Progression of definite and non-definite Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) and risk of major adverse cardiac events

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Background: In patients with Arrhythmogenic right ventricular cardiomyopathy (ARVC, also called"Arrhythmogenic Cardiomyopathy"), it is a challenge to predict those at greatest risk of major adverse cardiac events (MACE). Our hypothesis is that risk of arrhythmia may be preceded by change in ventricular structure and function.

Purpose: To assess the association between change in ventricular structure and function over time and risk of (MACE) in ARVC.

Methods: 101 definite and non-definite ARVC patients (defined as per Revised Task Force criteria (TFC)) were included with at least two sequential echocardiography and ECGs between 2010 and 2022. Structural progression was defined as development of new 2010 TFC on echocardiography during follow-up. MACE were defined as ventricular fibrillation (VF), sustained ventricular tachycardia (Sus VT), appropriate implantable cardio-defibrillator (ICD) therapy (shock/anti-tachycardia pacing (ATP)), heart failure, cardiac transplantation and death.

Results: Of the 101 patients, 51 had a definite diagnosis of ARVC, and 50 had a non-definite 'early' diagnosis, of whom a total of 66 (68%) carried a pathogenic variant associated with ARVC. Most were male 58 (57%), and the median age at presentation was 39 years (IQR: 27 - 53). Palpitations 41 (41%) and syncope 25 (25%) were the most common symptoms at baseline. 21 (23%) of the entire population were engaged in competitive exercise. At baseline, 22/101 (22%) patients presented with MACE, in which 20 (91%) definite patients met either minor or major imaging criteria at inclusion. During 4 years follow up (IQR: 2 – 6), 22 patients experienced MACE, in which 11 with history of MACE and 11 without, of those (15 (68%)) had structural progression. Additionally, 9 patients had structural progression of which 5 patients had history of MACE and no second event during follow up and 4 patients had no MACE at baseline or during follow up. Results showed that the odds of structural progression were significantly higher in patients with MACE than without (Table 1).

Conclusion: Structural progression was strongly associated with MACE events. This finding raises the possibility that tracking change over time identifies those patients at greatest risk of arrhythmia, with significant changes in right ventricular measurements.
<table>
<thead>
<tr>
<th>Markers</th>
<th>With MACE (n=33)</th>
<th>Without MACE (n=68)</th>
<th>Univariable OR (95% CI)</th>
<th>P value</th>
<th>Multivariable OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVOT PLAX (cm)</td>
<td>3.56 (0.86)</td>
<td>2.77 (0.54)</td>
<td>6.49 [2.87;14.66]</td>
<td>&lt;0.001</td>
<td>5.63 [1.18;26.74]</td>
<td>0.029</td>
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<tr>
<td>RVOT PSAX (cm)</td>
<td>3.74 (0.72)</td>
<td>3.04 (0.51)</td>
<td>6.70 [2.74;16.40]</td>
<td>&lt;0.001</td>
<td>3.15 [1.07;9.28]</td>
<td>0.037</td>
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<tr>
<td>RVFAC (%)</td>
<td>32.82 (9.68)</td>
<td>46.55 (7.19)</td>
<td>0.83 [0.77;0.89]</td>
<td>&lt;0.001</td>
<td>0.85 [0.77;0.93]</td>
<td>0.001</td>
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<tr>
<td>LVEF (%)</td>
<td>50.86 (16.23)</td>
<td>62.86 (5.67)</td>
<td>0.85 [0.77;0.94]</td>
<td>0.001</td>
<td>0.87 [0.75;1.01]</td>
<td>0.080</td>
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</tbody>
</table>

Structural progression

<table>
<thead>
<tr>
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<th>No</th>
<th>Yes</th>
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<tbody>
<tr>
<td>No</td>
<td>13 (39%)</td>
<td>20 (61%)</td>
</tr>
<tr>
<td>Yes</td>
<td>64 (94%)</td>
<td>4 (6%)</td>
</tr>
</tbody>
</table>

**Abbreviation:** RVOT PLAX: right ventricular outflow tract parasternal long axis; RVOT PSAX: right ventricular outflow tract parasternal short axis; RVFAC: right ventricular fractional area change; LVEF: left ventricular ejection fraction