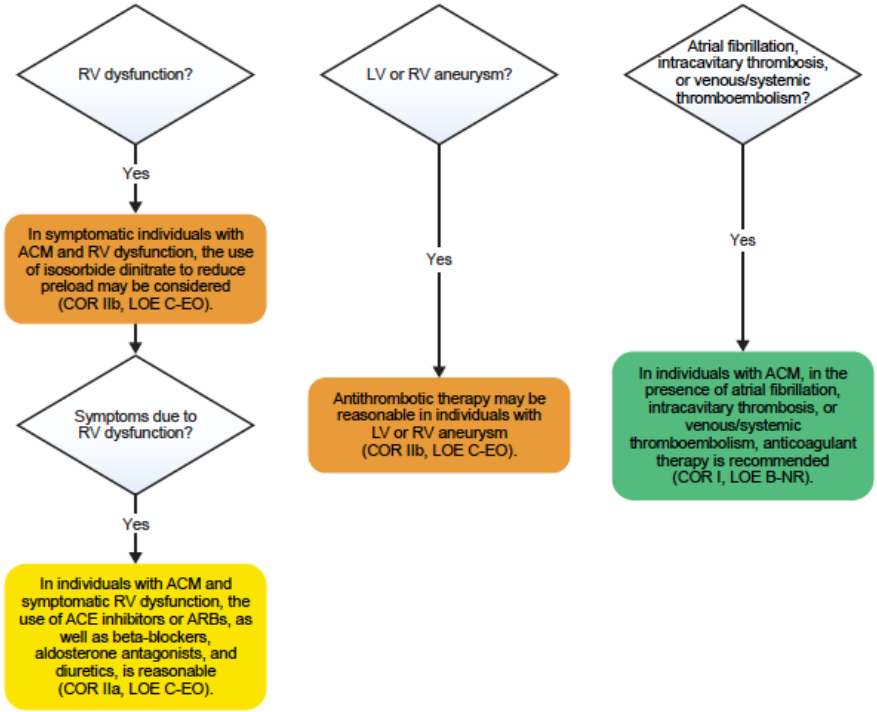


Figure 12. Recommendations for ventricular dysfunction and antithrombotic medical therapy in individuals with arrhythmogenic cardiomyopathy (ACM).

ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; COR = Class of Recommendation; LOE = Level of Evidence; LV = left ventricular; RV = right ventricular

Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019.

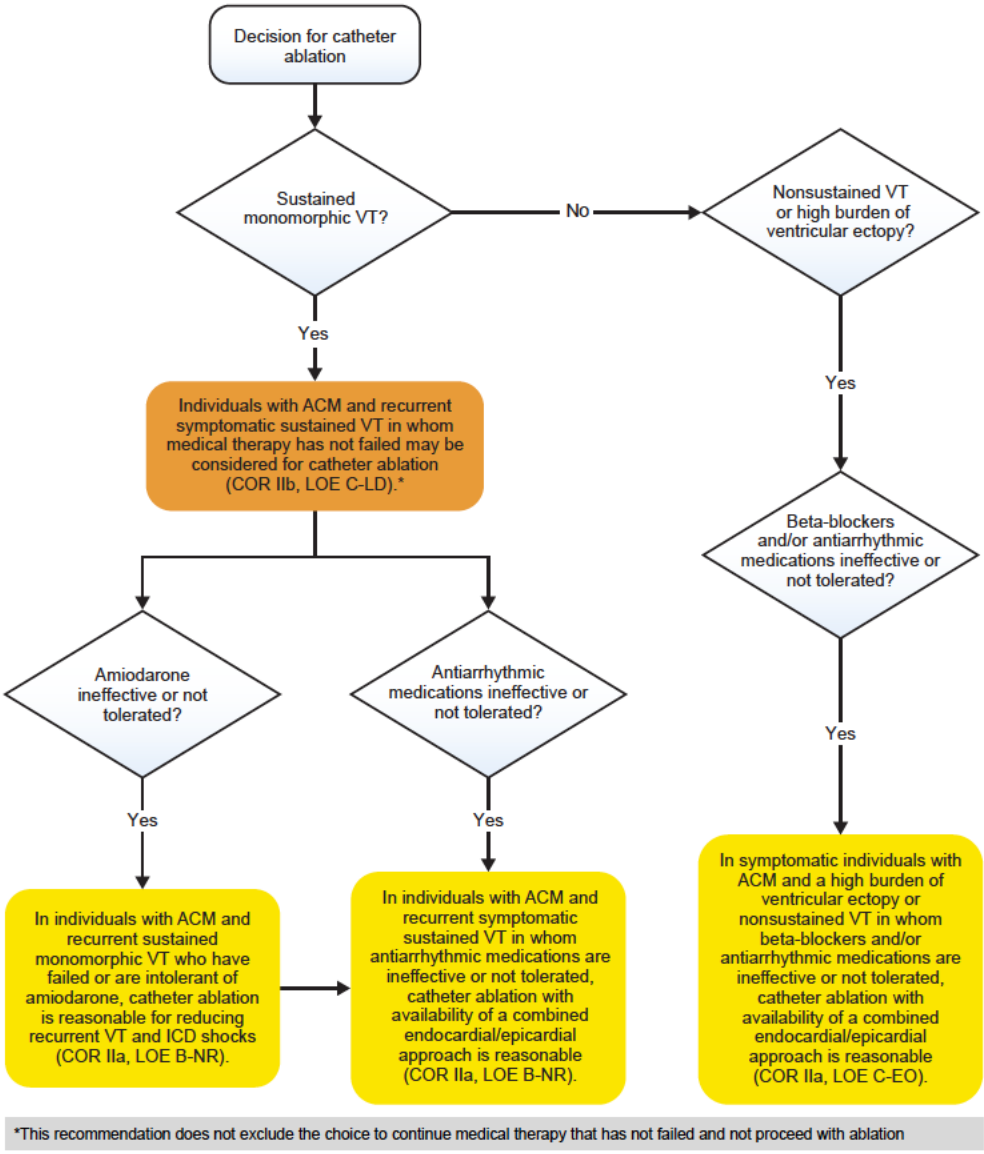


Figure 13. Catheter ablation recommendations for individuals with arrhythmogenic cardiomyopathy (ACM).

ICD = implantable cardioverter defibrillator; LOE = Level of Evidence; VT = ventricular tachycardia.

Towbin JA, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019.

Table 9. ESC 2023 GL on Cardiomyopathies. Exercise recommendations for patients with cardiomyopathy

Avoidance of high-intensity exercise, including competitive sport, may be considered in genotype-positive/phenotype-negative individuals in families with ARVC	IIb	C
Moderate- and/or high-intensity exercise, including competitive sport, is not recommended in individuals with ARVC	III	B

Table 10. ESC 2025 GL on pregnancy. ARVC

Flecainide, in addition to beta-blockers, should be considered as the anti-arrhythmic drug of choice in pregnant women with ARVC.[148]	**IIa**	**C**
Sotalol may be considered as an anti-arrhythmic drug in pregnant women with ARVC, with careful evaluation of QTc and while monitoring for foetal bradycardia and foetal growth and neonate hypoglycaemia.	**IIb**	**C**