

ARVD: What You Need to Consider

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CardioCase presentation

Freda's Rapid Heart Beat



Freda, 45, previously healthy, presents to the ER with complaints of a rapid heart beat of two hours duration, which started at the beginning of her regular exercise class. She denies dizziness, syncope or near syncope.

She has no cardiac risk factors. Her family history is unremarkable.

Upon examination, her BP is 100/60 mmHg and her heart rate is 160 bpm. Jugular venous pressure is 3 cm above the sternal angle. The first and second heart sounds are normal and there are no added sounds or murmurs. Her chest is clear to auscultation. Freda's ECG

(Figure 1) shows wide complex tachycardia (WCT), 154 bpm.

She was initially diagnosed as having supraventricular tachycardia (SVT) with aberrancy. She was given 6 mg and 12 mg of adenosine intravenously (IV) with no response. Later, she was given 2.5 mg and 5 mg of verapamil, and her systolic BP dropped to 75 mmHg. She was sedated with an IV of propofol and received a biphasic, 100 joules, shock to convert her to sinus rhythm. She was referred electively for an electrophysiology study. Figure 2 shows her ECG post-cardioversion.

For more on Freda, see page 20.



Figure 1. ECG upon presentation. WCT 154/ min with left bundle branch block (LBBB) morphology and left axis deviation (LAD).

CardioCase discussion

Freda's rapid heart beat continued...

Three months later she presents to the ER with the same complaints. Her follow up ECG in the ER is shown in Figure 3. Her BP was low and she was cardioverted to sinus rhythm with a biphasic, 100 joules, shock. This time, she was diagnosed as having VT, originating from the RV. She was started on oral amiodarone and referred to electrophysiology service.

Differential Diagnosis

VT in young patients with structural heart disease may be caused by:

- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Arrhythmogenic right ventricular dysplasia (ARVD)
- Dystrophica myotonica

In young patients without structural heart disease, causes of VT may include:

- Long QT syndrome
- Brugada syndrome
- Catecholaminergic polymorphic ventricular tachycardia

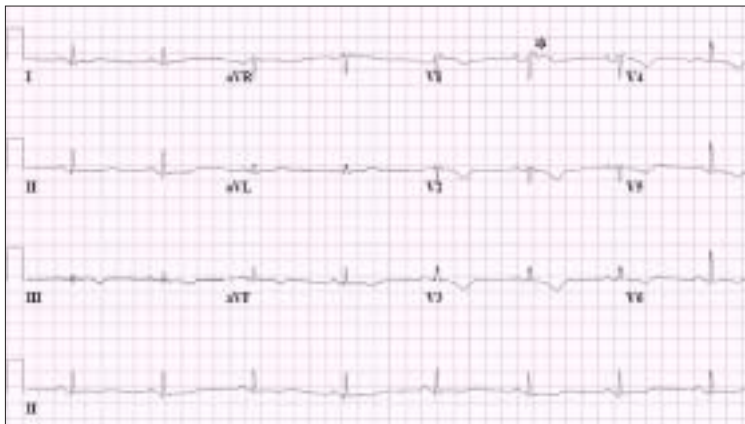


Figure 2. ECG post-cardioversion. Sinus bradycardia 52 bpm, with T-wave inversion in leads V₁-V₃ and epsilon wave.*



Figure 3. WQT 124/min, left bundle-branch block (LBBB) and left axis deviation (LAD) with fusion beat.**



Figure 4 A. Parasternal long axis.

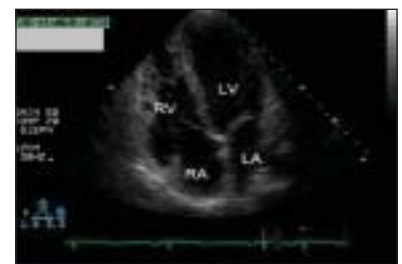


Figure 4 B. Apical 4-chamber RV enlargement.

