Cardiac Sarcoidosis

Sarcs and Recommendation

Amit C Patel, MD
Ascension St Vincent Indianapolis

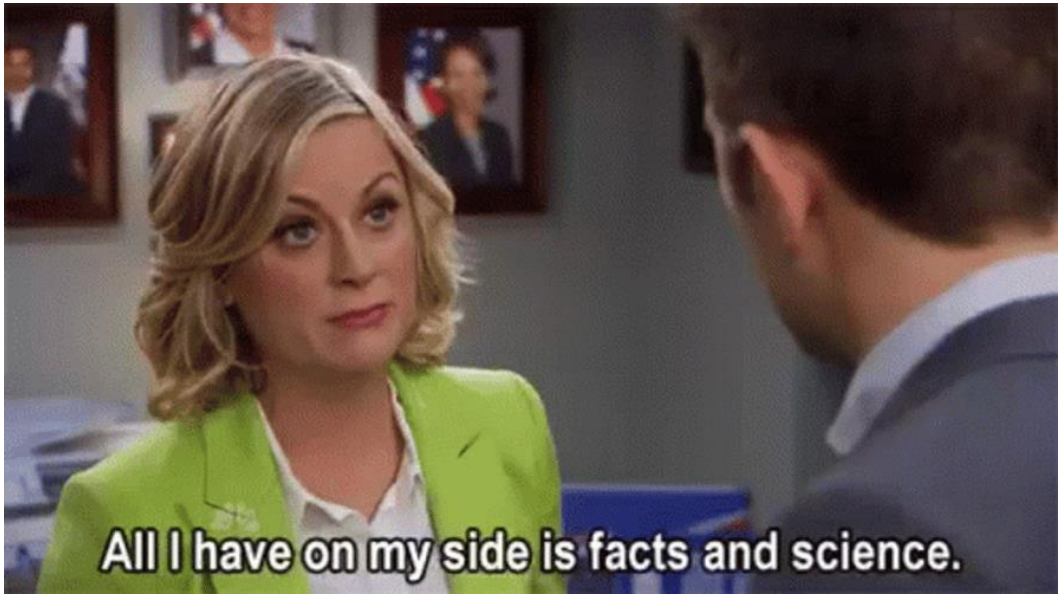
Disclosures

I have no actual or potential conflict of interest in relation to this program/presentation

Objectives

Objective One - BE SUSPICIOUS

Objective Two - Know The Diagnostic Pathway

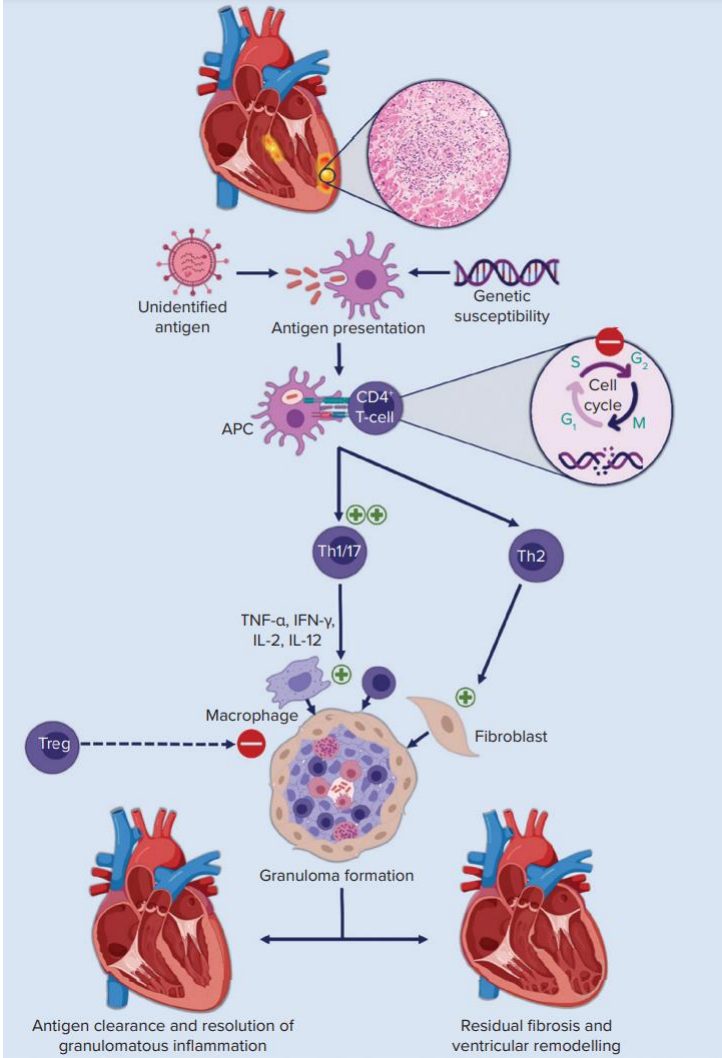


Objective Three - Understand treatment

What is Sarcoidosis?

What is Sarcoidosis?

- Multisystem inflammatory disease
- Non caseating granulomas
- Unknown etiology - suspect abnormal immunological response to a trigger in genetically predisposed individuals



