A Not-So-Common Case Of Cardiomyopathy

Tareq Al Saadi

12/18/2023
Initial Presentation

- 41 yo, PMHx of HIV [normal CD4 count and non-detected viral load], smoker, works as a truck driver
- No family history of SCD or cardiomyopathy.
- cc: syncope
- hsTroponin peaked at 600, TWI on EKG
- ESR/CRP normal
- CTPE negative for PE.
- CTA aorta negative for dissection.
- CCTA: no CAD, calcium score of 0

Echocardiogram

- LVEF 57%
- No regional wall motion abnormalities.
- Borderline RV enlargement
- No significant valve abnormalities.

Telemetry

- 2 symptomatic NSVT episodes
Major II. Tissue characterization of wall

- Residual myocytes < 60% by morphometric analysis (or 50% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy

Minor
- Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy

2010 revised criteria for diagnosis of ARVC

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
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</thead>
<tbody>
<tr>
<td>RV akinesia, dyssynergy, or aneurysm</td>
<td>Regional RV akinesia or dyssynergy or dysynchronous RV contraction</td>
</tr>
<tr>
<td>1 of the following:</td>
<td>1 of the following:</td>
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<tr>
<td>- PIAX: RVOT &gt; 32 mm (corrected for body size PIAX/BSA &gt; 10 mm/m²)</td>
<td>- Ratio of RV end-diastolic volume to BSA ≥ 110 mL/m² (male) or ≥ 100 mL/m² (female)</td>
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<tr>
<td>- RV fractional area change ≤ 33%</td>
<td>- or RV fractional area change &gt; 40%</td>
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</tbody>
</table>

3. Depolarization/conduction abnormalities

- Inverted T waves in leads V1, V2, and V3 or beyond in individuals > 14 years of age (in the absence of complete right bundle-branch block)
- Nonsustained or sustained ventricular tachycardia of RV outflow configuration, left bundle-branch block morphology with inferior axis
- History of ARVC/D in a first-degree relative

Diagnostic terminology:
- Definite diagnosis: 2 major or 1 major and 2 minor criteria or 4 minor from different categories.
- Borderline: 1 major and 1 minor or 3 minor criteria from different categories.
- Possible: 1 major or 2 minor criteria from different categories.
## 2010 revised criteria for diagnosis of ARVC

### I. Global or regional dysfunction and structural alterations

**Major**
- By 2D echo:
  - Regional RV akinesia, dyskinesia, or aneurysm
  - 1 of the following:
    - Ratio of RV end-diastolic volume to BSA ≥ 110 mL/m² (male) or ≥ 100 mL/m² (female)
    - Fractional area change ≥ 50%
- By MRI:
  - Regional RV akinesia, dyskinesia, or aneurysm

**Minor**
- By 2D echo:
  - Regional RV akinesia, dyskinesia, or aneurysm
  - 1 of the following:
    - Ratio of RV end-diastolic volume to BSA ≥ 110 mL/m² (male) or ≥ 100 mL/m² (female)
    - Fractional area change ≥ 50%
- By MRI:
  - Regional RV akinesia, dyskinesia, or aneurysm

### II. Tissue characterization of wall

**Major**
- Residual myocytes < 60% by morphometric analysis (or 50% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 4 of 34
- Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of tissue on endomyocardial biopsy

**Minor**
- Residual myocytes < 75% by morphometric analysis (or 60% if estimated), with fibrous replacement of the RV free wall myocardium
- Residual myocytes 75% to 90% by morphometric analysis (or 65% to 75% if estimated), with fibrous replacement of tissue on endomyocardial biopsy

### III. Repolarization abnormalities

**Major**
- Inverted T waves in leads V1, V2, and V3 in individuals ≥ 14 years of age in the absence of complete right bundle-branch block or QRS ≥ 120 ms

**Minor**
- Inverted T waves in lead V1, V2, and V3 in individuals ≥ 14 years of age in the absence of complete right bundle-branch block

### IV. Depolarization/conduction abnormalities

**Major**
- Early repolarization (proportional low-amplitude signals between end of QRS complex to onset of the T wave) in the right precordial leads (V1 to V3)