Figure 4 A and B show RV enlargement.

About the authors...

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What next?

Freda's echocardiogram (Figure 4 A and 4 B) reveals an enlarged RV with reduced RV systolic function.

Her nuclear scan shows:

LVEF 0.62 (Normal > 0.50)
RVEF 0.22 (Normal > 0.45).

EF: Ejection Function

Her cardiac MRI is presented in Figures 5 A and 5 B, which shows diffused intramural fatty infiltration and fat suppression in the RV free wall. Figures 6 A and 6 B presents her RV angiogram.

What's wrong with Freda?

Based on ECG changes, VT of RV origin on presentation and RV changes, she is diagnosed with arrhythmogenic right ventricular dysplasia (ARVD). She receives an implantable cardioverter defibrillator (ICD) for primary prevention of sudden cardiac death (SCD) and was started on sotalol, 80 mg, twice daily.

What is ARVD?

ARVD is a heart disease, often familial and characterized by structural and functional abnormalities of the RV due to replacement of the myocardium by fatty and fibrous tissue. LV involvement may occur late in the course of the disease and have a worse prognosis. ARVD is familial in 30% to 90% of cases. The most common pattern of inheritance is autosomal dominant with variable penetrance.

How does ARVD present?

ARVD includes various arrhythmias, generally of RV origin, including isolated extrasystoles, non-sustained or sustained VT and ventricular

fibrillation leading to syncope or sudden death. Symptoms are usually exercise related. Congestive heart failure is also observed in the most severe forms of the disease.

What are the characteristics?

ARVD generally appears as a diffuse or segmental loss of the myocardium of the RV free wall, which is then replaced by fatty tissue. Only the subendocardial layers are preserved and are frequently occupied by dissecting fibrosis. Persisting strands of cardiomyocytes bordered by or embedded in a variable extent of fibrosis are observed in the epicardial and mediomural layers. This leads to a major reduction of conduction velocity within myocardium and may constitute, in some cases, an arrhythmogenic substrate and may explain mysterious cases of sudden death.

Pathologic patterns seen in ARVD

Fatty infiltration

Confined to the RV, fatty infiltration involves a partial or near-complete substitution of myocardium with fatty tissue without wall thinning. Predominantly, the apical and infundibular regions of the RV are involved. The LV and ventricular septum are usually spared. No inflammatory infiltrates are seen in this form.

The fibrofatty form

Myocytes are replaced with fibrofatty tissue. A patchy myocarditis is involved in up to two-thirds of cases, with inflammatory infiltrates (mostly T cells) seen on microscopy. This leads to thinning of the RV free wall (to < 3 mm thickness). The RV inflow tract, the RV outflow tract and the RV apex are the regions generally affected. The LV is involved in 50% to 67% of individuals, which is usually late in the course of disease, resulting in a poor prognosis.