Grunewald, N Engl J Med 2021; 385:1018-1032
DOI: 10.1056/NEJMra2101555

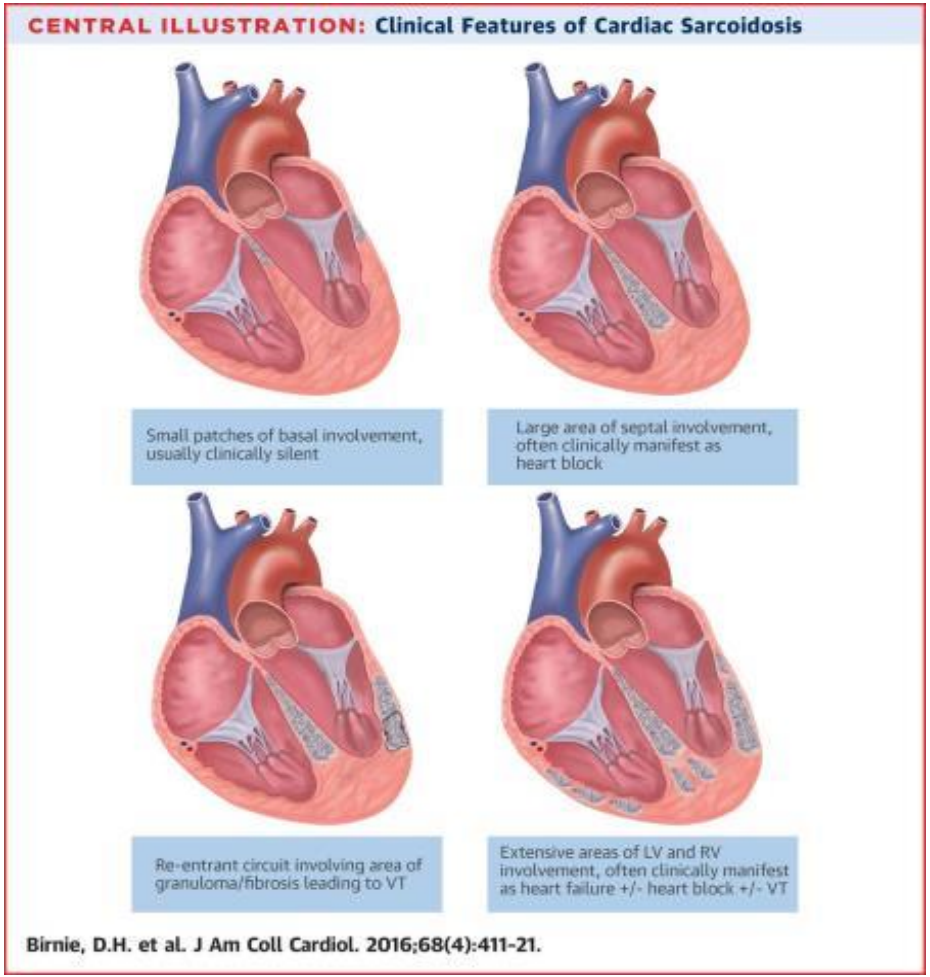
Giblin, Card Fail Rev. 2021 Mar; 7: e17. doi: 10.15420/cfr.2021.16

Epidemiology

- Clinically manifest cardiac involvement is estimated to occur in approximately 25–50% of systemic sarcoidosis depending on the means of ascertainment.
- Cardiac involvement - worse prognosis

Giblin, Card Fail Rev. 2021 Mar; 7: e17. doi: 10.15420/cfr.2021.16

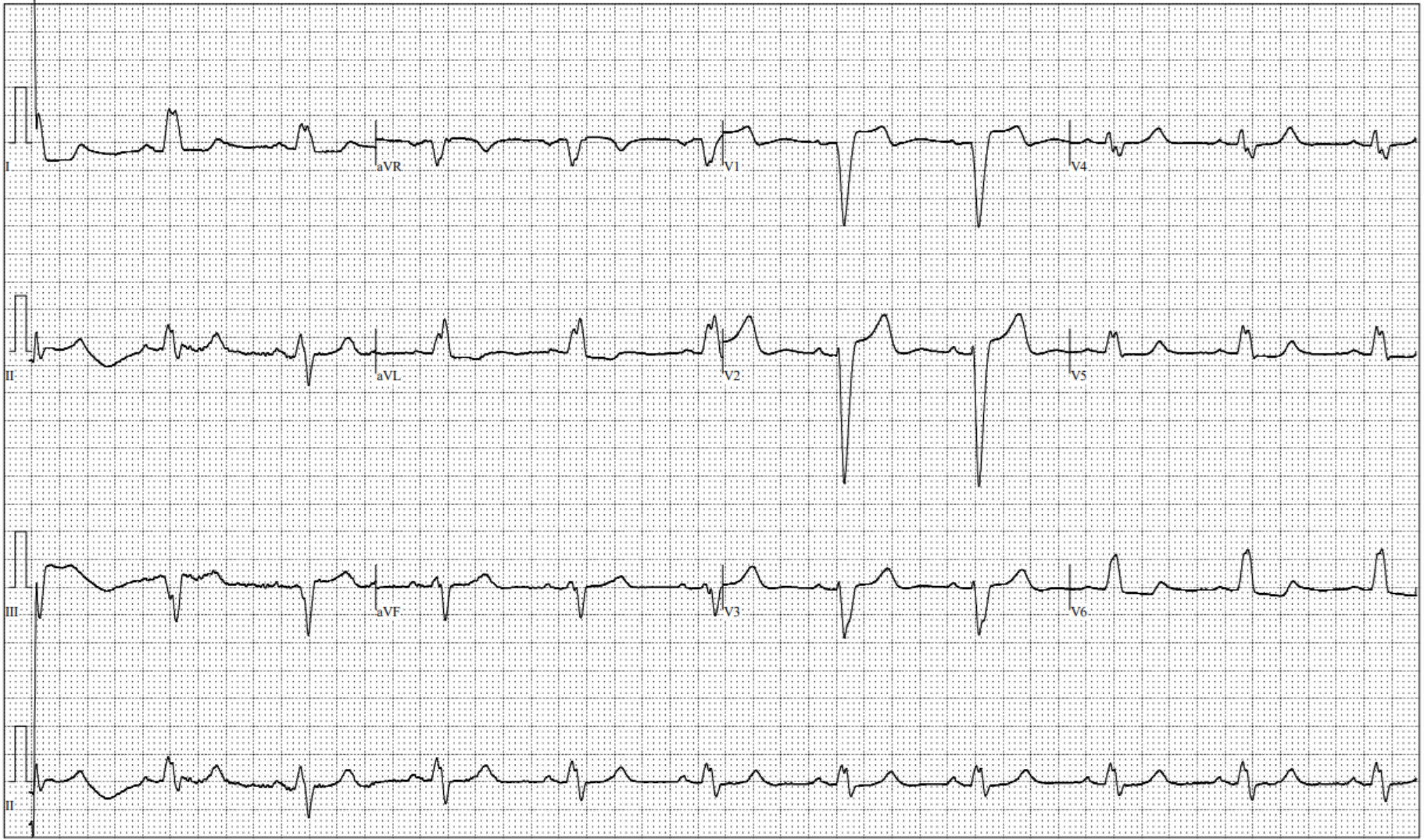
Symptom	
AV Block	Most common (44%), Younger age than other etiologies
Ventricular Arrhythmias	SVT or NSVT or PVCs, Second most common (33%)
Supraventricular Arrhythmias	Flutter, Fib, Sinus arrest. Fib is the most common. (32%)
Sudden Cardiac Death	
Cardiomyopathy/CHF	Dilated or Restrictive. Isolated RV failure possible as well
Vasculitis	Great Vessels and coronaries as well (not much data)