**Minor**
- Late potentials by SAE CG in ≥ 1 of 3 parameters in the absence of a QRS duration of ≥ 110 ms on the standard ECG
  - Filtered QRS duration (QRSf) ≤ 114 ms
  - Duration of terminal QRS ≥ 40 ms (low-amplitude signal duration) ≤ 38 ms
  - Root mean square voltage (v) of terminal 40 ms ≤ 20 V
- Terminal activation duration of QRS ≥ 55 ms measured from the nadir of the T wave to the end of the QRS, including R, V1, V2, or V3, in the absence of complete right bundle-branch block

### V. Arrhythmia

**Major**
- Nonsustained or sustained ventricular tachycardia of left bundle-branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and aVF and positive in lead aVL)
  - Regional RV akinesia, dyskinesia, or aneurysm
- Nonsustained or sustained ventricular tachycardia of RV outflow configuration, left bundle-branch block morphology with inferior axis (positive QRS in leads II, III, and aVL and negative in lead aVL) or of unknown axis
  - Regional RV akinesia, dyskinesia, or aneurysm
- History of ARVC/D in a first-degree relative in whom it is not possible or practical to determine whether the family member meets current Task force criteria
  - Regional RV akinesia, dyskinesia, or aneurysm
- History of ARVC/D in a first-degree relative who meets current Task force criteria
  - Regional RV akinesia, dyskinesia, or aneurysm
- Premature sudden death (< 35 years of age) due to suspected ARVC/D in a first-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- ARVC/D confirmed pathologically or by current Task Force criteria in a second-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm

**Minor**
- History of ARVC/D in a second-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- Premature sudden death (≥ 35 years of age) due to suspected ARVC/D in a second-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- Premature sudden death (≥ 35 years of age) or nonsudden death from ARVC/D in a second-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- Nonsustained or sustained ventricular tachycardia of RV outflow configuration, left bundle-branch block morphology with inferior axis (negative QRS in leads II, III, and aVL and positive in lead aVL) or of unknown axis
  - Regional RV akinesia, dyskinesia, or aneurysm

### VI. Family History

**Major**
- ARVC/D confirmed in a first-degree relative who meets current Task force criteria
  - Regional RV akinesia, dyskinesia, or aneurysm
- ARVC/D confirmed pathologically at autopsy or surgery in a first-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- Identification of a pathogenic mutation* categorized as associated or probably associated with ARVC/D in the patient and under evaluation
  - Regional RV akinesia, dyskinesia, or aneurysm

**Minor**
- History of ARVC/D in a first-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- Premature sudden death (≥ 35 years of age) due to suspected ARVC/D in a first-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm
- ARVC/D confirmed pathologically or by current Task Force criteria in a second-degree relative
  - Regional RV akinesia, dyskinesia, or aneurysm

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*Identification of a pathogenic mutation determined by next-generation sequencing.
ICD implanted
Primary prevention of sudden cardiac death

Recurrent presentations with PVCs and NSVT
Symptoms of near syncope and exertional intolerance
Beta blockers then amiodarone added

?Sarcoidosis
FDG-PET scan

18-FDG PET/CT (Outside hospital)

FDG uptake in the basal septal, inferior, and inferolateral wall segments of the LV. Mild uptake in the apical LV and RV free wall.

Corresponding area of decreased perfusion on N-13 Ammonia perfusion study.

Multiple hypermetabolic cervical nodes and naso-oropharynx likely secondary to covid 19 infection.

No mediastinal, hilar adenopathy, or lung findings to suggest sarcoidosis.
Biopsies

Cervical lymph node: Negative for metastatic tumor and granuloma.

