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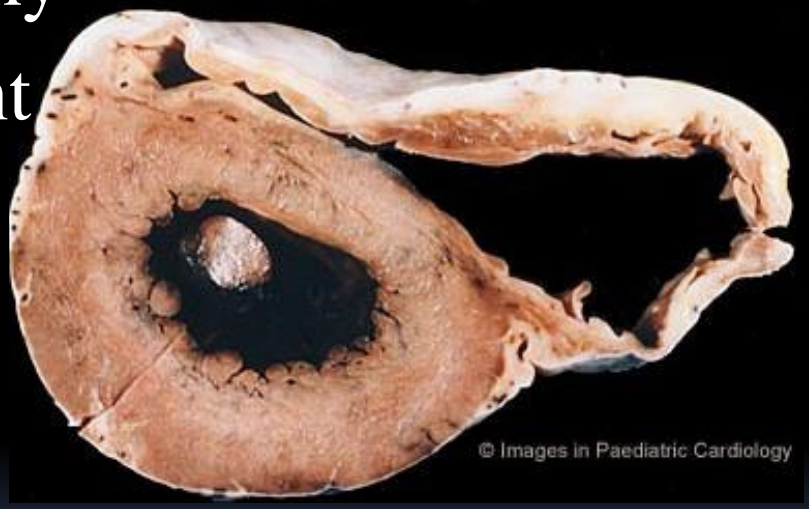
ARRHYTHMOGENIC RIGHT VENTRICULAR DISPLASIA (ARVD): recent advances and limitations of diagnostic criteria

ARVD

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



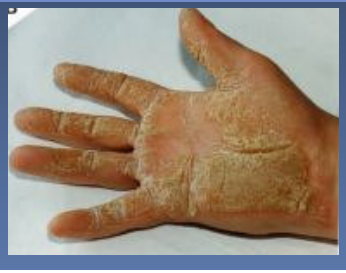
ARVD - incidence

- 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

Type	Chromosomal Locus	Genetic Mutation
ARVD1	14q23-q24	
ARVD2	1q42-q43	Mutation in the ryanodine receptor, type 2 (RYR2)
ARVD3	14q12-q22	
ARVD4	2q32.1-q32.3	
ARVD5	3p23	
ARVD6	10p14-p12	
ARVD7	10q22.3	
ARVD8	6p24	Mutation in desmoplakin
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

McKenna WJ, et al. Br Heart J 1994

ARVD – 1994 Task Force criteria

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

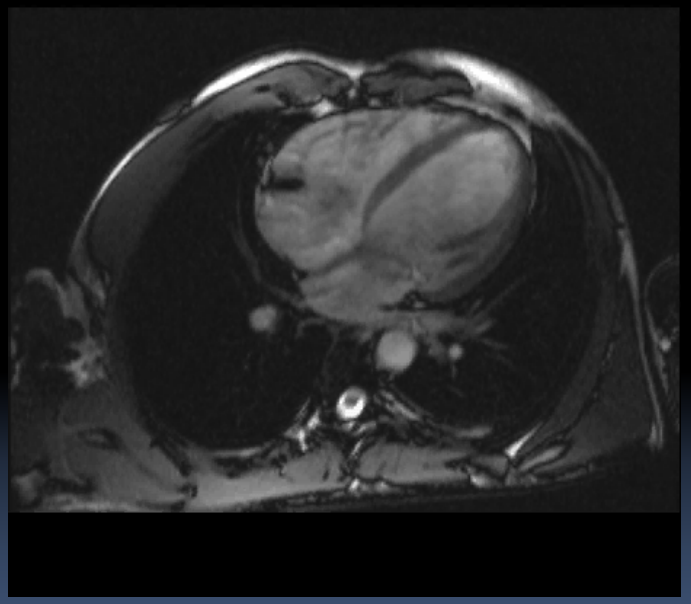
MAJOR CRITERIA:

1. • Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
2. • Localized right ventricular aneurysms (akinetic 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

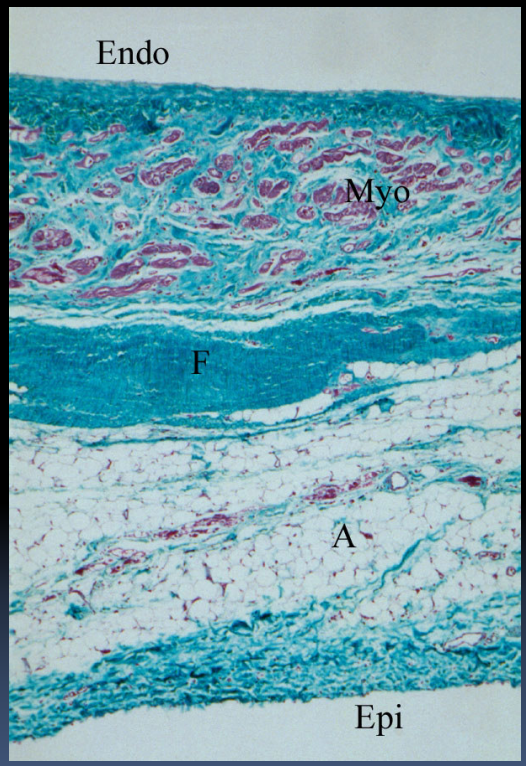


ARVD – 1994 Task Force criteria

II. Tissue Characterization of Walls

MAJOR CRITERIA:

