ARRHYTHMOGENIC RIGHT VENTRICULAR DISPLASIA (ARVD):
recent advances and limitations of diagnostic criteria
ARVD

- Genetic cardiomyopathy
- Fibro-fatty replacement of the right ventricular (RV) musculature
- Ventricular arrhythmias
- RV failure
ARVD - incidence

- 5 % of sudden deaths < 35 in US
- 25 % of exercise related deaths in the Veneto region
- Prevalence estimated 1 / 5000
- Death rate for patients with ARVD – 2,5 % / year
- 2,7 male / 1 female
### ARVD - etiology

- Desmosomal dysfunction
- Sporadic forms
- Familial forms (30 – 80 %)
- Success rate of genotyping < 50 %
- Autosomal dominant inheritance (30 – 50 %)
- Variable phenotype expression
- Naxos Disease
  - Autosomal recessive
  - Greece

<table>
<thead>
<tr>
<th>Type</th>
<th>Chromosomal Locus</th>
<th>Genetic Mutation</th>
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</thead>
<tbody>
<tr>
<td>ARVD1</td>
<td>14q23-q24</td>
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<tr>
<td>ARVD2</td>
<td>1q42-q43</td>
<td>Mutation in the ryanodine receptor, type 2 (RYR2)</td>
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<td>ARVD3</td>
<td>14q12-q22</td>
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<td>ARVD4</td>
<td>2q32.1-q32.3</td>
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<tr>
<td>ARVD5</td>
<td>3p23</td>
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<td>ARVD6</td>
<td>10p14-p12</td>
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<tr>
<td>ARVD7</td>
<td>10q22.3</td>
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<td>ARVD8</td>
<td>6p21</td>
<td>Mutation in desmoplakin</td>
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</tbody>
</table>

Naxos Disease | 17q21 | Mutation in plakoglobin; woolly hair and keratoderma |
ARVD - diagnosis

- 1994 Task Force
- Diagnostic criteria would be fulfilled by the presence of:
  - 2 major criteria or
  - 1 major plus 2 minor criteria or
  - 4 minor criteria

I. Global and/or Regional Dysfunction and Structural Alterations*

**MAJOR CRITERIA:**
1. • Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
2. • Localized right ventricular aneurysms (akineti c or dyskinetic areas with diastolic bulging)
3. • Severe segmental dilatation of the right ventricle

**MINOR CRITERIA:**
1. • Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle
2. • Mild segmental dilatation of the right ventricle
3. • Regional right ventricular hypokinesia

* Detected by echocardiography, angiography, magnetic imaging, or radionuclide scintigraphy
II. Tissue Characterization of Walls

**MAJOR CRITERIA:**

- Fibrofatty replacement of myocardium on endomyocardial biopsy

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**Image:**

- Endo
- Myo
- F
- A
- Epi
III. Repolarisation Abnormalities

MINOR CRITERIA:

- Inverted T waves in right preordial leads (V2 and V3) (people aged>12 years, in absence of right bundle branch block)
IV. Depolarisation/Conduction Abnormalities

MAJOR CRITERIA:
• Epsilon waves or localised prolongation (>110ms) of the QRS complex in right precordial leads (V1-V3)

MINOR CRITERIA:
• Late potentials (signal averaged ECG)
ARVD – 1994 Task Force criteria

V. Arrhythmias

MINOR CRITERIA:
- Left bundle branch block type ventricular tachycardia (sustained and nonsustained) ECG, Holter, exercise testing
- Frequent ventricular extrasystoles (>1000/24 hours) (Holter)

VI. Family History

MAJOR CRITERIA:
- Familial disease confirmed at necropsy or surgery

MINOR CRITERIA:
- Familial history of premature sudden death (<35 years) due to suspected right ventricular dysplasia.
- Familial history (clinical diagnosis based on present criteria)
ARVD – MR Assessment

- Morphological abnormalities
  - Intramyocardial fat
ARVD – MR Assessment

- Morphological abnormalities
  - Intramyocardial fat
ARVD – MR Assessment

- Morphological abnormalities
  - Wall thinning
  - Wall hypertrophy
  - Trabecular disarray
ARVD – MR Assessment