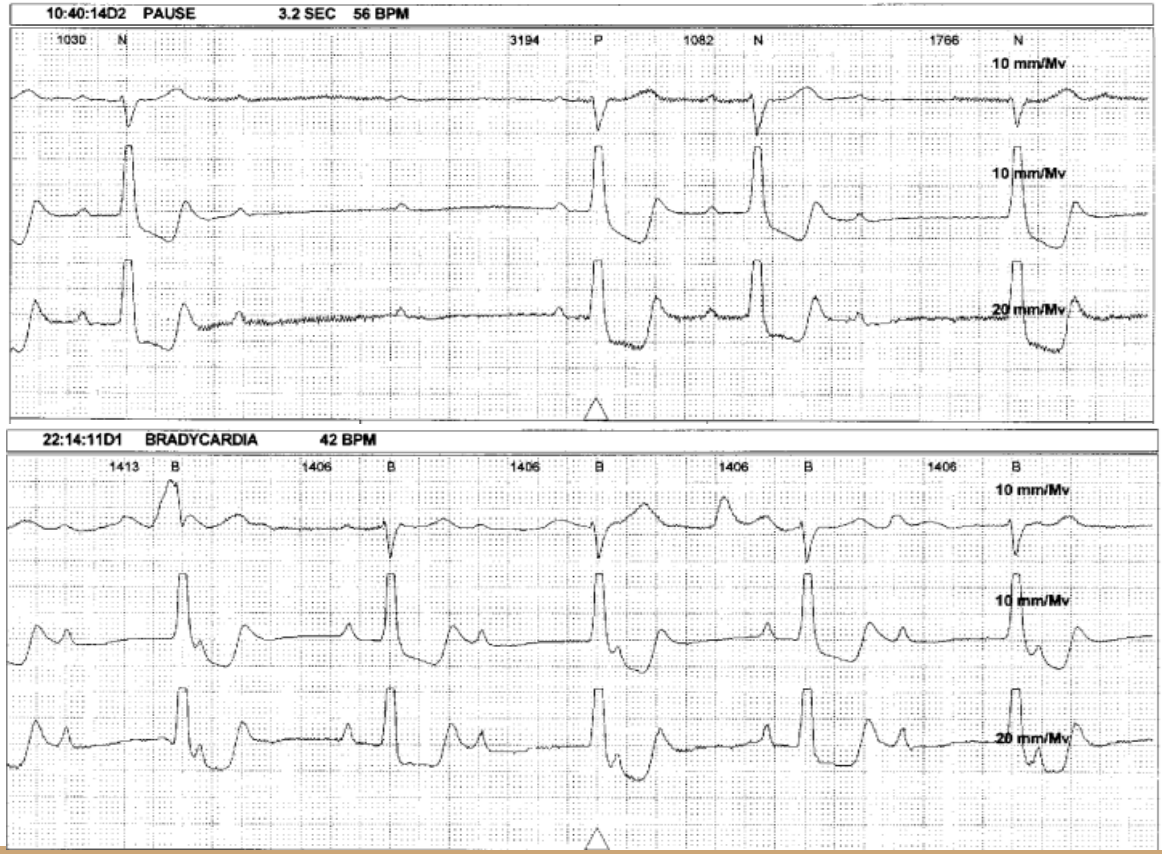
DIAGNOSIS

Case #1

- 67 y/o African American Female
- PMH – Asthma and HTN, **Remote history of pulmonary sarcoidosis in her 20's** was on steroids briefly and it hasn't been an issue since. By report biopsy proven.
- Referred for **shortness of breath and fatigue**
- CC: **SOB and Palpitations**


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Case #1 - Holter



Diagnosis

- 2014 HRS/WASOG
- 2017 Japanese Criteria

2014 HRS/WASOG

Expert Consensus Recommendations on ***Criteria for the Diagnosis of CS***

There are 2 pathways to a diagnosis of Cardiac Sarcoidosis:

1. Histological Diagnosis from Myocardial Tissue
   CS is diagnosed in the presence of non-caseating granuloma on histological examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable).
2. Clinical Diagnosis from Invasive and Non-Invasive Studies:
   It is probable* that there is CS if:
   a) There is a histological diagnosis of extra-cardiac sarcoidosis
   and
   b) One or more of following is present
      - Steroid +/- immunosuppressant responsive cardiomyopathy or heart block
      - Unexplained reduced LVEF (<40%)
      - Unexplained sustained (spontaneous or induced) VT
      - Mobitz type II 2nd degree heart block or 3rd degree heart block
      - Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
      - Late Gadolinium Enhancement on CMR (in a pattern consistent with CS)
      - Positive gallium uptake (in a pattern consistent with CS)
   and
   c) Other causes for the cardiac manifestation(s) have been reasonably excluded

*In general, 'probable involvement' is considered adequate to establish a clinical diagnosis of CS.[33]

Birnie et Al, Heart Rhythm, V 11, N 7, 1304-1323; 2014

WASOG

	Highly Probable	At Least Probable	Possible	No Consensus
Cardiac		Treatment responsive CM or AVNB (12-7-1) Reduced LVEF in the absence of other clinical risk factors (2-13-4) Spontaneous or inducible sustained VT with no other risk factor (6-12-1) Mobitz type II or 3rd degree heart block (11-6-2) Patchy uptake on dedicated cardiac PET (10-8-1) Delayed enhancement on CMR (12-5-1) Positive gallium uptake (8-11-0) Defect on perfusion scintigraphy or SPECT scan (4-11-3) T2 prolongation on CMR (2-11-5)	Reduced LVEF in the presence of other risk factors (e.g., HTN, DM) (0-1-17) Atrial dysrhythmias (0-4-15)	Frequent ectopy (>5% QRS) (0-6-13) Bundle branch block (2-8-9) Impaired RV function with a normal PVR (0-8-10) Fragmented QRS or pathologic Q waves in ≥2 anatomically contiguous leads (0-7-10) At least one abnormal SAECG domain (0-6-10) Interstitial fibrosis or monocyte infiltration (4-8-7)

Judson et al. Official journal of WASOG / World Association of Sarcoidosis and Other Granulomatous Disorders. 31. 19-27. 2014

Japanese Criteria - Cardiac Involvement in Sarcoidosis

Table 1 (cont.)
Clinical findings defining cardiac involvement

Cardiac findings should be assessed based on the major criteria and the minor criteria. Clinical findings that satisfy the following 1) or 2) strongly suggest the presence of cardiac involvement.
1) Two or more of the five major criteria (a) to (e) are satisfied .
2) One of the five major criteria (a) to (e) and two or more of the three minor criteria (f) to (h) are satisfied.