- Fibrofatty replacement of myocardium on endomyocardial biopsy

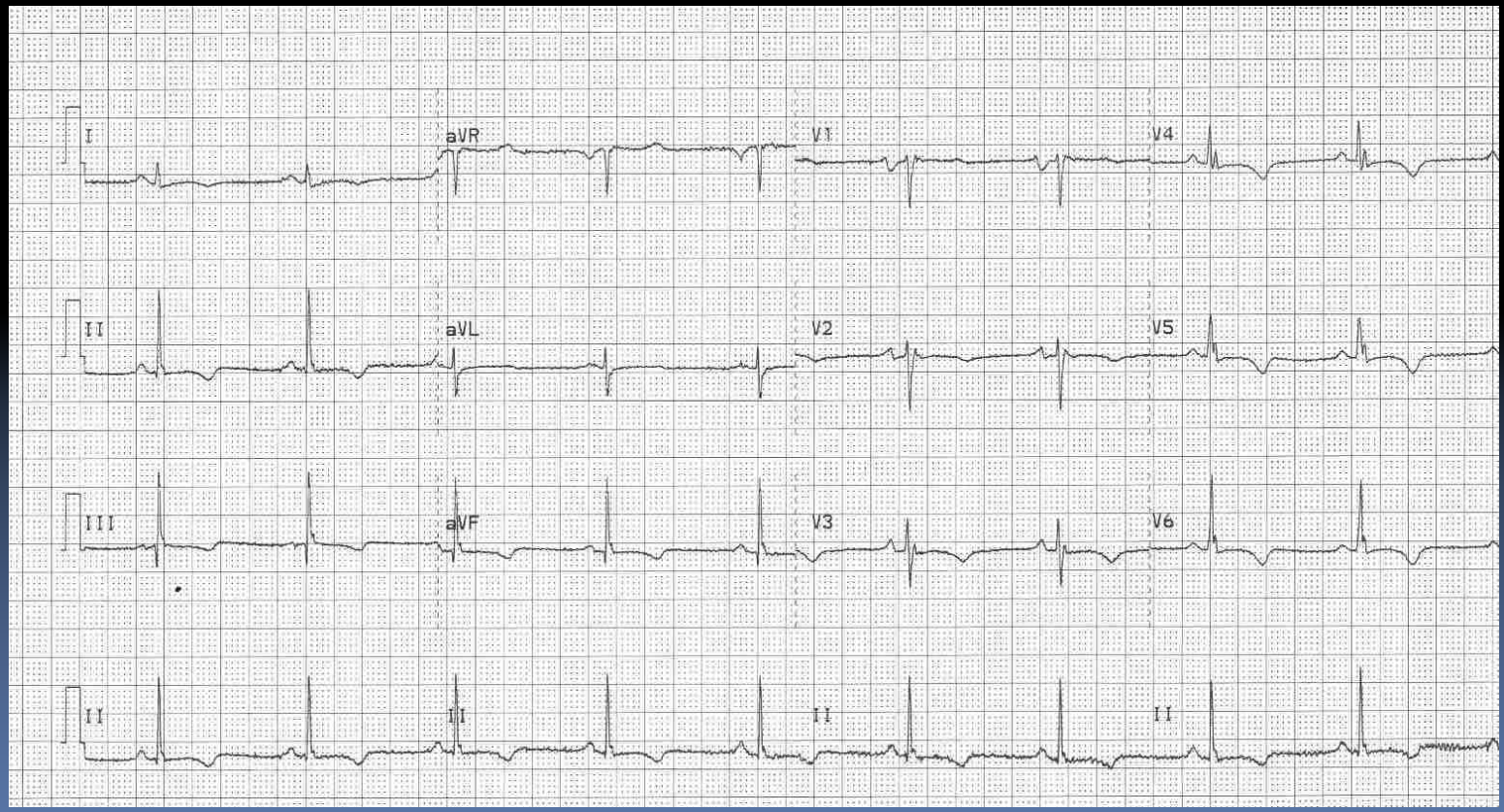


ARVD – 1994 Task Force criteria

III. Repolarisation Abnormalities

MINOR CRITERIA:

- Inverted T waves in right precordial leads (V2 and V3) (people aged>12 years, in absence of right bundle branch block)



ARVD – 1994 Task Force criteria

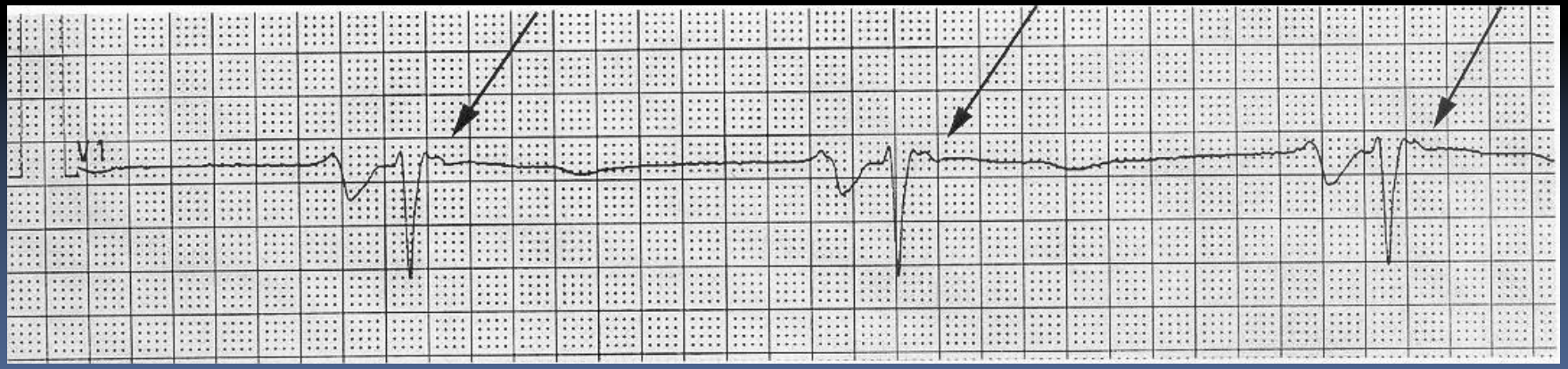
IV. Depolarisation/Conduction Abnormalities

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:

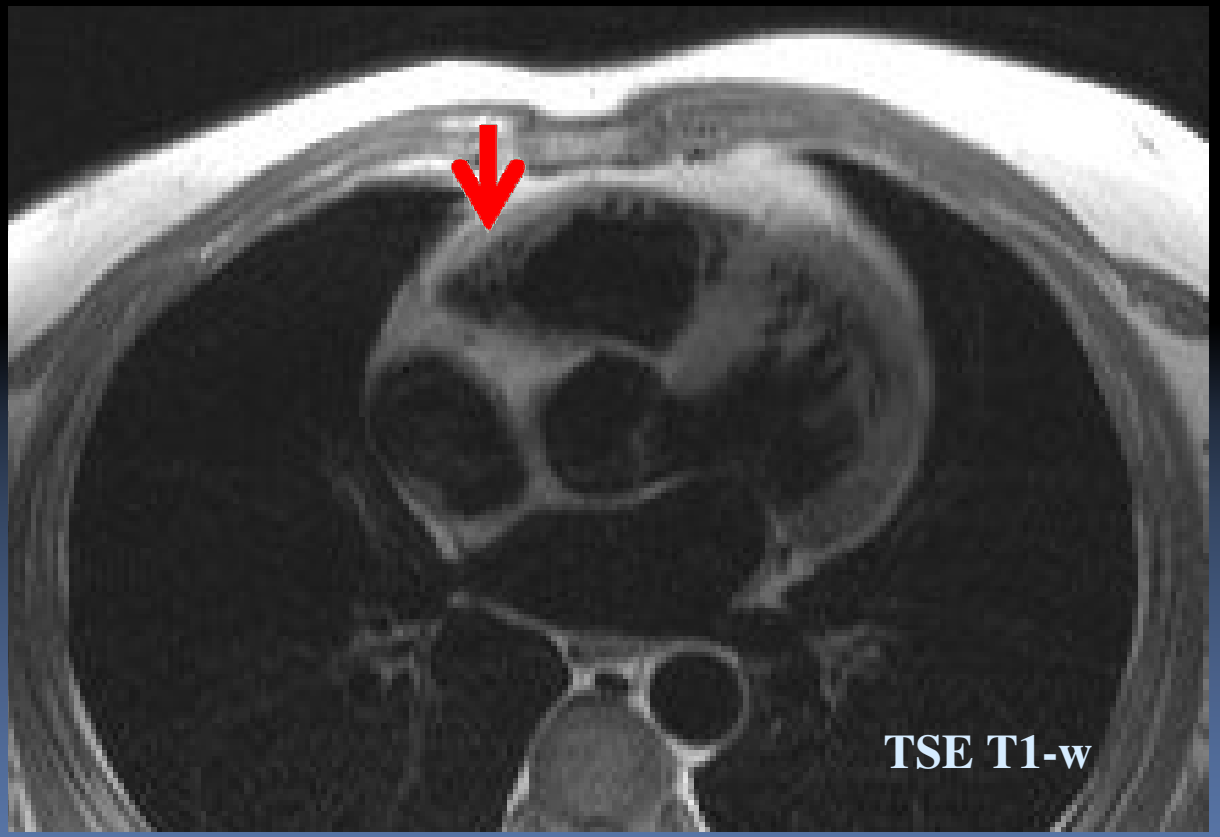
- Familial disease confirmed at necropsy or surgery

