Update on use of cardiac MRI in ARVC/D

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Outline

• Background
• Diagnosis
• Characteristic imaging findings
• Genetics of ARVC
  – Genotype – phenotype correlation
  – LV predominant ARVC
• Pitfalls and mimics
  – Evaluation of RV fat
  – Normal RV structural variants
  – Sarcoidosis
• Role of cardiac MRI in treatment of ARVC
  – DCE for scar mapping prior to ablation
Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

- Rare inherited genetic disorder
- Fibrofatty replacement of the right ventricular myocardium
- Electrical and structural abnormalities of the right ventricle
- Sudden cardiac death
Epidemiology

- Prevalence estimated at 1:1000 – 1:5000
- 20% of sudden death in young athletes
- Male > female
- Age typically 20s-30s at presentation
Clinical

- Palpitations, dizziness, or syncope most common
- Sudden death may be first presentation
- Family history of sudden death
- ECG abnormalities, PVC’s on Holter monitoring, NSVT of LBBB morphology
Diagnosis

- Diagnostic challenges are well known, particularly in early disease and screened family members.

- In one series, of 89 patients referred to a tertiary care center for the diagnosis of ARVC, only 27% met criteria after expert evaluation.\(^\dagger\)

- Differential includes normal, RVOT tachycardia, sarcoidosis, and myocarditis.

Task Force Criteria

- Task Force Criteria (TFC) for diagnosis established major and minor criteria in 1994 and revised 2010
  - Personal history of SCD
  - Family history of ARVC or sudden death
  - Genetic testing results
  - EKG and Holter findings
  - Non-invasive imaging
  - Biopsy
TFC 2010: MRI Criteria

QUANTITATIVE

RV Regional Wall Motion Abnormality
*Dyskinesia, Akinesia, Dyssynchronous Contraction*

AND

QUALITATIVE

Reduced RV Function (↓EF)

*or*

RV Dilation (↑RVEDV)
MAJOR

By MRI:
- Regional RV akinesia or dyskinesia or dyssynchronous RV contraction
- and 1 of the following:
  - Ratio of RV end-diastolic volume to BSA $\geq 110$ mL/m$^2$ (male) or $\geq 100$ mL/m$^2$ (female)
  - or RV ejection fraction $\leq 40$

MINOR

By MRI:
- Regional RV akinesia or dyskinesia or dyssynchronous RV contraction
- and 1 of the following:
  - Ratio of RV end-diastolic volume to BSA $\geq 100$ to $< 110$ mL/m$^2$ (male) or $\geq 90$ to $< 100$ mL/m$^2$ (female)
  - or RV ejection fraction $> 40\%$ to $\leq 45\%$
Figure 2. Proportional Incidence of Original and Revised ARVC Criteria

The graph shows the different incidence of patients with major criteria, minor criteria, or without criteria according to the original cardiac magnetic resonance criteria (green bars) and the revised criteria (orange bars). Abbreviation as in Figure 1.
MRI Findings in TFC Positive ARVC
24M Marine who presented with sustained ventricular tachycardia (HR 230) after a workout
24M Marine who presented with sustained ventricular tachycardia (HR 230) after a workout; genetic testing negative
14F with SCD during volleyball game, resuscitated
gene positive
Genetics

- Mutations in genes encoding desmosomal proteins
- Autosomal dominant inheritance pattern
- Variable penetrance and severity
- ~50-60% of patients will have a gene identified
Genotype – Phenotype Correlation

- **Desmoplakin (DSP):**
  - severe course
  - LV abnormalities >> RV in many patients
  - more common mutation in some European cohorts

- **Plakophilin-2 (PKP2)**
  - Most common mutation in U.S. cohorts
  - Classical RV dominant disease most common phenotype
  - Biventricular involvement seen, but typically RV more severely affected
Left ventricle in ARVC

• LV involvement increasingly recognized

• >80% of a 200 patient cohort from the U.K. showed evidence of LV pathology†

• Others have seen prevalence of LV pathology in ARVC as low as 16%‡

• Delayed enhancement, fat, LV dilation, and reduced function may be seen

†Circ 2007;115:1710-20
‡JACC 1997;30:1512-20
30F with palpitations and syncope
Mutation positive (DSG2)

49F with syncope and abnormal EKG
Mutation positive (DSP)
Pitfalls and mimics of ARVC

- Misdiagnosis is common and lead to inappropriate ICD implantation

- Often, the incorrect diagnosis hinges on MRI findings

- Qualitative MRI findings (particularly RV fat and regional wall motion abnormalities) may lead to diagnosis

- Clinicians often unaware of the TFC criteria
Johns Hopkins ARVD/C Program

• Established in 1999 to care for patients with ARVD/C and to systematically study the disease

• Many of these patients are referred from outside institutions to our ARVD/C program for re-evaluation

• A recurring pattern of mistakes leads to the majority of misdiagnoses
Intramyocardial fat