(Note: English translation of tables has been provided by the authors.)

Table 1 Criteria for cardiac involvement of sarcoidosis

1. Major criteria
(a) High-grade atrioventricular block (including complete atrioventricular block) or fatal ventricular arrhythmia (e. g., sustained ventricular tachycardia and ventricular fibrillation)
(b) Basal thinning of the ventricular septum or abnormal ventricular wall anatomy (ventricular aneurysm, thinning of the middle or upper ventricular septum, regional ventricular wall thickening)
(c) Left ventricular contractile dysfunction (left ventricular ejection fraction less than 50%)
(d) ^{67}Ga citrate scintigraphy or ^{18}F-FDG PET reveals abnormally high tracer accumulation in the heart
(e) Gadolinium-enhanced MRI reveals delayed contrast enhancement of the myocardium
2. Minor criteria
(f) Abnormal ECG findings: Ventricular arrhythmias (nonsustained ventricular tachycardia, multifocal or frequent premature ventricular contractions), bundle branch block, axis deviation, or abnormal Q waves
(g) Perfusion defects on myocardial perfusion scintigraphy (SPECT)
(h) Endomyocardial biopsy: Monocyte infiltration and moderate or severe myocardial interstitial fibrosis

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Terasaki et al Annals of nucl cardiol 2017: 3(1): 42-45

Comparison

Expert Consensus Recommendations on ***Criteria for the Diagnosis of CS***

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   It is probable* that there is CS if:
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Terasaki et al Annals of nucl cardiol 2017: 3(1): 42-45

Japanese Criteria - Isolated Cardiac Sarcoidosis

Table 1 Criteria for cardiac involvement of sarcoidosis

Table 3 Diagnostic guidelines for isolated cardiac sarcoidosis

Prerequisite

1. No clinical findings characteristic of sarcoidosis are observed in any organs other than the heart. (The patient should be examined in detail for respiratory, ophthalmic, and skin involvements of sarcoidosis. When the patient is symptomatic, other etiologies that can affect the corresponding organs must be ruled out.)
2. ^{67}Ga scintigraphy or ^{18}F-FDG PET reveals no abnormal tracer accumulation in any organs other than the heart.
3. A chest CT scan reveals no shadow along the lymphatic tracts in the lungs or no hilar and mediastinal lymphadenopathy (minor axis > 10 mm).

1) Histological diagnosis group
Isolated cardiac sarcoidosis is diagnosed histologically when endomyocardial biopsy or surgical specimens demonstrate non-caseating epithelioid granulomas.
2) Clinical diagnosis group
Isolated cardiac sarcoidosis is diagnosed clinically when the criterion (d) and at least three other criteria of the major criteria (a)-(e) are satisfied (Table 1).

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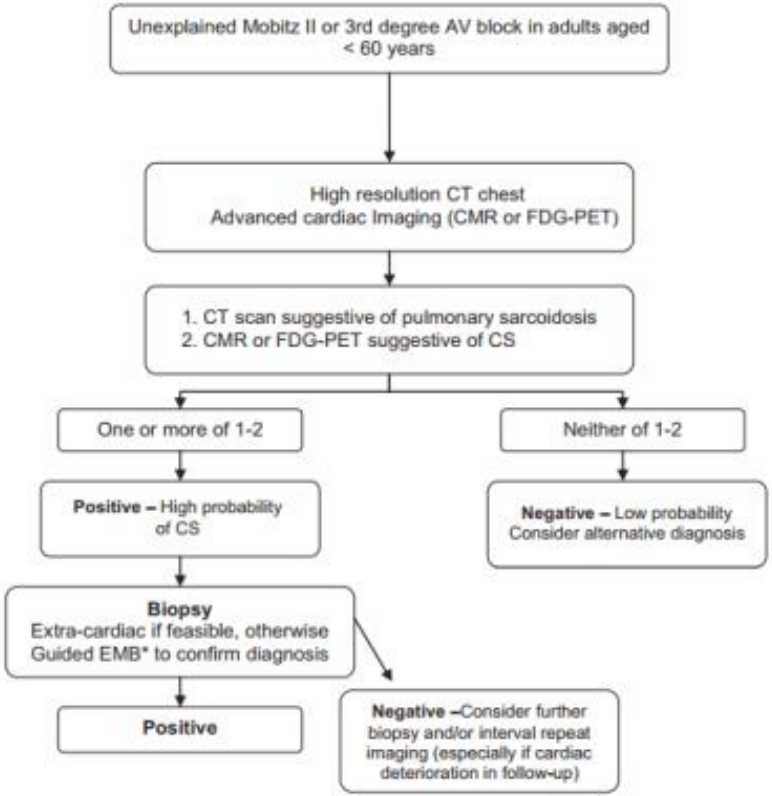
Terasaki et al Annals of nucl cardiol 2017: 3(1): 42-45

BEING SUSPICIOUS - Heart Block

Expert Consensus Recommendations on Screening for CS in Patients With Specific Cardiac Presentations	
Class IIa	1. Screening for CS in patients younger than 60 years with unexplained second-degree (Mobitz II) or third-degree AV block **can be useful**. 2. If initial screening tests are suggestive of sarcoidosis, biopsies **can be useful**. Biopsies should be extracardiac if feasible, otherwise guided endomyocardial (see text for details).