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
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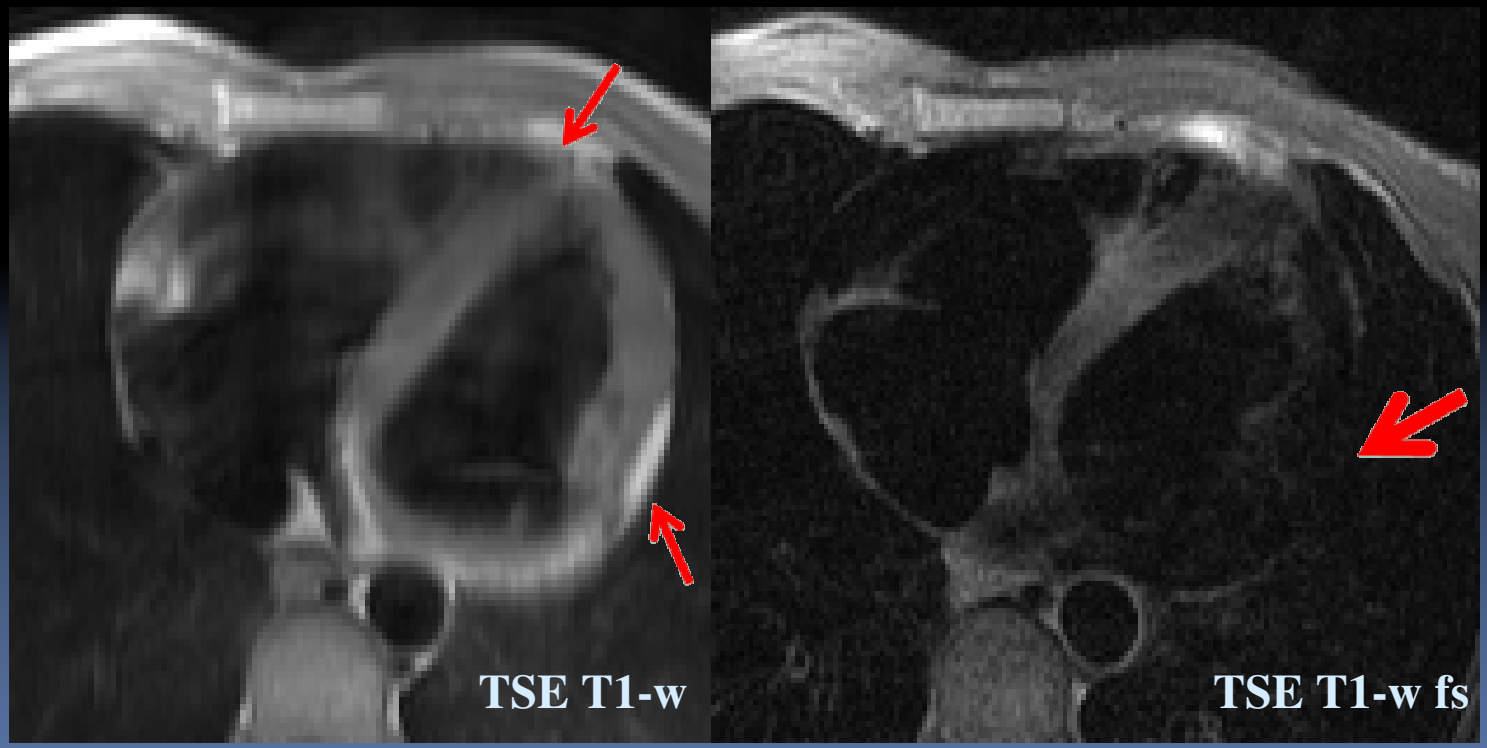
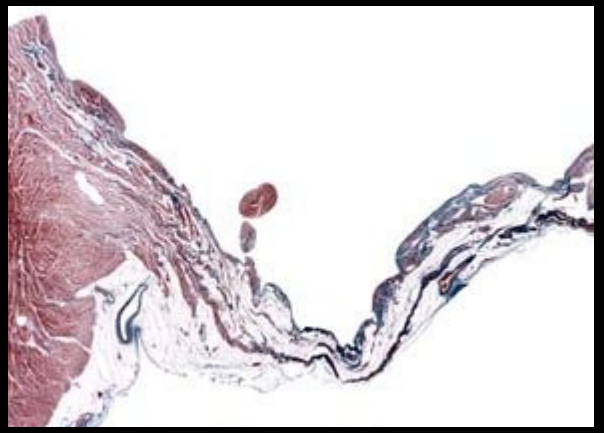
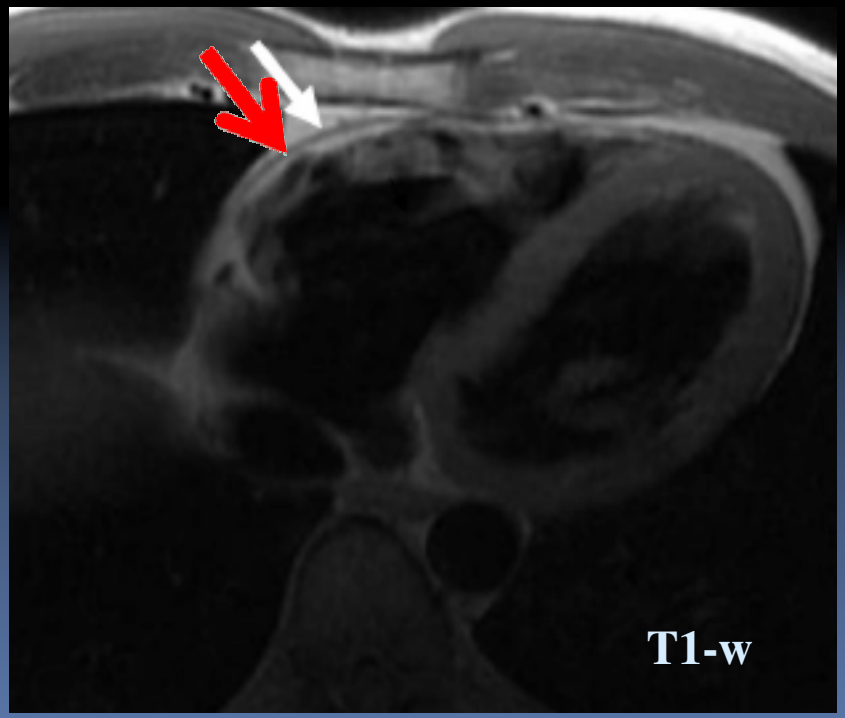