- Notoriously difficult to diagnose
- Overlap between ARVC and physiologic fat infiltration
- Among those misdiagnosed by MRI, fat was the only reported abnormality 77% of the time†
- In one study, presence of fat infiltration was the same among controls, suspected ARVC, and definite ARVC patients‡

† J Cardiovasc Electrophysiol 2004;15:300-6
‡ JACC 1997;30:1512-20
57M with sister who had SCD and ARVC at autopsy; Multiple PVCs and PKP2 mutation
57M with sister who had SCD and ARVC at autopsy; Multiple PVCs and PKP2 mutation
57M with sister who had SCD and ARVC at autopsy; Multiple PVCs and PKP2 mutation
Physiologic fat

48F evaluated for suspected shunt with normal MRI
Pitfalls in assessment of RV wall motion abnormalities
Normal RV wall motion

- High prevalence of subjective RV wall motion abnormalities at CMR in normal patients that can be mistaken for ARVD/C
  - 29 healthy subjects underwent CMR: 93% had “disordered” RV wall motion
    - Most commonly on axial images (86%)
    - 79% involved the apicolateral wall
  - 30 healthy volunteers were evaluated at Johns Hopkins, focal systolic outpouching of the apicolateral free wall was seen in 63% of patients with axial views and 10% with horizontal long axis views

Sievers et al. J Cardiovasc Mag Reson 2004
Fritz et al. J Comput Assist Tomogr 2005
Pectus excavatum

- Restricted motion of the basolateral and inferolateral walls.
- Narrowed base and enlarged apex give the appearance of intrinsic focal wall motion abnormality. There is a banana-shaped RV.
RV tether
Sarcoidosis mimicking ARVC
Sarcoidosis and ARVC

- Sarcoid can present with RV predominant involvement; may meet criteria for ARVC
- Numerous case reports exist documenting patients misdiagnosed with ARVC, but with sarcoid on biopsy
- In a small cohort of 20 consecutive patients with probable or definite ARVC, 3 had eventual diagnosis of sarcoidosis†

† J Cardiovasc Electrophysiol 2009;20:473-6
## Imaging sarcoidosis vs. ARVC

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CS (n = 40)</th>
<th>ARVC (n = 21)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>66 ± 14</td>
<td>55 ± 10</td>
<td>0.073</td>
</tr>
<tr>
<td>Left ventricular mass (g)</td>
<td>129 ± 18</td>
<td>130 ± 38</td>
<td>0.425</td>
</tr>
<tr>
<td>Left ventricular systolic volume (cm³)</td>
<td>36 ± 16</td>
<td>72 ± 31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular diastolic volume (cm³)</td>
<td>103 ± 3</td>
<td>155 ± 42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right ventricular ejection fraction (%)</td>
<td>49 ± 11</td>
<td>40 ± 9</td>
<td>0.017</td>
</tr>
<tr>
<td>Right ventricular mass (g)</td>
<td>78 ± 30</td>
<td>80 ± 34</td>
<td>0.618</td>
</tr>
<tr>
<td>Right ventricular systolic volume (cm³)</td>
<td>62 ± 29</td>
<td>104 ± 42</td>
<td>0.002</td>
</tr>
<tr>
<td>Right ventricular diastolic volume (cm³)</td>
<td>124 ± 44</td>
<td>176 ± 63</td>
<td>0.004</td>
</tr>
<tr>
<td>Delayed enhancement</td>
<td>29 (73%)</td>
<td>4 (19%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Short inversion time inversion-recovery</td>
<td>16 (40%)</td>
<td>3 (14%)</td>
<td>0.047</td>
</tr>
<tr>
<td>Right ventricular involvement</td>
<td>19 (48%)</td>
<td>21 (100%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Isolated right ventricular involvement</td>
<td>8 (20%)</td>
<td>16 (76%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular involvement</td>
<td>25 (63%)</td>
<td>5 (24%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Isolated left ventricular involvement</td>
<td>21 (53%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mediastinal lymphadenopathy</td>
<td>27 (68%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal involvement</td>
<td>17 (43%)</td>
<td>0</td>
<td>0.001</td>
</tr>
<tr>
<td>Septal or mediastinal lymphadenopathy or isolated left ventricular involvement</td>
<td>38 (95%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
46M with multisystemic sarcoidosis and arrhythmia
Cardiac MRI and Treatment
Figure 5. Agreement analysis of wall motion abnormalities identified by cine cardiac magnetic resonance (CMR) with electro-anatomical scar (EAS) and delayed contrast enhancement (DCE) scars for different right ventricular (RV) regions. Gray bars indicate the level of agreement between wall motion abnormalities (WMAs) identified by cine-CMR and EAS; black bars, level of agreement between WMA and DCE. *P values were obtained using a χ² contingency table.
Conclusions

- MRI is useful to assess structural abnormalities in suspected ARVD
- Both quantitative and qualitative abnormalities should be present to meet diagnostic criteria
- Left ventricular involvement in ARVD is increasingly recognized and is increased for certain genotypes
- Several commonly normal variants of RV motion on cardiac MRI can lead to misdiagnosis
- Sarcoidosis should be considered in the differential of ARVD