Birnie et Al, Heart Rhythm, V 11, N 7, 1304-1323; 2014



*voltage guided or advanced imaging guided endomyocardial biopsy (see text in Section 4 for details)

Birnie et Al, Heart Rhythm, V 11, N 7, 1304-1323; 2014

BEING SUSPICIOUS - VT

- HRS 10/14 voted in favor of screening for Sarcoid but did not reach threshold to become recommendation

Birnie et Al, Heart Rhythm, V 11, N 7, 1304-1323; 2014

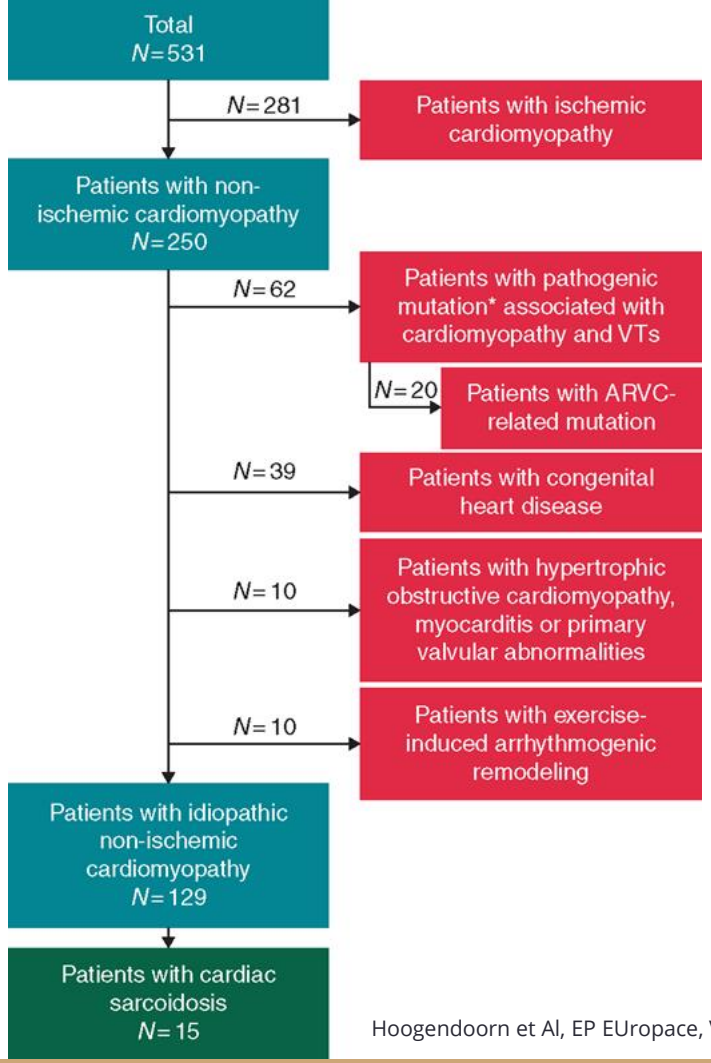
BEING SUSPICIOUS - VT

- Prospective study of patients with VT
  - Excluded OT VT, Fascicular VT, VT secondary to CAD, or prior Cardiac Sarcoid
  - Patients underwent FDG-PET
  - If positive -> biopsy
  - 14 patients met inclusion criteria and 4 had CS (29%)

Nery PB, Pacing Clin Electrophysiol. 2014 Mar;37(3):364-74. doi: 10.1111/pace.12277. Epub 2013 Sep 17

BEING SUSPICIOUS - VT

Leiden VT ablation registry retrospective data from 2008 to 2018



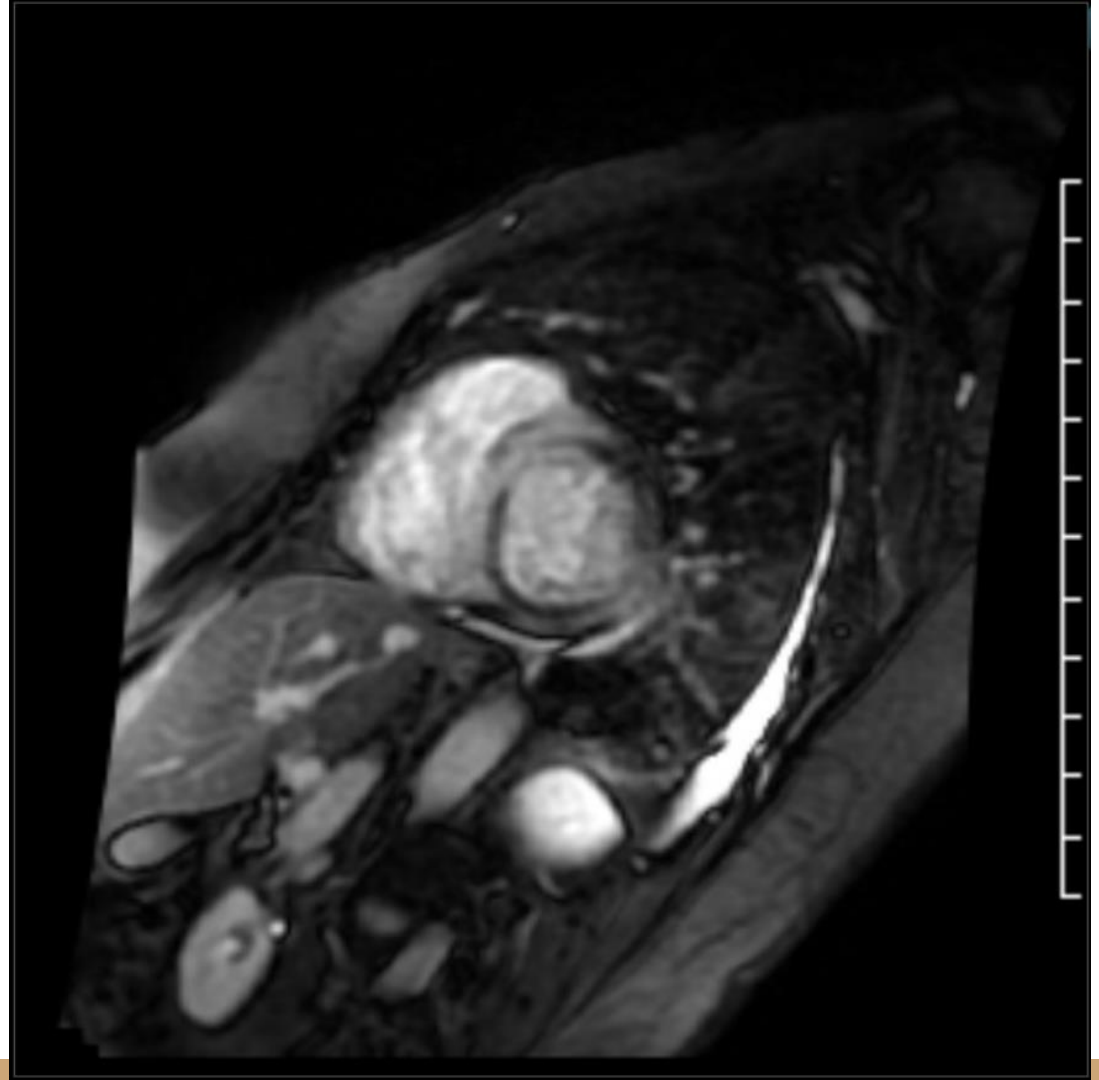
Hoogendoorn et Al, EP EUropace, V 22, N 9, 1376-1383; 2020