ARVD – MR Assessment

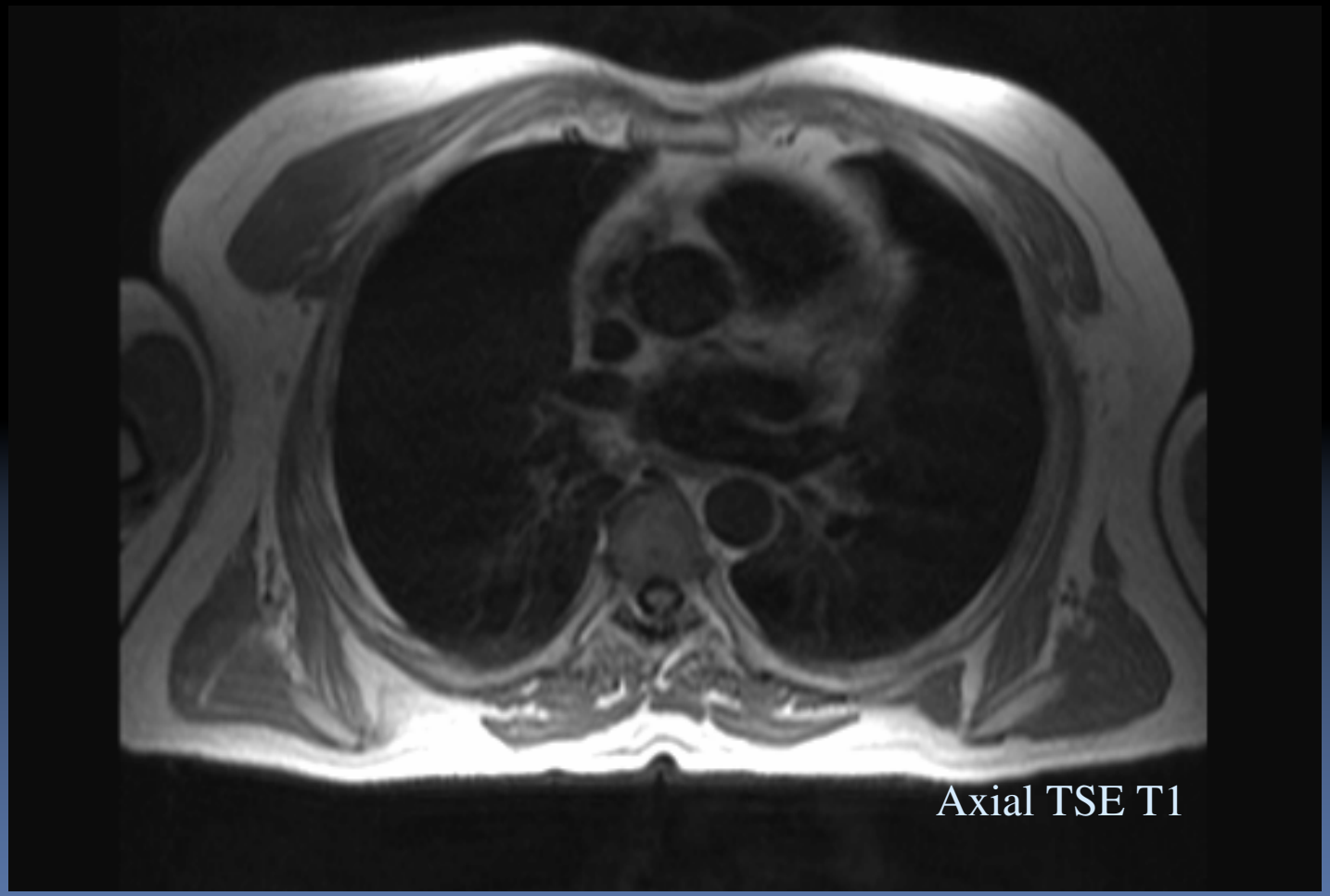
- Morphological abnormalities
  - Wall thinning
  - Wall hypertrophy
  - Trabecular disarray





ARVD – MR Assessment

- Morphological abnormalities
  - RVOT enlargement



ARVD – MR Assessme

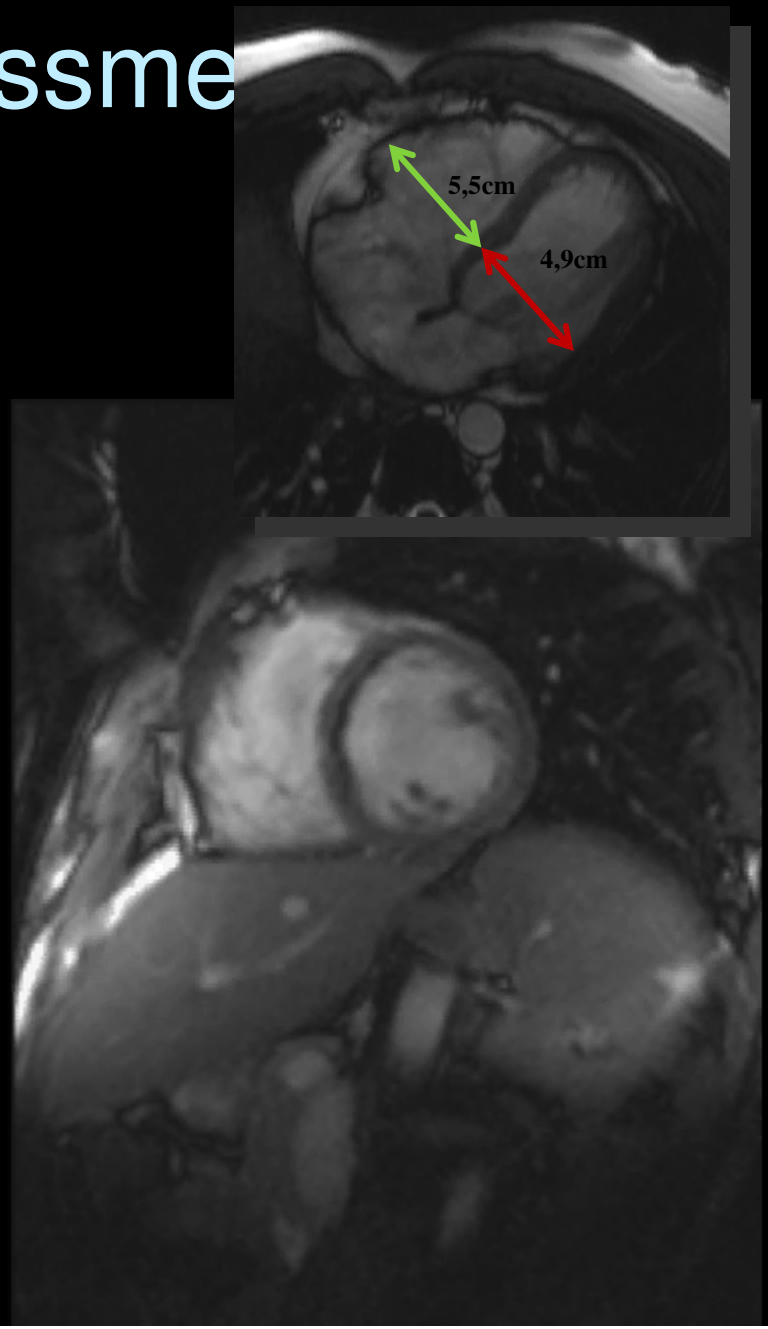
- Functional abnormalities
  - Global RV dilatation / dysfunction