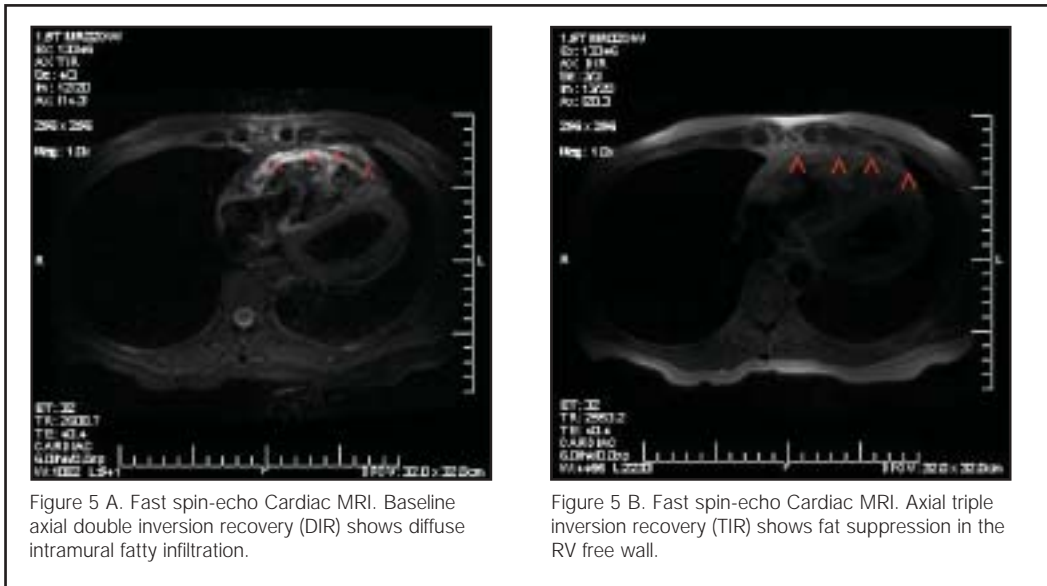


Figure 5 A and 5 B show Freda's fast spin-echo Cardiac MRI.



Figure 6 A and B present Freda's RV angiogram. (See diagnostic testing for ARVD).

The loss of RV myocardium has been related to three basic mechanisms:

1. Apoptosis or programmed cell death
2. Inflammatory phenomenon
3. Major replacement of myocardium by fat.

Differential Diagnosis

See Table 1.

Diagnostic Criteria

To make a diagnosis of ARVD requires either two major criteria *or* one major and two minor criteria, *or* four minor criteria (Table 2).

Management

When managing ARVD, the goal is to decrease the incidence of sudden cardiac death (SCD). Certain individuals are at high risk of SCD.

Table 1 Differential diagnosis of ARVD

Congenital heart disease	Acquired heart disease	Miscellaneous
Repaired tetralogy of Fallot	Tricuspid valve disease	Pre-excited AV re-entry tachycardia
Ebstein's anomaly	Pulmonary hypertension	Idiopathic RVOT tachycardia
Uhl's anomaly	RV infarction	
Atrial septal defect	Bundle-branch re-entrant tachycardia	
Partial anomalous venous return	Tricuspid valve disease	

AV: Atrioventricular
RV: Right ventricle

RVOT: Right ventricular outflow tract

Examples of those at high risk of SCD include:

- Young age
- Competitive sports activity
- Malignant familial history
- Extensive RV disease with decreased RV EF
- LV involvement
- Syncope
- Episode of ventricular arrhythmia

Family screening

All first degree family members of the affected individual should be screened for ARVD. This is used to establish the pattern of inheritance. Screening should begin during the teenage years unless otherwise indicated.

Tests include:

- Echocardiogram
- ECG
- Signal averaged ECG
- Holter monitoring
- Cardiac MRI
- Exercise stress test

Diagnostic testing for ARVD includes:

ECG

The most common ECG abnormality seen in arrhythmogenic right ventricular dysplasia (ARVD) is T-wave inversion in leads V1 to V3. However, this is a non-specific finding, and may be considered a normal variant in right bundle-branch block (RBBB), women and children under 12 years of age. The epsilon wave is found in about 50% of those with ARVD. This is described as a terminal notch in the QRS complex due to slowed intraventricular conduction.

Echocardiography

Echocardiography reveals an enlarged, hypokinetic right ventricle (RV) with a paper-thin RV free wall. The dilatation of the RV will cause dilatation of the tricuspid valve annulus, with subsequent tricuspid regurgitation. Paradoxical septal motion may also be present. Due to trabeculations and non-visibility of RV structure, milder forms of the disease may be difficult to diagnose.

Cardiac MRI

Fatty infiltration of the RV free wall can be visible on cardiac MRI. Fat has increased intensity in T1-weighted images. However, it may be difficult to differentiate intramyocardial fat and the epicardial fat which is commonly seen adjacent to the normal heart. Also, the sub-tricuspid region may be difficult to distinguish from the atrioventricular sulcus, which is rich in fat. Cardiac MRI can visualize the extreme thinning and akinesis of the RV free wall. However, the normal RV free wall may be about 3 mm thick, making the test less sensitive.