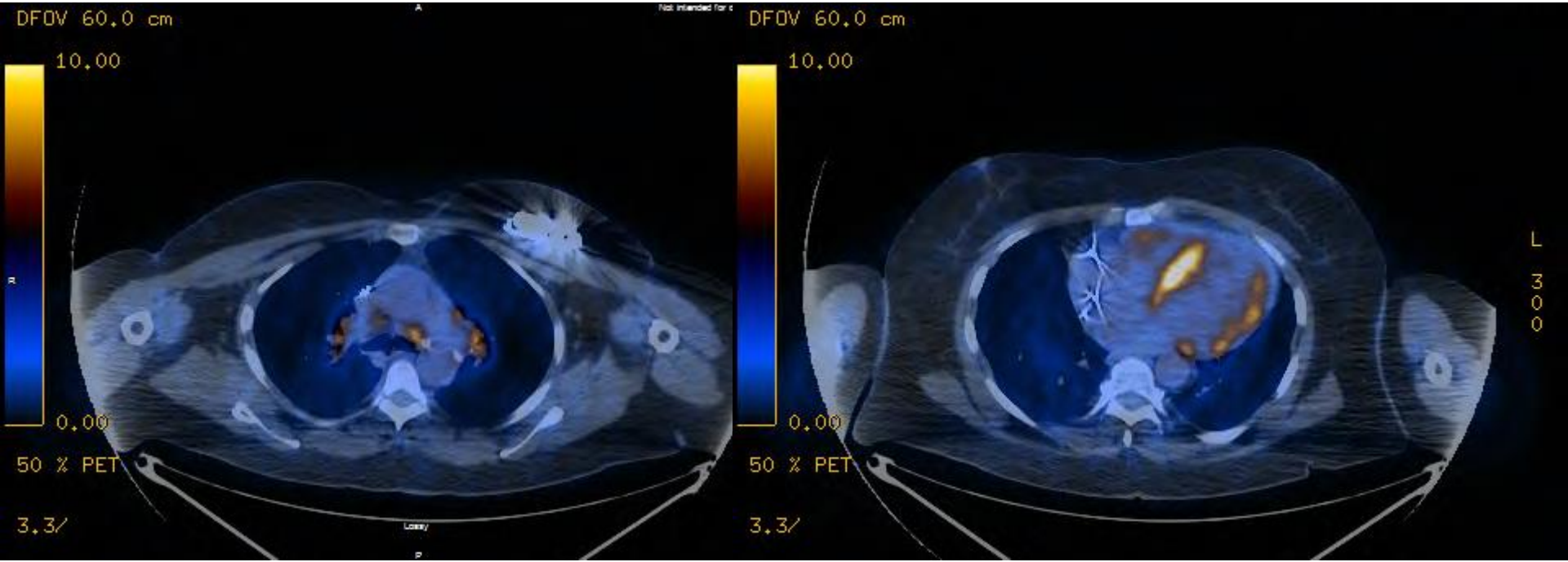
Take home points

- Multimodality imaging
  - MRI
  - FDG PET +/- Perfusion
  - ECHO
- EKG/Holter/MCOT
- Pathology - when possible

Case #1

- What Next?
- MRI and FDG PET




DFOV 60.0 cm
10.00
0.00
50 % PET
3.3/
DFOV 60.0 cm
10.00
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50 % PET
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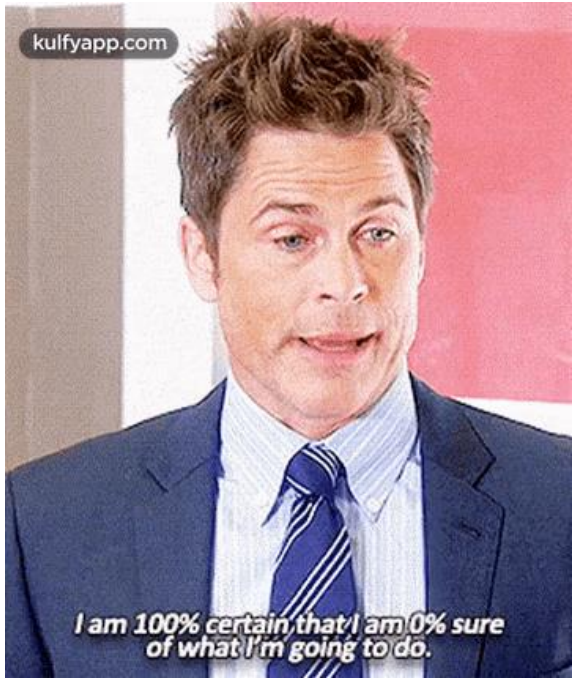
Case #1- SLAM DUNK

- 67 y/o African American Female w systemic sarcoidosis and cardiac involvement
  - +Heart Block
  - +FDG Uptake
  - +MRI LGE
  - +MRI Shows EF now 40-45%


kulfyapp.com
I am 100% certain that I am 0% sure
of what I'm going to do.

Treatment

Case #1

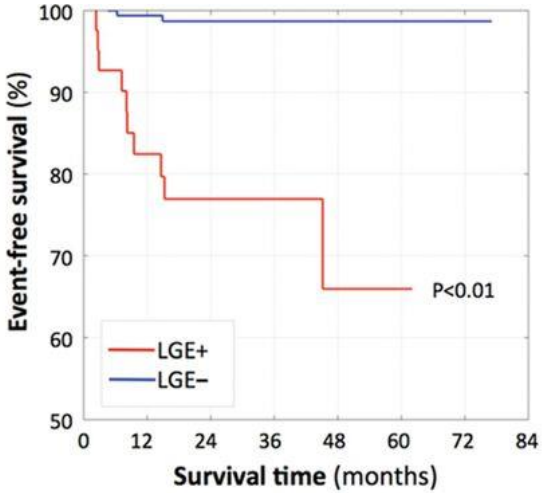
- What to do next?
  - A. PPM
  - B. ICD
  - C. Immunosuppression
  - D. B and C