Myocardium: patchy fibrosis. Negative for myocarditis, sarcoidosis, iron overload, amyloidosis, and ischemic changes.
18-FDG-PET/CT

- Resting myocardial perfusion with rubidium was normal.
- With 18 FDG imaging there was uptake in the basal anteroseptal, anterolateral, inferior, inferoseptal, inferolateral, lateral and septal walls. SUV max: 5.4.
- There was no evidence of abnormal extracardiac activity.
Treatment for cardiac sarcoidosis

**Corticosteroids**
- First line agents
- High rates of recurrence in monotherapy

**Immunomodulators**
- Upfront addition to corticosteroids in cases of rapidly progressive heart failure, life-threatening arrhythmias, and extensive inflammation on cardiac PET
- Methotrexate, azathioprine, mycophenolate mofetil, leflunomide, and cyclophosphamide

**Biologic anti-tumor necrosis factor (TNF)**
- Third line agents
- Infliximab and adalimumab

Sarcoidosis treatment started

**Immunosuppression:** Prednisone and Mycophenolate Mofetil

**Prophylactic TMP/SMX, nystatin, calcium + Vitamin D supplements.**


**Expert Consensus Recommendations for the Management of Ventricular Arrhythmias**

*Class IIa*

1. Assessment of myocardial inflammation with FDG-PET can be useful in CS patients with ventricular arrhythmias.
2. Immunosuppression can be useful in CS patients with frequent ventricular ectopy or nonsustained VT and evidence of myocardial inflammation.
3. Immunosuppression can be useful in CS patients with sustained ventricular arrhythmias and evidence of myocardial inflammation.
4. Antiarrhythmic medication therapy can be useful in patients with ventricular arrhythmias refractory to immunosuppressive therapy.
5. Catheter ablation can be useful in patients with CS and ventricular arrhythmias refractory to immunosuppressive and antiarrhythmic therapy.
6. Catheter ablation can be useful in patients with incessant ventricular arrhythmias.
18-FDG-PET/CT - 5 months later

- Resting myocardial perfusion with rubidium was normal.
- With 18 FDG imaging there was uptake in the basal anteroseptal, inferior, inferoseptal, and inferolateral walls. SUV max: 4.7.
- There was no evidence of abnormal extracardiac activity.

Ongoing ventricular arrhythmias
Switching between different antiarrhythmics (amiodarone, sotalol, mexiletine)
Cardiac function slowly decreasing down to LVEF of 30%
Transplant evaluation

Uptitration of immunosuppressive regimen
PVC/VT ablation
Apical inferior RV PVC ablated. Numerous other pleomorphic PVCs seen but not pursued for ablation.
Adalimumab started
HIV infection still considered relative contraindication to heart transplantation at most centers...

**Perception of HIV-positive patients as high risk recipients to be avoided given scarce organ supply**

**Concern for immunosuppression-triggered progression of HIV to AIDS**

**Drug interactions which could worsen outcomes**

- Impact of certain antiretrovirals on cytochrome P-450 metabolism

**From kidney transplant data:**

- HIV remained stable post-transplantation
- HIV positive recipients have higher rejection rates

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**Heart Transplantation Survival Outcomes of HIV Positive and Negative Recipients**

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Admission for recurrent VT requiring multiple shocks and ATP

Orthotopic heart transplant

Discharge home

Admission for acute rejection

Listed for transplant

Post-op tamponade requiring return to OR

Post-op pericarditis

Explanted heart pathology
How sensitive and specific is 18-FDG PET for cardiac sarcoidosis?


Abstract

Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heritable heart muscle disease that causes sudden cardiac death in the young. Inflammatory myocardial infiltrates have been described at autopsy and on biopsy, but there are few data on the prevalence of myocarditis in living patients with ARVC using non-invasive imaging techniques. FDG-PET is a validated technique for detecting myocardial inflammation in clinically suspected myocarditis. We aimed to determine the prevalence of myocardial inflammation in patients with ARVC using 18F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Methods and results: We performed a retrospective analysis of a single-center cohort of patients with ARVC referred for FDG-PET scans between 2012 and 2017 for investigation of symptoms or suspected device infection. Sixteen patients (12 male; age 42 ± 13 years) with a definite diagnosis of ARVC were identified. Seven had positive FDG-PET scans, two of whom had cardiac sarcoidosis co-existing myocarditis. Of the remaining five, two had pathologic desmosomal mutations. FDG uptake was found in the left ventricular myocardium in all cases. One patient also had right ventricular uptake.

Conclusion: In this exploratory study, we show that some patients with ARVC have evidence for myocardial inflammation on FDG-PET, suggesting that myocarditis plays a role in disease pathogenesis.
How common is inflammation in patients with ACM?