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

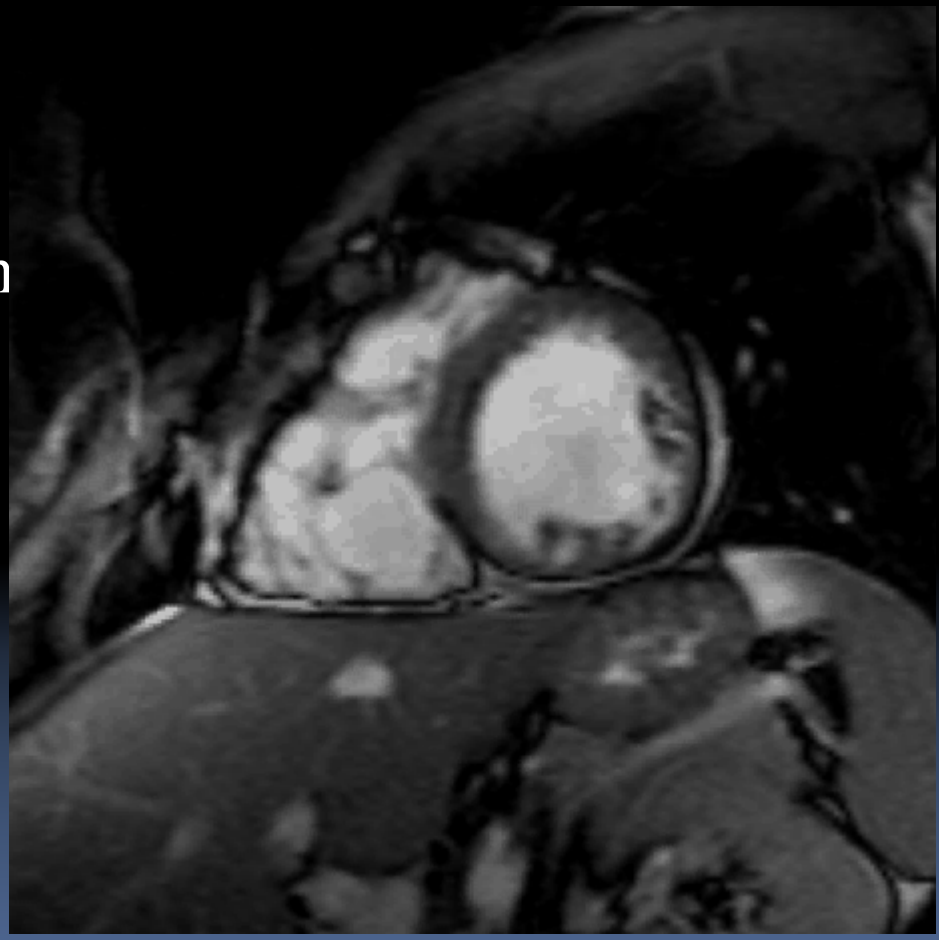


ARVD – MR Assessment

- Functional abnormalities
  - Regional dysfunction

MAJOR CRITERIA:

• Localized right ventricular aneurysms (akinetic or dyskinetic areas with diastolic bulging)

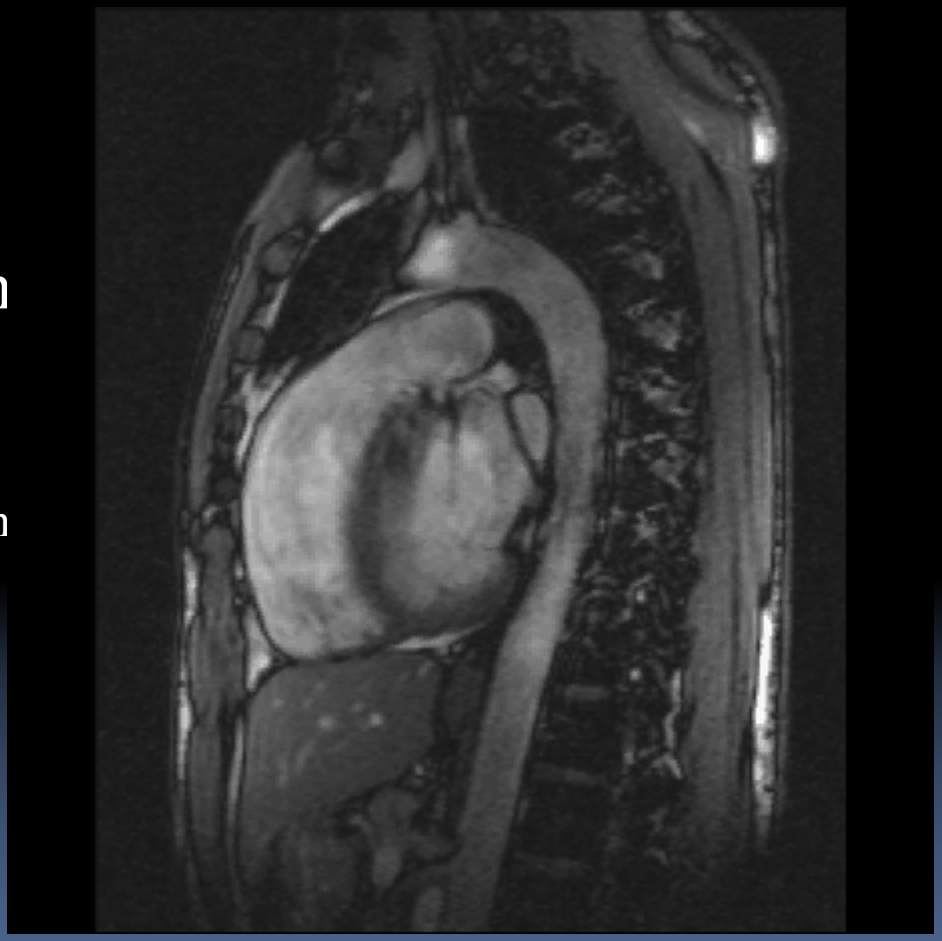


ARVD – MR Assessment

- Functional abnormalities
  - Regional dysfunction

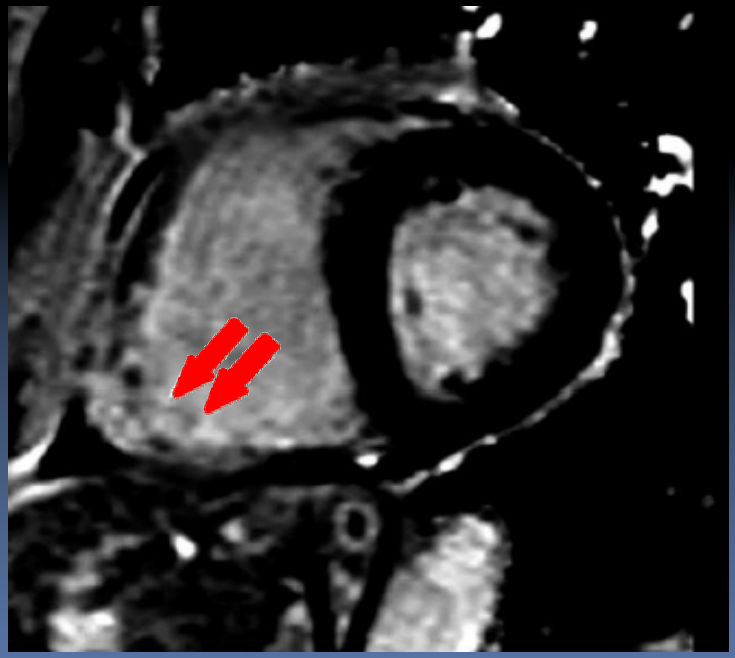
MINOR CRITERIA:

- Mild segmental dilatation of the righ ventricle
- Regional right ventricular hypokinesia