ICD GUIDELINES

COR	LOE	Recommendations
I	B-NR	1. In patients with cardiac sarcoidosis who have sustained VT or are survivors of SCA or have an LVEF of 35% or less, an ICD is recommended, if meaningful survival of greater than 1 year is expected.[S7.6-1–S7.6-5]
IIa	B-NR	2. In patients with cardiac sarcoidosis and LVEF greater than 35% who have syncope and/or evidence of myocardial scar by cardiac MRI or positron emission tomographic (PET) scan, and/or have an indication for permanent pacing, implantation of an ICD is reasonable, provided that meaningful survival of greater than 1 year is expected.[S7.6-6–S7.6-10]
IIa	C-LD	3. In patients with cardiac sarcoidosis and LVEF greater than 35%, it is reasonable to perform an electrophysiological study and to implant an ICD, if sustained VA is inducible, provided that meaningful survival of greater than 1 year is expected.[S7.6-11,S7.6-12]
IIa	C-LD	4. In patients with cardiac sarcoidosis who have an indication for permanent pacing, implantation of an ICD can be beneficial.[S7.6-13]

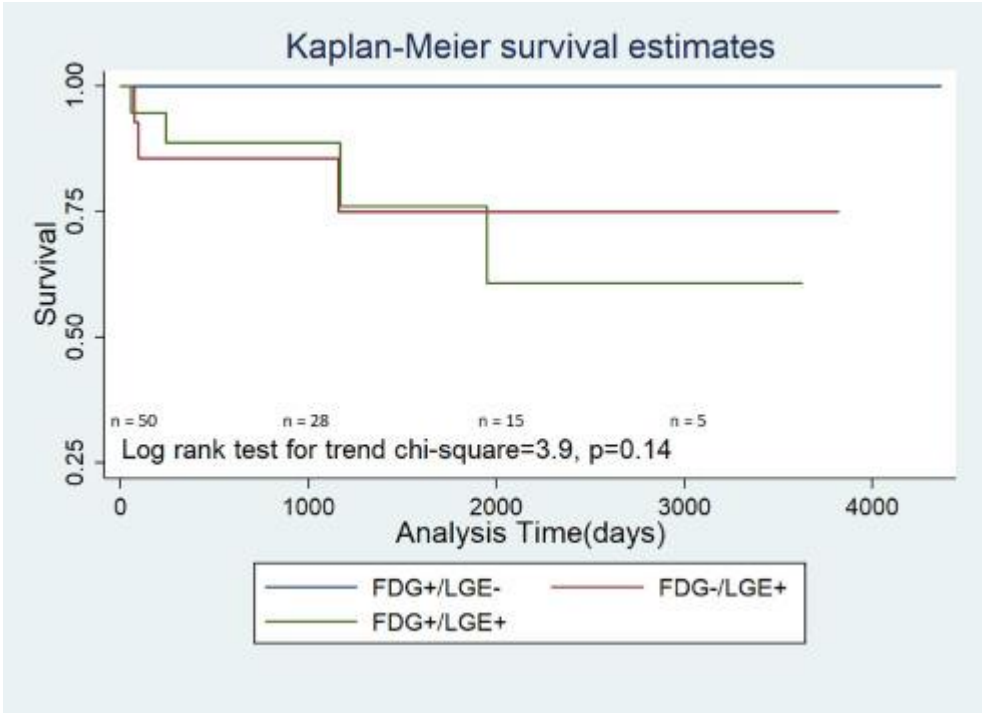
Al-Khatib et al,
AHA/ACC/HRS Guideline
For management of SCD
2017

VT Free Survival



Months	0	12	24	36	48	60	72	84
LGE +	41	32	21	12	5	1	0	0
LGE −	164	149	124	92	60	14	2	0

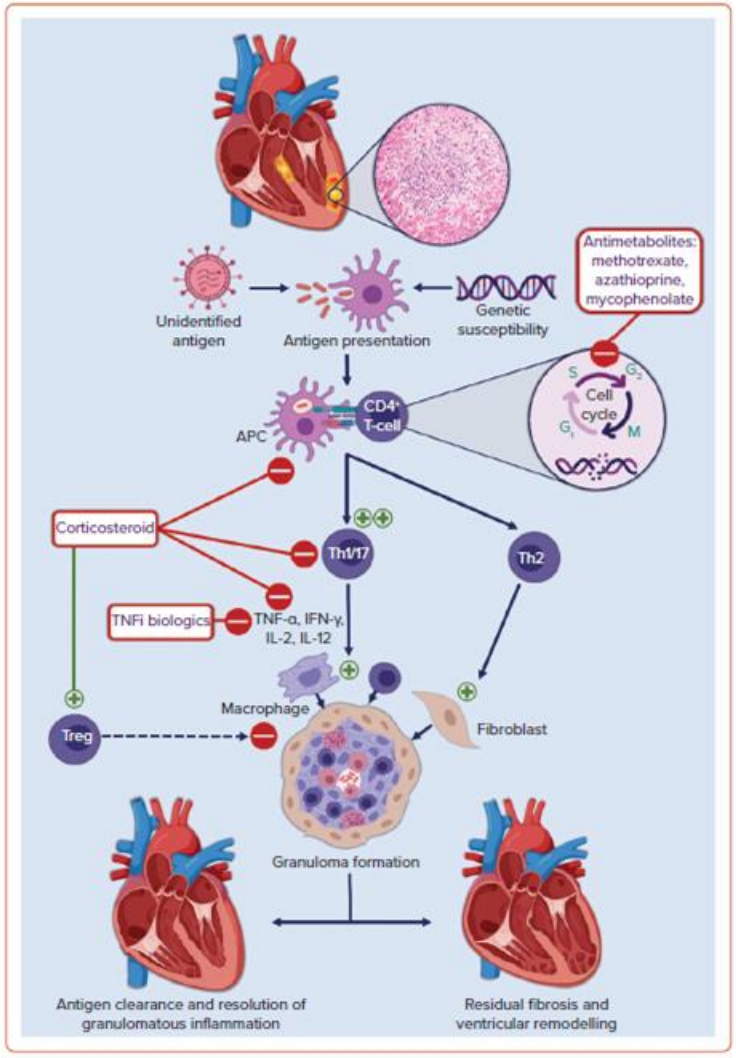
Number at risk



Murtagh et al. Circ Imaging 2016 January VOl 9:1

Gowani et Al, Am Journal Cardiology, 2020 Aug 15;S0002-9149(20)