Where does inflammation fall in the pathogenesis of ACM?
• Thank you!
Disclosure

• I have no financial disclosure or conflicts of interest with the presented material in this presentation.
• Any photos of patients have been used with permission and are for teaching purposes only

Kenya

• Gained independence from Great Britain in 1963
• Population: 53.1 million people (2021)
• Official languages are Swahili and English
Epidemiology

- Life expectancy 67.7 years
- Median age is 19.6 years
- Prevalence of rheumatic heart disease (RHD) is ~15% in East Africa (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10522432)
- 300,000-400,000 deaths per year worldwide (vast majority are women, ~85%, and common ages of death second and third decade of life and in pregnancy)

World Health Organization Data: Kenya

<table>
<thead>
<tr>
<th>Top causes of death for females</th>
<th>Top causes of death for males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths per 100,000 population, Kenya, 2019</td>
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<tr>
<td>Neocnatal conditions</td>
<td>42.5</td>
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<tr>
<td>Lower respiratory infections</td>
<td>39.3</td>
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<tr>
<td>HIV/AIDS</td>
<td>35.1</td>
</tr>
<tr>
<td>Stroke</td>
<td>29.8</td>
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<tr>
<td>Diarrhoeal diseases</td>
<td>25.9</td>
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<tr>
<td>Tuberculosis</td>
<td>24.6</td>
</tr>
<tr>
<td>Malaria</td>
<td>21.8</td>
</tr>
<tr>
<td>Maternal conditions</td>
<td>21.3</td>
</tr>
<tr>
<td>Cirrhosis of the liver</td>
<td>20.4</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>20.4</td>
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<tr>
<td>Neonatal conditions</td>
<td>55.2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>50.3</td>
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<td>Lower respiratory infections</td>
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<td>Road injury</td>
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<tr>
<td>Ischaemic heart disease</td>
<td>25.2</td>
</tr>
</tbody>
</table>
World Health Organization Data: United States

Top causes of death for females
Deaths per 100,000 population, United States, 2019

- Ischaemic heart disease: 135
- Alzheimer disease and other dementias: 116
- Chronic obstructive pulmonary disease: 62
- Stroke: 55
- Trachea, bronchus, lung cancers: 43
- Breast cancer: 29
- Kidney diseases: 25
- Hypertensive heart disease: 20
- Lower respiratory infections: 19
- Colon and rectum cancers: 18

Top causes of death for males

- Ischaemic heart disease: 172
- Alzheimer disease and other dementias: 58
- Chronic obstructive pulmonary disease: 57
- Trachea, bronchus, lung cancers: 52
- Stroke: 41
- Drug use disorders: 29
- Kidney diseases: 27
- Self-harm: 25
- Diabetes mellitus: 22
- Prostate cancer: 22

Eldore and Kapsowar
RHD Screening

2023 World Heart Federation guidelines for the echocardiographic diagnosis of rheumatic heart disease

Criteria for pathological MR (requires all):
- Observed in two views
- Minimum MR jet length (1.5 cm for patients weighing <30 kg and 2.0 cm for patients weighing ≥30 kg) observed in one view
- Velocity >3.0 m/s^b
- Pan-systolic jet^b

Criteria for pathological AR (requires all):
- Observed in two views
- Velocity >3.0 m/s^b
- Pan-diastolic jet^b

RHD morphological criteria:
- MV anterior leaflet thickening and/or MV chordal thickening
- MV leaflet restriction and/or excessive anterior leaflet tip motion
- AV thickening, prolapse or restricted leaflet motion
12 year old male presents with his father for RHD Screening
Saving time saves lives! A time focused evaluation of a single-view echocardiographic screening protocol for subclinical rheumatic heart disease

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Background: Rheumatic heart disease affects 33 million people in low and middle income countries and is the leading cause of cardiovascular death among children and young adults. Evidence increasingly supports that simplified screening protocols can identify at risk children with good accuracy. One of the more proximal and pragmatic hurdles that has not been completely explored is the time required for executing the screening exam.

Methods: We conducted an observational study comparing three different echocardiographic strategies in four separate school-based screening programs in Kenya and Cameroon.

