Αρρυθμιογόνος μυοκαρδιοπάθεια. Πότε επαρκεί και πότε όχι η υπερηχογραφική μελέτη;

NIKOLAOS KADOGLOU
METROPOLITAN HOSPITAL, ATHENS, GREECE
OXFORD UNIVERSITY, UNITED KINGDOM
Arrhythmogenic (right) ventricular cardiomyopathy/dysplasia (ARVC/D)

It is considered to be an inherited disease with autosomal dominant inheritance and variable penetrance and phenotype expression.

It is characterized by a fibrous and fatty replacement of primarily right ventricular (RV) and potentially left ventricular (LV) myocardium, and an increased risk of ventricular arrhythmias and sudden cardiac death (SCD).

It may account for up to 25% of exercise-related SCD in young individuals.

Diagnosis has previously been based on the revised 2010 Task Force criteria involving different categories: Imaging, tissue characterization of walls, repolarization abnormalities, depolarization/conduction abnormalities, arrhythmias, family history.

Ackerman MJ et al, Europace 2013; Marcus FI et al Circulation 2010
# ARVC/D Diagnostic Criteria

## Major Echocardiogram/MRI Criteria

**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/m²)
  - PSAX RVOT ≥ 36 mm (corrected for body size [PSAX/BSA] ≥ 21 mm/m²)
  - or fractional area change ≤ 33%

**By MR:**
- Regional RV akinesia or dyskinesia or dyssynchronous RV contraction
- and 1 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 Echocardiogram/MRI Criteria

**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 MR:**
- 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/m² (male) or ≥ 90 to < 100 mL/m² (female)
  - or RV ejection fraction > 40% to ≤ 45%

**Definite diagnosis:** 2 major or 1 major and 2 minor criteria or 4 minor from different categories

---

*Marcus FI et al Circulation 2010*
ARVC diagnosis – echocardiogram
ARVC diagnosis – echocardiogram
ARVC diagnosis – echocardiogram
ARVC diagnosis – echocardiogram

➢ The echocardiogram is immediately available and may confirm or reject clinical suspicion of ARVC/D.

➢ Requires operator experience and good quality of acoustic window.

The most conspicuous echocardiogram findings:
- RV dilation, isolated RVOT dilation, enhanced moderator band
- Localized aneurysms, decreased fractional area change & akinesia/dyskinesis of the inferior wall and RV apex
- RA dilation
ARVC relative screening - echocardiogram

Clinical examination / history
ECG

**Echocardiogram**
Signal average ECG
Ambulatory ECG recording (holter)
CMR
Genetic testing?
ARVC diagnosis / prognosis – novel echocardiogram techniques

Contrast echocardiogram improves endocardial border delineation and enhances RV opacification – systolic function estimation

Perhaps 3D reconstruction and novel indices are required beyond 2D echocardiogram images
ARVC diagnosis / prognosis – novel echocardiogram techniques

The new **3D-based technique** is promising and has shown lower inter-individual variability than 2D measurements.

**BUT many patients do not offer adequately good acoustic windows** that allow the entire RV evaluation by 3D.
ARVC diagnosis / prognosis – novel echocardiogram techniques

2D – strain: segmental strain analysis was able to define the presence of impaired RV function in ARVC patients which otherwise would have been missed by current standard parameters.
Imaging in ARVC

- Diagnostic challenge
- Overemphasis to Imaging may be problematic
- RV Imaging – not the gold standard

<table>
<thead>
<tr>
<th></th>
<th>TTE</th>
<th>CMR</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial resolution</td>
<td>0.5–1 mm</td>
<td>1–2 mm</td>
<td>0.5 mm</td>
</tr>
<tr>
<td>Temporal resolution</td>
<td>15–60 ms</td>
<td>25–50 ms</td>
<td>50–100 ms</td>
</tr>
<tr>
<td>Availability</td>
<td>++</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Low cost</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Functional analysis</td>
<td>+</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Radiation dose</td>
<td>None</td>
<td>None</td>
<td>Moderate for cine CT (5–10 mSv)</td>
</tr>
<tr>
<td>Tissue characterization</td>
<td>N/A</td>
<td>++ (fat/water/fibrosis)</td>
<td>+ (fat)</td>
</tr>
<tr>
<td>Remarks</td>
<td>RV imaging requires special emphasis/expertise; cardiac devices are acceptable</td>
<td>Not influenced by habitus; sensitive to arrhythmia; generally not compatible with cardiac devices</td>
<td>Sensitive to arrhythmia; cardiac devices are acceptable</td>
</tr>
</tbody>
</table>
Pitfalls of echocardiogram, where CMR may be preferable for ARVC/D diagnosis

1. **Quality of acoustic window** → lower diagnostic accuracy of TTE and limited reproducibility.

2. **Operator’s experience** → affects sensitivity of echocardiogram to detect subtle regional RV wall abnormalities.