Other radiologic tests include:

Cardiac CT scan and nuclear scan can be used to assess RV function and structure.

RV angiography

Findings consistent with ARVD are an akinetic or dyskinetic bulging localized to the infundibular, apical and subtricuspid regions of the RV. The specificity is 90%; however, the test is observer dependent.


RV biopsy

Transvenous biopsy of the RV can be highly specific for ARVD, but has low sensitivity. False positives include other conditions with fatty infiltration of the ventricle, (such as chronic alcohol abuse and Duchenne/Becker muscular dystrophy). The disease is segmental in nature and false negatives are common because the disease progresses typically from the epicardium to the endocardium (with the biopsy sample coming from the endocardium). Also, due to the paper-thin RV free wall, most biopsy samples are taken from the ventricular septum, which is often not involved in the disease process.

Table 2 Major and minor criteria for diagnosing ARVD

	RV dysfunction	Tissue characterization	Conduction abnormalities	Family history
Major criteria	<ul style="list-style-type: none"> Severe dilatation and reduction of RV EF with little or no LV impairment Localized RV aneurysms Severe segmental dilatation of the RV 	<ul style="list-style-type: none"> Fibrofatty replacement of myocardium on endomyocardial biopsy 	<ul style="list-style-type: none"> Epsilon waves V1-V3 Localized prolongation (>110 ms) of QRS in V1-V3 	<ul style="list-style-type: none"> Familial disease confirmed on autopsy/surgery
Minor criteria	<ul style="list-style-type: none"> Mild global RV dilatation and/or reduced EF with normal LV Mild segmental dilatation of the RV Regional RV hypokinesis 		<ul style="list-style-type: none"> Inverted T-waves in V2 and V3 in an individual 12 years or more in the absence of RBBB Late potentials on signal averaged ECG VT with a LBBB morphology Frequent PVCs (> 1000 PVCs/24 hours) 	<ul style="list-style-type: none"> Familial history of SCD before age 35 due to suspected ARVD Family history of ARVD
EF: Ejection fraction LV: Left ventricle RV: Right ventricle		LBBB: Left bundle branch block RBBB: Right bundle branch block VT: Ventricular tachycardia		SCD: Sudden cardiac death

Conclusion

ARVD is a rare, but serious, heart disease that may cause SCD in young people. Its diagnosis is difficult and depends on disease awareness and multiple diagnostic investigations. The management of ARVD is not standardized, but mostly involves ICD implantation, especially in high risk patients, and the use of antiarrhythmic drugs. 

Managing ARVD:

Pharmacology

Therapy with beta blockers, sotalol or amiodarone may be effective in suppressing ventricular arrhythmias and possibly in preventing sudden cardiac death.

Catheter ablation

Catheter ablation may be used to treat intractable ventricular tachycardia (VT). It has a 60% to 90% acute success rate. Unfortunately, recurrence is common (60% recurrence rate). Indications for catheter ablation include: drug-refractory VT and frequent recurrence of VT after implantable cardioverter defibrillator (ICD) placement, causing frequent discharges of the ICD.

Surgery

Surgical disarticulation of the right ventricular (RV) free wall from its attachments to the left ventricle (LV) and septum can prevent the electrical propagation of ventricular arrhythmias from the RV to the LV. This was an effective means to prevent sudden death prior to the availability of the ICD, but resulted in severe RV failure.

Cardiac transplant surgery is rarely performed in ARVD. It may be indicated if the arrhythmias associated with the disease are uncontrollable or if there is severe bi-ventricular heart failure that is not manageable with pharmacologic therapy.

Placement of an ICD

Placement of an ICD is the most effective prevention against SCD.

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