ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

Arrhythmogenic right ventricular cardiomyopathy (ARVC) or dysplasia (ARVD) is a category of cardiomyopathy characterized by fibrous or fibro-fatty replacement of myocardium in the inflow tract, outflow tract and/or apex of the right ventricle. In its most severe form it is called Uhl's disease or parchment right ventricle.

ARVC is difficult to diagnose by echocardiography due to limited sensitivity and specificity of echocardiographic features. The 2010 revised Task Force major echocardiographic criterion[1] was developed to yield 95 percent specificity and requires regional right ventricular akinesis / dyskinesis or aneurysm plus either right ventricular outflow dilatation or reduced fractional area change. Both the original and revised criteria are divided into minor and major criteria and are classified into six categories:

- Global and/or regional dysfunction and structural alterations
- Tissue characterization of wall
- Repolarization abnormalities on the ECG
- Depolarization/conduction abnormalities on the ECG
- Arrhythmias
- Family history

Definite diagnosis of ARVC using the 2010 revised Task Force Criteria requires the presence of:

- Two major criteria **OR**
- One major and two minor criteria **OR**
- Four minor criteria from different categories

Borderline diagnosis of ARVC using the 2010 revised Task Force Criteria requires the presence of:

- One major and one minor criteria **OR**
- Three minor criteria from different categories

Possible diagnosis of ARVC using the 2010 revised Task Force Criteria requires the presence of:

- One major criteria **OR**
- Two minor criteria from different categories

2010 revised Task Force criteria for the diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

	Revised Task Force criteria
I. Global or regional dysfunction and structural alterations*	
Major	**By 2D echo:** ▪ Regional RV akinesia, dyskinesia, or aneurysm ▪ *and* 1 of the following (end diastole): • PLAX RVOT ≥32 mm (corrected for body size [PLAX/BSA] ≥19 mm/m^2) • PSAX RVOT ≥36 mm (corrected for body size [PSAX/BSA] ≥21 mm/m^2) • *or* fractional area change ≤33 percent
	By MRI: ▪ Regional RV akinesia or dyskinesia or dyssynchronous RV contraction ▪ *and* 1 of the following: • Ratio of RV end-diastolic volume to BSA ≥110 mL/m^2 (male) or ≥100 mL/m^2 (female) • *or* RV ejection fraction ≤40 percent
	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/m^2) • PSAX RVOT ≥32 to <36 mm (corrected for body size [PSAX/BSA] ≥18 to <21 mm/m^2) • *or* fractional area change >33 percent to ≤40 percent
	By MRI: ▪ Regional RV akinesia or dyskinesia or dyssynchronous RV contraction ▪ *and* 1 of the following: • Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m^2 (male) or ≥90 to <100 mL/m^2 (female) • *or* RV ejection fraction >40 percent to ≤45 percent
II. Tissue characterization of wall	
Major	▪ Residual myocytes <60 percent by morphometric analysis (or <50 percent 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 percent to 75 percent by morphometric analysis (or 50 percent to 65 percent 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 (V_1, V_2, and V_3) 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 V_1 and V_2 in individuals >14 years of age (in the absence of complete right bundle-branch block) or in V_4, V_5, or V_6 ▪ Inverted T waves in leads V_1, V_2, V_3, and V_4 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 (V_1 to V_3)
Minor	▪ Late potentials by SAECG in ≥1 of the following 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 µV (low-amplitude signal duration) ≥38 ms • Root-mean-square voltage of terminal 40 ms ≤20 µV ▪ Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R', in V_1, V_2, or V_3, 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, left bundle-branch block 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

Diagnostic terminology for revised criteria:
- Definite diagnosis: 2 Major, OR 1 Major and 2 Minor criteria, OR 4 Minor from different categories
- Borderline diagnosis: 1 Major and 1 Minor, OR 3 Minor criteria from different categories
- Possible diagnosis: 1 Major, OR 2 Minor criteria from different categories

In a study using 2-D echocardiography, tricuspid annulus plane systolic excursion (TAPSE) and RV fractional area change predicted adverse outcomes[2].

A study using 3-D echocardiography with Doppler tissue imaging demonstrated that patients with ARVC had lower right ventricular ejection fraction, decreased lateral right ventricular and LV systolic annular velocity, and decreased regional systolic strain compared with age-matched controls[3].

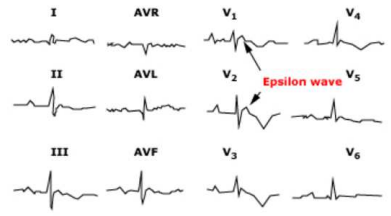
In another study that included genotypically abnormal (desmosomal gene) relatives of ARVC probands (without phenotypic abnormality) and controls, reduced global and regional strain was present in patients with ARVC mutation but not in controls[4].