Immunosuppression



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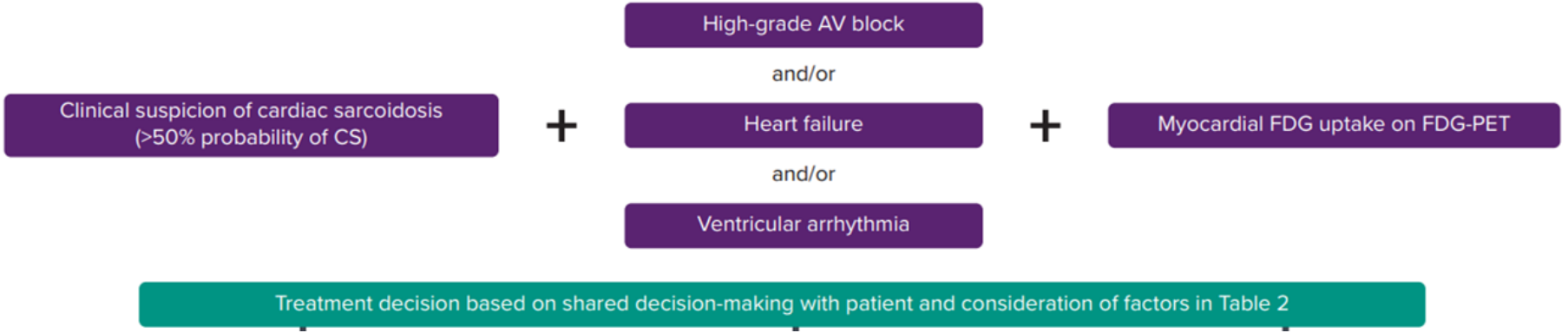
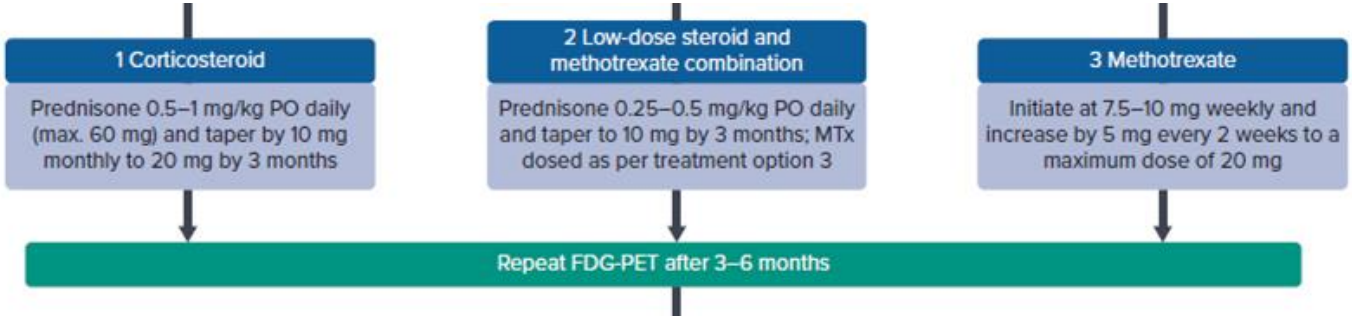
Immunosuppression



Decisions in Cardiac Sarcoidosis

Factors
Degree of LV dysfunction and established fibrosis at diagnosis
Extent of inflammation on cardiac PET
Ventricular arrhythmia burden
Presence of systemic sarcoidosis also warranting immunosuppressive therapy
Metabolic complication risk
Opportunistic infection risk
Malignancy risk with chronic immunosuppression

Immunosuppressive regimens



Clinical and FDG pet response to help guide therapy decsions

Methotrexate has the most data behind it but it is still very limited data

- Our center uses approach similar to #2 but with mycophenolate

Consider TNF-Alpha inhibitor or alternative immunosuppressive therapy

Giblin, Card Fail Rev. 2021 Mar; 7: e17. doi: 10.15420/cfr.2021.16

Case #1

- What to do next?
  - A. PPM
  - B. ICD
  - C. Immunosuppression
  - **D. B and C**

Case #1

- We ended up placing dual chamber ICD
- And immunosuppression with steroids
- Patient eventually developed VT the VT storm and went on to cardiac transplantation now doing great
- Get permission to use patient image at son's wedding here.

Post Lecture Question?

What range of patients with systemic sarcoidosis have cardiac involvement

A. 0-25%

B. 25-50%

C. 50-75%

D. 75-100%

E. Nobody knows

Post Lecture Question?

What range of patients with systemic sarcoidosis have cardiac involvement

A. 0-25%

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C. 50-75%

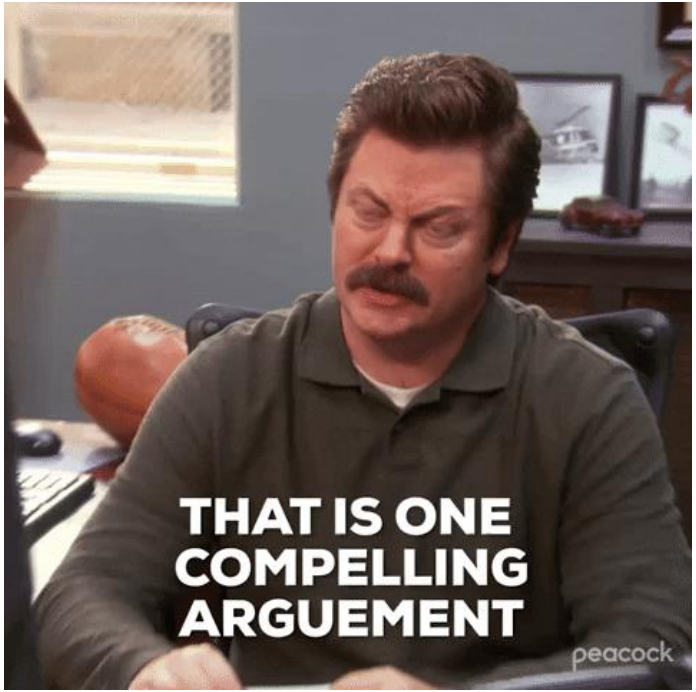
D. 75-100%

E. Nobody knows

- Questions?
- Comments?
- Snide Remarks?

Email
amit.patel@ascension.org

Cell
469-693-4867



Objective One - BE SUSPICIOUS