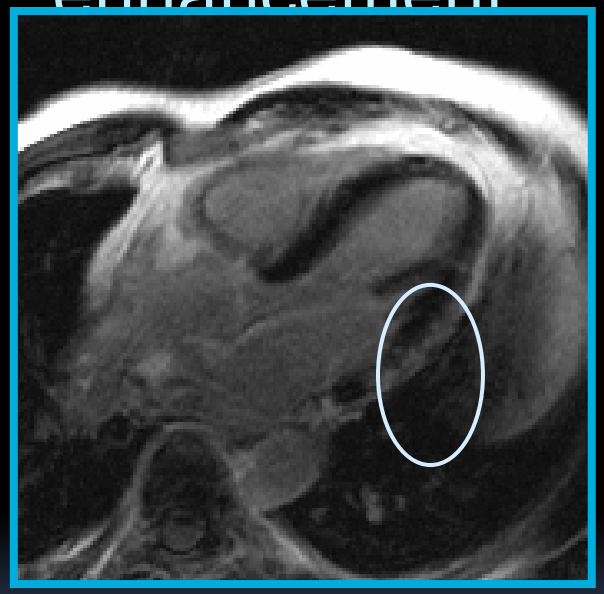
ARVD – MR Assessment

- Delayed enhancement
  - Most significant advance of the recent years
  - Tandri et al. (2005)
    - 67 % patients with ARVD
    - Fibrofatty replacement on biopsy

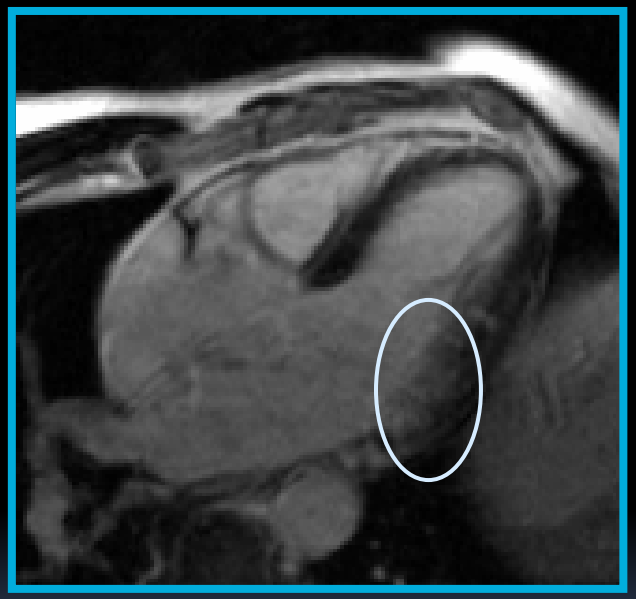


ARVD suspicion

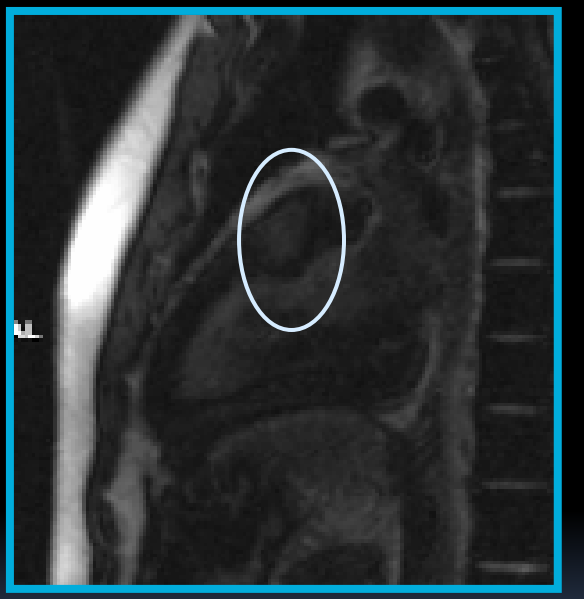
Identification: Alternative Diagnosis - MR late enhancement



Previous myopericarditis



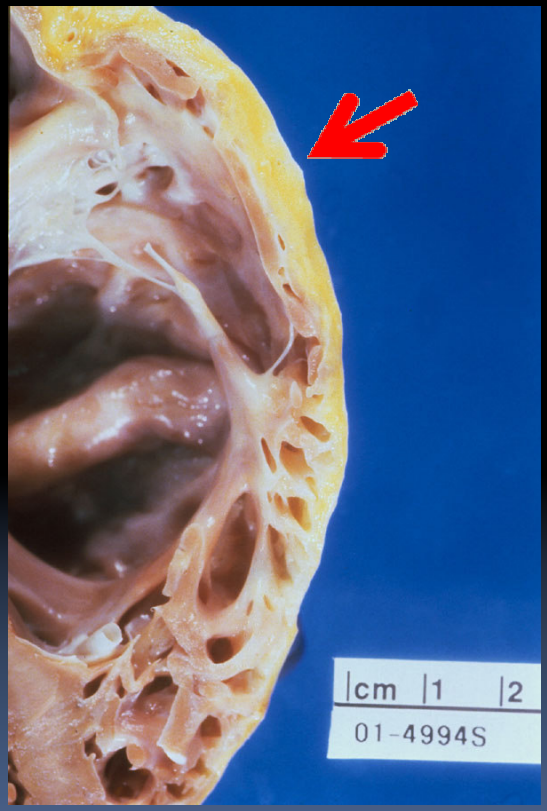
Previous infarct



Scar on Hypertrophic cardiomyopathy

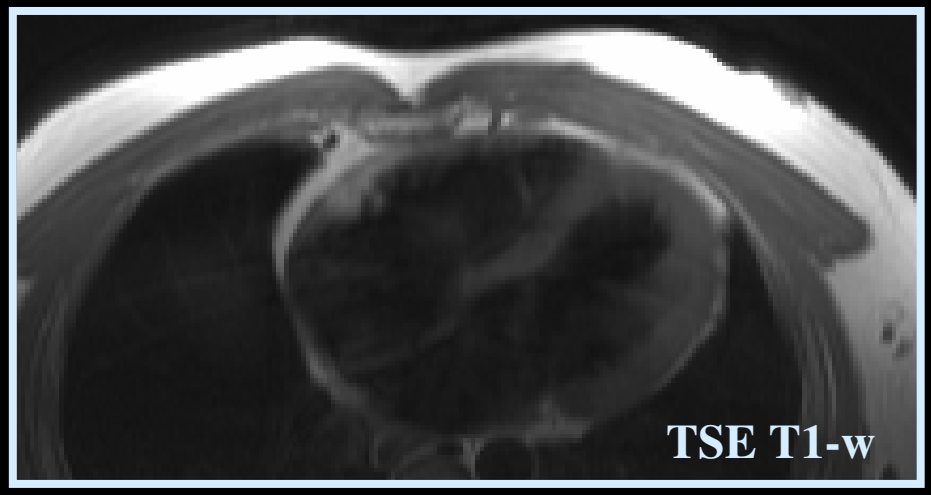
ARVD – MR Assessment
Limitations - Intramyocardial fat