Sensitivity and specificity of proposed RV imaging criteria for ARVC*

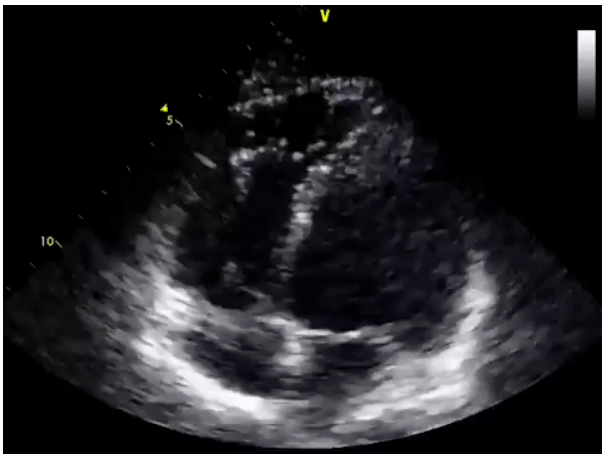
	Value	Sensitivity, percent	Specificity, percent
Echocardiogram			
Major			
PLAX RVOT (diastole)	≥32 mm	75	95
Corrected for body size (PLAX/BSA)	≥19 mm/m^2		
PSAX RVOT (diastole)	≥36 mm	62	95
Corrected for body size (PSAX/BSA)	≥21 mm/m^2		
Fractional area change	≤33 percent	55	95
Minor			
PLAX RVOT (diastole)	≥29 mm	87	87
Corrected for body size (PLAX/BSA)	≥16 to ≤18 mm/m^2		
PSAX RVOT (diastole)	≥32 mm	80	80
Corrected for body size (PSAX/BSA)	≥18 to ≤20 mm/m^2		
Fractional area change	≤40 percent	76	76
MRI[1]			
Major			
Ratio of RV end-diastolic volume to BSA			
Males	≥110 mL/m^2	76	90
Females	≥100 mL/m^2	68	98
or RV ejection fraction	≤40 percent		
Minor			
Ratio of RV end-diastolic volume to BSA			
Males	≥100 mL/m^2	79	85
Females	≥90 mL/m^2	89	97
or RV ejection fraction	≤45 percent		

The diagnosis of ARVC is most commonly made in patients with suspicious clinical manifestations (eg, palpitations, ventricular tachyarrhythmias, etc) using information obtained from surface ECG and cardiac imaging (typically echocardiography with or without CMR).

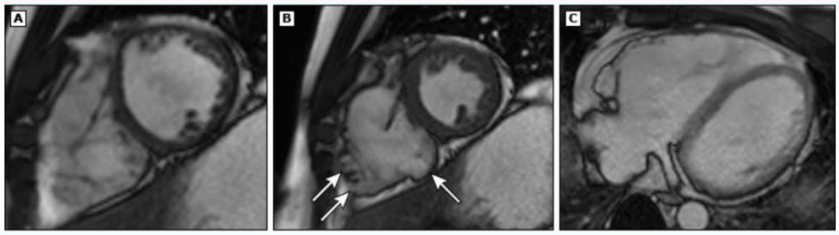
12-lead electrocardiogram (ECG) showing epsilon wave and T wave inversions in arrhythmogenic right ventricular cardiomyopathy (ARVC)



Twelve lead electrocardiogram in a patient with arrhythmogenic right ventricular cardiomyopathy (ARVC) showing deep T wave inversions in V2 to V4, compatible with right ventricular disease, and epsilon waves representing delayed right ventricular depolarization just after the QRS complex (arrows).



CMR in patient with ARVC



(A) End diastole, short-axis cine bright blood image.
(B) End systole, short-axis image from same level as (A). Arrows – dyskinetic regions in the lateral and inferior walls.
(C) End diastole, axial cine image showing dilated RV.

The diagnosis of ARVC can be challenging, requiring a high degree of clinical suspicion and frequently multiple diagnostic tests or procedures to arrive at the correct diagnosis. Because many of the clinical findings and test results have reduced sensitivity and / or specificity for ARVC, diagnostic criteria have been published by professional societies in an effort to standardize the process of arriving at the correct diagnosis.

References:

1. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Circulation 2010; 121:1533.
2. Saguner AM, Vecchiati A, Baldinger SH, et al. Different prognostic value of functional right ventricular parameters in arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circ Cardiovasc Imaging 2014; 7:230.
3. Kjaergaard J, Hastrup Svendsen J, Sogaard P, et al. Advanced quantitative echocardiography in arrhythmogenic right ventricular cardiomyopathy. J Am Soc Echocardiogr 2007; 20:27.
4. Réant P, Hauer AD, Castelletti S, et al. Epicardial myocardial strain abnormalities may identify the earliest stages of arrhythmogenic cardiomyopathy. Int J Cardiovasc Imaging 2016; 32:593.

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