3. **Complex RV shape and probe angulation** → inherently difficult to assess both the size and systolic function in a reproducible fashion in 2D images.

4. **Indices of RV systolic function** → 2D plane, regionally affected.

Gotschy A et al EHJ Cardiov Imag 2018; Borquist R et al EHJ Cardiov Imag 2014
ARVC diagnosis – Pros and cons of cardiac MRI (CMR)

1. Better visualization of RVOT and RV free wall, non operator-dependent in experienced centers → More accurate assessment of RV size and function, even in extreme thinning and akinesis of the RV free wall.

Normal RV free wall may be about 3 mm thick, making the test less sensitive.

2. Fat has increased intensity in T1-weighted images → Fatty infiltration of the RV free wall can be visible on CMR.

Difficult to differentiate intramyocardial and epicardial fat - adjacent to the normal heart.

LGE → fibrosis assessment – risk of SCD
ARVC diagnosis – fat characterization by cardiac MRI (CMR)

Murphy DT et al Am J Roentgen 2010
CMR may be preferable over echocardiogram for ARVC/D diagnosis

A significant proportion of patients with imaging-positive ARVC by CMR did not fulfil echocardiographic ARVC 2010 criteria.

**On the other hand...** applying CMR data as the ‘gold standard’ may lead to over-diagnosing of small regional abnormalities in the RV.

### Table 6
ARVC minor or major diagnostic imaging criteria by echocardiography or CMR in probands only

<table>
<thead>
<tr>
<th></th>
<th>CMR negative</th>
<th>CMR positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative (n)</td>
<td>11</td>
<td>30</td>
<td>41</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>6</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td>positive (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>63</td>
<td>80</td>
</tr>
</tbody>
</table>

Diagnostic performance for echocardiography when compared with CMR. PPV 85%, NPV 27%, sensitivity 52% and specificity 64%. $P = 0.21$.

### Table 4
ARVC minor or major diagnostic imaging criteria by echocardiography or CMR (as defined by 2010 Task Force criteria)

<table>
<thead>
<tr>
<th></th>
<th>CMR negative</th>
<th>CMR positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative (n)</td>
<td>21</td>
<td>36</td>
<td>57</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>9</td>
<td>36</td>
<td>45</td>
</tr>
<tr>
<td>positive (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>72</td>
<td>102</td>
</tr>
</tbody>
</table>

Diagnostic performance for echocardiography when compared with CMR. PPV 80%, NPV 37%, sensitivity 50% and specificity 70%. $P = 0.06$.
ARVC subtypes – imaging techniques not only focused on the right...

Three subtypes have been proposed:
1. the classical right-dominant subtype
2. biventricular forms
3. left-dominant subtypes with predominant LV involvement.

Te Riele A et J C MR 2019
Case ARVC/D

➢ 38 M

➢ Personal history: SoB on walking flat ground (NYHA II). **Syncope on sitting position (2015)**

➢ Family history: Father – SCD (44y), mother death (36y) after the delivery of the 3\textsuperscript{rd} child, sister passed away after pulmonary oedema (16y), brother syncopes but never seek for medical attendance (**1minor?**)

➢ CV risk factors: Diabetes, Hypertension, Hyperlipidemia, Obesity (BMI=38kg/m2)

➢ ECG: SR, T-wave inversion in right precordial leads V1-V3 (**1major**)
Case ARVC/D
Case ARVC/D

➢ Echocardiogram: Dilated RV with free-wall akinesia, RVOT SAX: 44mm. LV normal **(1 major)**

➢ 24h ambulatory ECG: SR, 4512 VEs, 1 episode NSVT **(1 minor)**

➢ Coronary angiogram: Non-obstructed coronaries

➢ Genetic testing: Plakophilin-2 and desmoplakin mutations **(1 major)**

➢ EPS: Monomorphic VT

➢ ICD implantation & interrogation: Frequent NSVT episodes; 1 appropriate shock

➢ Medications: Enalapril 20mg x2, Bisoprolol 5mg x1, Atorvastatin 20mg x1, Fenofibrate 145mg x1, Furosemide 40mg x1
Case ARVC/D

Indexed RV end-diastolic volume = 208 ml/m², RVEF 27%
Case ARVC/D

38 male with ARVC gene, syncope, ICD implantation and strong family of SCD
Case ARVC/D
Take home messages

➢ Echocardiogram still remains the first diagnostic choice in ARVC/D with significant limitations.

➢ From one hand, it is important to identify asymptomatic patients with subtle structural changes. This maximizes prevention benefits.

➢ From the other hand, in subjects with non-specific symptoms and/or subtle abnormalities, there is also a risk of over-diagnosing disease.

➢ More unambiguous imaging data are required from large-scale studies.

*Echocardiogram and CMR are not competitive but complementary techniques to maximize sensitivity and specificity for correctly diagnosing ARVC/D*