Results: In a sample of 911 children, we found that a single-view screening strategy can be obtained in an average time of 1.2 min/child, the two-view in an average of 2.1 min/child, and multi-view in an average of 5 min/child.

Conclusions: Our study demonstrates that there are significant differences in the time required to execute different screening protocols and is an essential consideration in the feasibility of large scale populations based rheumatic heart disease screening programs.

[15]. However, we used a modified version of the WHF criteria that did not require the application of continuous-wave Doppler, rather identifying visually pandiastolic AR or pathological pansystolic MR. [6,12] We additionally considered eccentric, visually identified pansystolic mitral regurgitation abnormal if the length was more than 1 cm. These
RHD Secondary Prevention

Table 10.1: Recommended antibiotic regimens for secondary prophylaxis

<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylpenicillin (BPG)</td>
<td>1,250,000 units (30 kg)</td>
<td>Deep intramuscular</td>
<td>Every 28 days</td>
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<tr>
<td></td>
<td>500,000 units (20 kg)</td>
<td></td>
<td>Every 21 days</td>
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<tr>
<td></td>
<td>250,000 units (10 kg)</td>
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</table>

Second line (if 1st route is not possible or consistently declined)

| Penicillin G (penicillin V) | 250 mg | Oral | Twice a day |

Following documented penicillin allergy

| Erythromycin                | 250 mg | Oral | Twice a day |

1 For children weighing less than 15 kg, a dose of 15,000 units is generally recommended but seek paediatric advice.
2 Oral penicillins are the preferred regimens of secondary prophylaxis.
3 Some reports have used regimens of 15,000 units every 21 days to reduce the number of injections in high-risk groups.
4 If a patient has a documented history of ARF, 15,000 units every 21 days may be considered for patients who have bloodstream ARF despite complete adherence to a 15,000 units every 21 days regimen, or those without a high risk of adverse consequences (e.g., anemia, severe RHD, or a history of heart valve surgery).


2020 ACC/AHA Guidelines

Severe MS MVA ≤1.5 cm²

Symptomatic

Stage D

Asymptomatic

Stage C

Exertional symptoms

Surgical candidate

Severe symptoms NYHA III-IV

PASP >50 mm Hg

New AF

Stress test

Hemodynamically significant MS

Sequal valve +2 MR

Sequal valve +2 MR

PMBC at CVC

PMBC at CVC

PMBC at CVC

PMBC at CVC

PMBC at CVC

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Case 1

- 12 year old male with history of rheumatic heart disease
- Worsening mitral stenosis with shortness of breath and weight loss
- Medically managed with metoprolol, furosemide, and spironolactone
Transseptal Puncture
Post mitral balloon valvuloplasty
2.1. Neointimal Restenosis

The restenosis rate after MBV has been reported as 39% at 7 years [Hernandez et al., 1999] and was lower (31%) at 19 years in our younger population (mean age 31.5 ± 11 years) [Fawzy et al., 2007; 2009; Ben Farhat et al., 2001] and was 29% in subgroup of patients with M5S ≤ 8. The actuarial freedom from restenosis rates for this population were 78 ± 2% at 10 years, 52 ± 3% at 15 years, and 26 ± 5% at 19 years and were significantly higher for patients with optimal morphology [Fawzy et al., 2007] (echo score < 8), namely 88 ± 2% at 10 years, 67 ± 4% at 15 years, 40 ± 6% at 19 years (Fig. 1). The predictors of being free from restenosis were a low echo score (P < 0.0001) and post-procedure MVA > 2.0 cm² [Fawzy et al., 2007; 2009; Ben Farhat et al., 2001; Jone et al., 1999].

![Image of restenosis graph]

**Figure 1.**
Freedom from restenosis by Kaplan-Meier estimates for all patients and for patients with M5S ≤ 8. Numbers at the bottom represent patients alive and uncensored at each year of follow-up.
Case 2

• 25 year old woman who was in the hospital to schedule an appointment
• Has been feeling short of breath and unable to walk on any incline
• Her father recently passed away from RHD
Course

• She was admitted overnight, diuresed, and beta blockade was initiated
• She underwent PBMV the following morning
• Mean gradient improved to 4 mmHg with no mitral regurgitation

Thank you!
Thank you!