- Morphological abnormalities
  - RVOT enlargement

Axial TSE T1
Functional abnormalities
  - Global RV dilatation / dysfunction

**MAJOR CRITERIA:**
- Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
- Severe segmental dilatation of the right ventricle

**MINOR CRITERIA:**
- Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle
ARVD – MR Assessment

- Functional abnormalities
  - Regional dysfunction

**MAJOR CRITERIA:**
- Localized right ventricular aneurysms (akinetc or dyskinetic areas with diastolic bulging)
ARVD – MR Assessment

- Functional abnormalities
  - Regional dysfunction

MINOR CRITERIA:
- Mild segmental dilatation of the right ventricle
- Regional right ventricular hypokinesia
ARVD – MR Assessment

- Delayed enhancement
  - Most significant advance of the recent years
  - Tandri et al. (2005)
    - 67% patients with ARVD
    - Fibrofatty replacement on biopsy
ARVD suspicion
Identification: Alternative Diagnosis - MR late enhancement

Previous myopericarditis
Previous infarct
Scar on Hypertrophic cardiomyopathy
ARVD – MR Assessment
Limitations - Intramyocardial fat

- Sensitivity and specificity remain unanswered
- Fatty replacement non specific
  - Healthy individuals
  - > 50 % elderly
  - Long term therapy with steroids
  - Other cardiomyopathies
  - Idiopathic ventricular tachycardia
ARVD – MR Assessment
Limitations - Intramyocardial fat

- Current spatial resolution is not enough to detect subtle RV intramyocardial fat
- Differentiation with normal epi and pericardial fat
ARVD – MR Assessment
Limitations

- Difficult triggering
  - Frequent extra-systoles
  - Poor image quality
- Insufficient resolution
  - Detect thinning of the 4-5 mm RV free wall
ARVD – MR Diagnosis

- MR
  - Most common reason for over-diagnosis of ARVD
  - Frustration with inability to provide definitive answers
  - Wide spectrum of phenotype expression
    - RV outflow tract tachycardia
    - Early bi-ventricular disease
ARVD – MR Diagnosis

- RV outflow tract tachycardia and Brugada syndrome
  - occult ARVD
  - diagnosis delayed after initial normal evaluation
  - A negative MR may indicate reevaluation
ARVD – MR Diagnosis

- Early bi-ventricular disease
  - RV wall motion abnormalities
  - Localized LV late enhancement
    - Subepicardial / midwall
    - In concordance with the pattern of fibrofatty substitution
  - Ventricular arrhythmia precede ventricular dysfunction (diferent dilated cardiomyopathy)
ARVD – MR Diagnosis

- Interobserver concordance
  - High (k scores 0.89 – 0.94)
    - Wall thinning
    - Outflow tract dilatation
    - Wall motion abnormalities
    - RV volume and function quantification
  - Low (k = 0.74)
    - Myocardial fatty replacement

Tandri H et al. J Am Coll Cardiol 2006
ARVD – MR Diagnosis

- **UK experience**
  - 2006

<table>
<thead>
<tr>
<th></th>
<th>N = 232</th>
<th>MR sensitivity</th>
<th>MR specificity</th>
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<tbody>
<tr>
<td>Task Force without familial criteria</td>
<td>100 %</td>
<td>29 %</td>
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<tr>
<td>Task Force with familial criteria</td>
<td>100 %</td>
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- **MR may detect disease at an earlier stage than Task Force Criteria**

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<th>Genotype Subset Identification</th>
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<tr>
<td>Task Force Criteria</td>
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<tr>
<td>MR</td>
<td>76 %</td>
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ARVD – MR Diagnosis

- Intramyocardial fat
  - Believed to be the most useful feature
  - Least reliable of all qualitative MR parameters
- Wall motion abnormalities
  - Reproducible among expert readers
- Quantitative volume analysis
  - Relatively robust
- Delayed enhancement
  - LV involvement
  - RV fibrofatty tissue
ARVD – MR Diagnosis

- Predictors of arrhythmic events
  - Structurally severe disease
  - LV involvement
  - Delayed enhancement
ARVD – MR Diagnosis

Conclusions

- Should not be seen as a stand-alone technique for diagnosis
- Help the Task Force guidelines accuracy
  - currently under revision
- Genetic testing does not replace MR evaluation
  - don’t determinate phenotypic expression