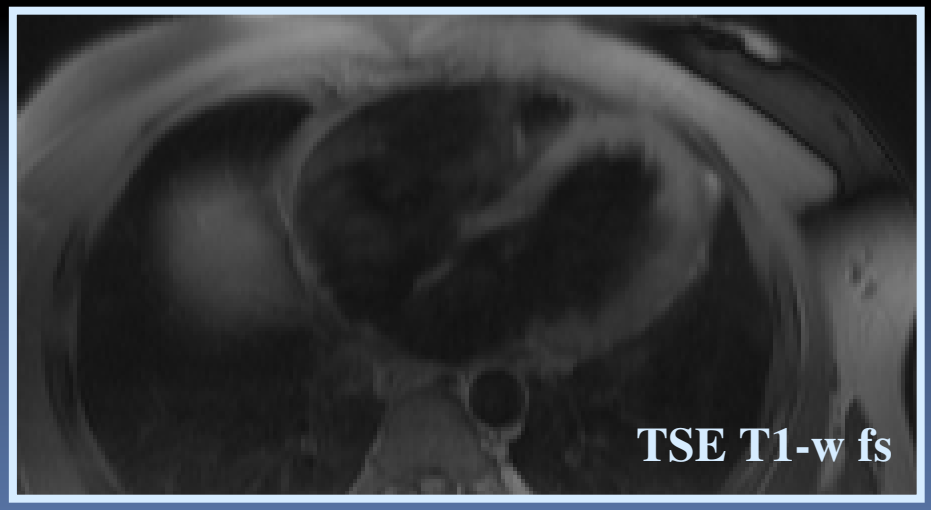
- Sensitivity and specificity remain unanswered
- Fatty replacement non specific
  - Healthy individuals
  - > 50 % elderly
  - Long term therapy with steroids
  - Other cardiomyopathies
  - Idiopathic ventricular tachycardia



ARVD – MR Assessment
Limitations - Intramyocardial fat

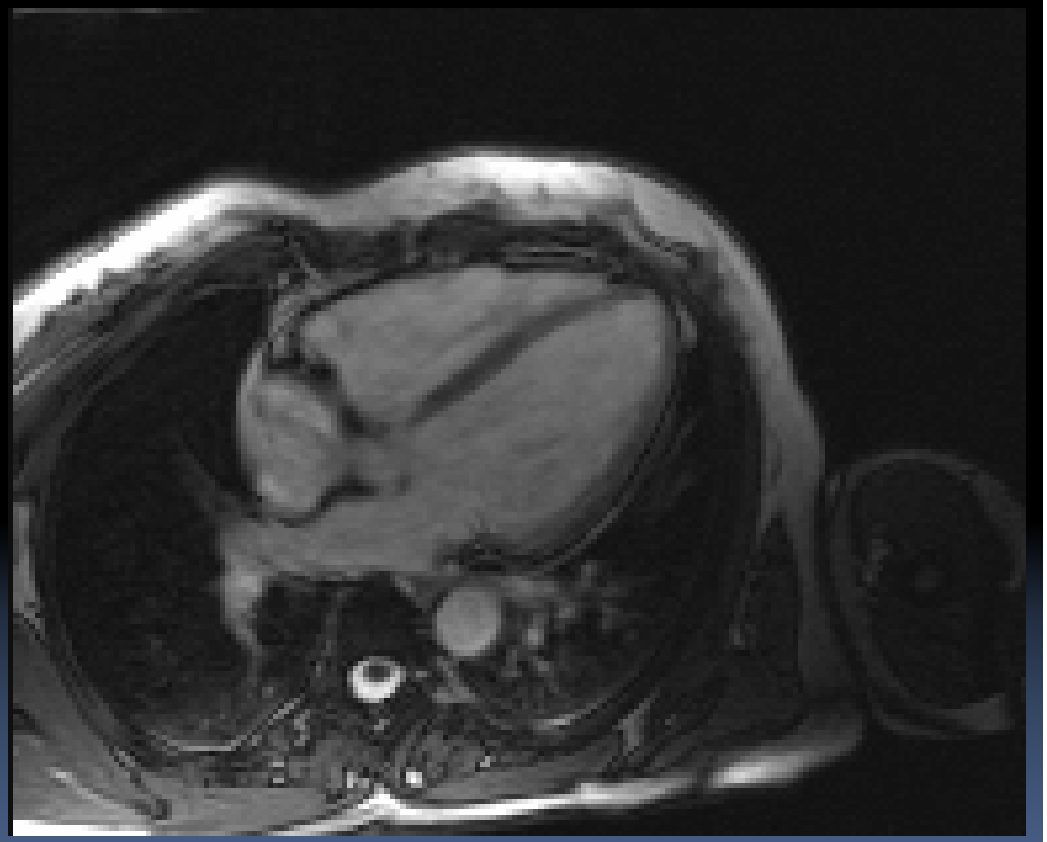
- Current spatial resolution is not enough to detect subtle RV intramyocardial fat
- Differentiation with normal epi and pericardial fat





ARVD – MR Assessment
Limitations

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

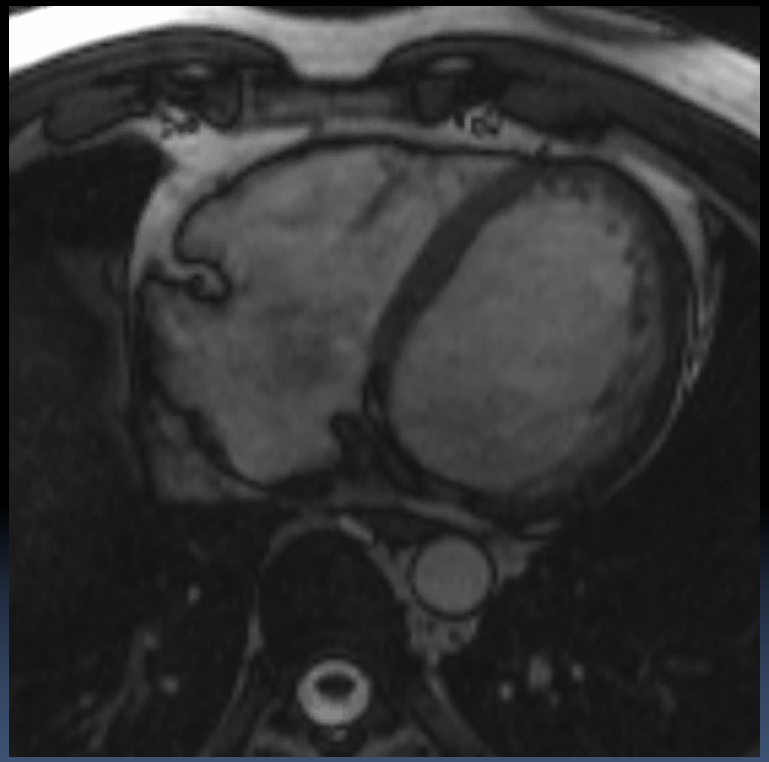


ARVD – MR Diagnosis

- 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

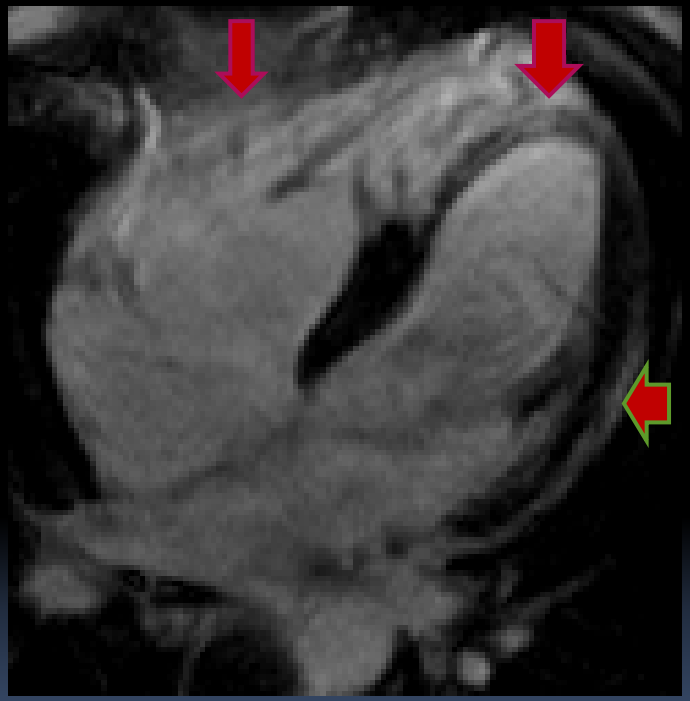
ARVD – MR Diagnosis

- 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

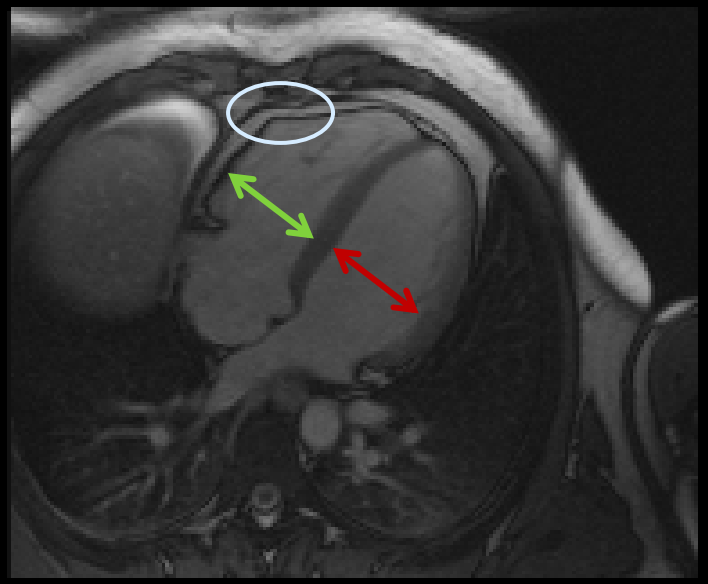
N = 232	MR sensitivity	MR specificity
Task Force without familial criteria	100 %	29 %
Task Force **with** familial criteria	100 %	50%

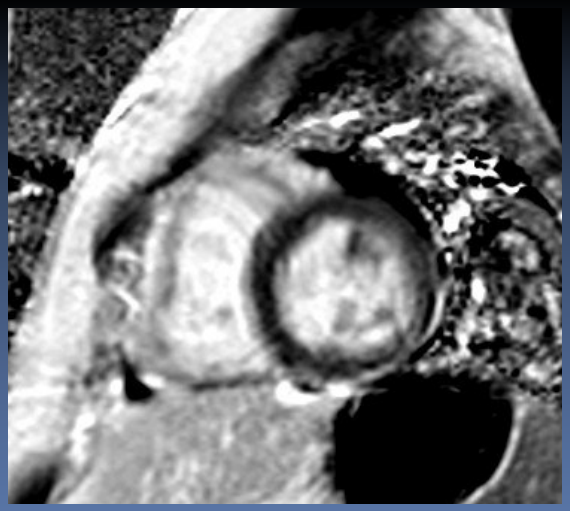
- MR may detect disease at an earlier stage than Task Force Criteria

N = 35	Genotype Subset Identification
Task Force Criteria	46 %
MR	76 %

ARVD – MR Diagnosis

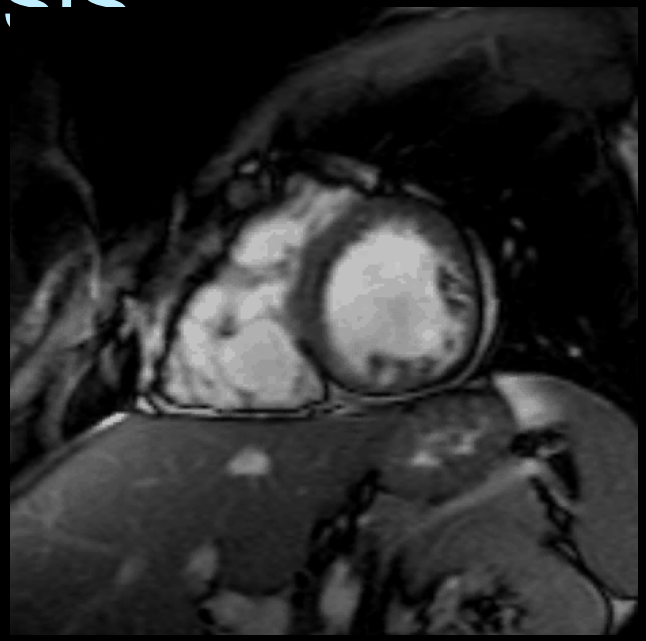
- Intramyocardial fat
  - Believed to be the most useful feature
  - Least reliable of all qualitative MR parameters
- Wall motion abnormalities
  - Reproducible among expert readers
- Quantitative volume analysis
  - Relatively robust
- Delayed enhancement
  - LV involvement
  - RV fibrofatty tissue

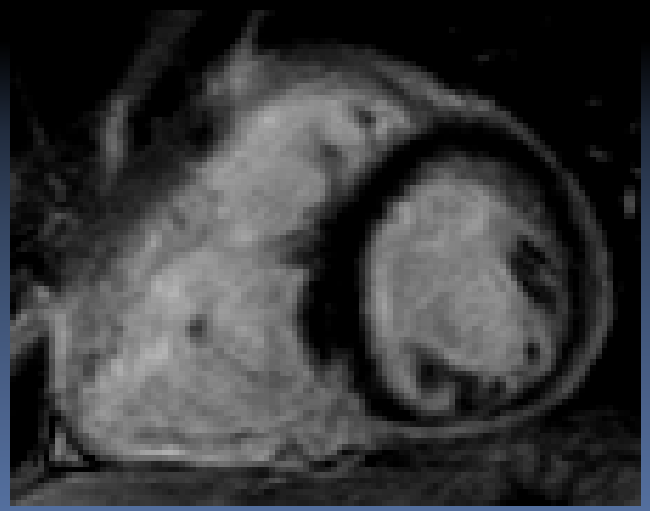




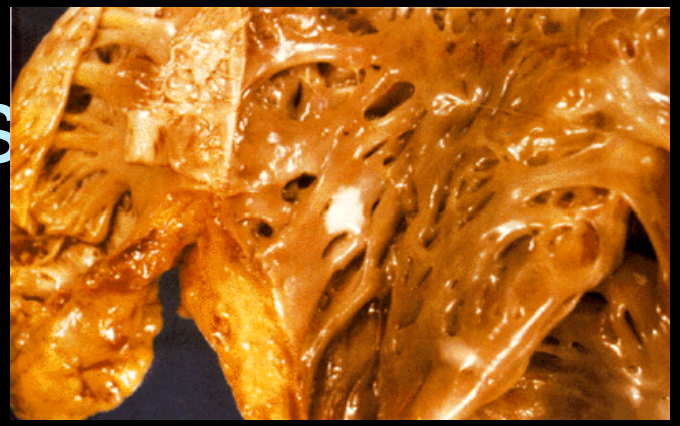
ARVD – MR Diagnosis

- Predictors of arrhythmic events
  - Structurally severe disease
  - LV involvement
    - Delayed enhancement





ARVD – MR Diagnos
Conclusion



- 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