Myocarditis: 2019

Oklahoma Heart Research
& Education Symposium

Tulsa, OK

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DISCLOSURE

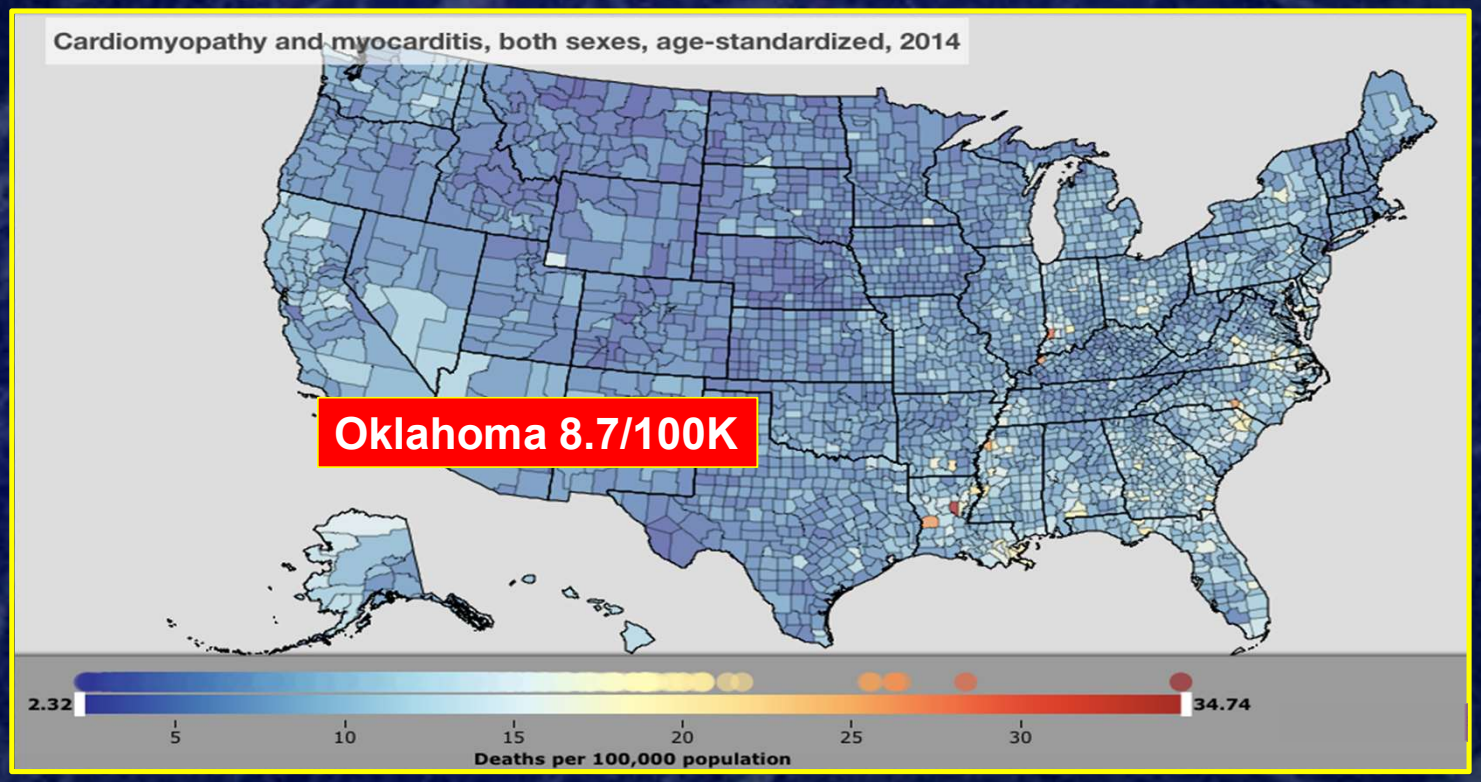
Relevant Financial Relationship(s)

None

Off Label Usage

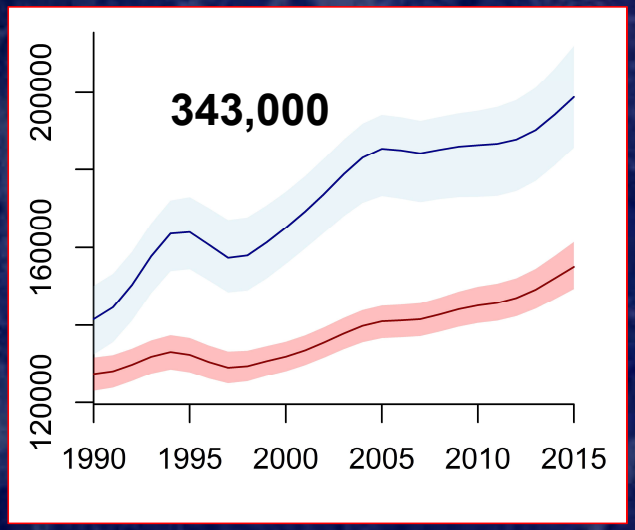
None

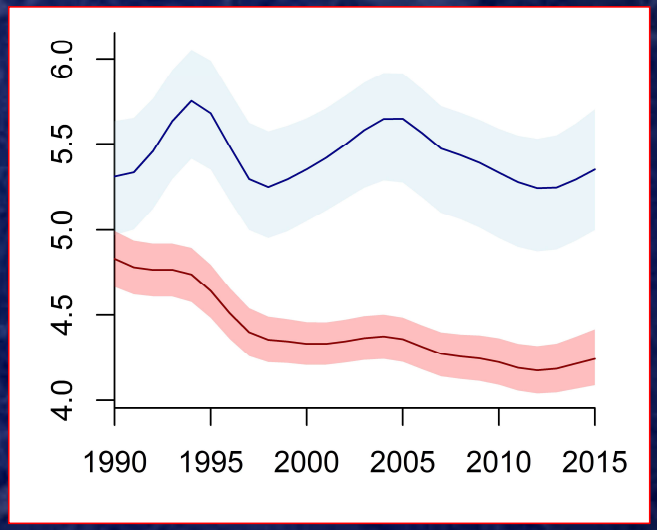
Death Rate due to Myocarditis and Cardiomyopathy



Source: 2016 Global Burden of Disease project

Myocarditis and Cardiomyopathy
Deaths and Death Rate /100,000
1990-2015





3.1M cases in 2017

JACC, Nov 29th 2016
Lancet November 10th, 2018

Articles

Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

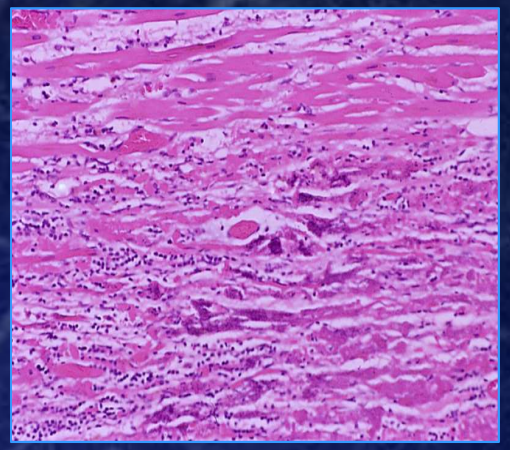
Global Burden of Disease Study 2013 Collaborators

Year	Myocarditis Cases	#/100,000
1990	961,000	22.8
2013	1,481,000	22.0

The Lancet, published online June 7th, 2015

Myocarditis

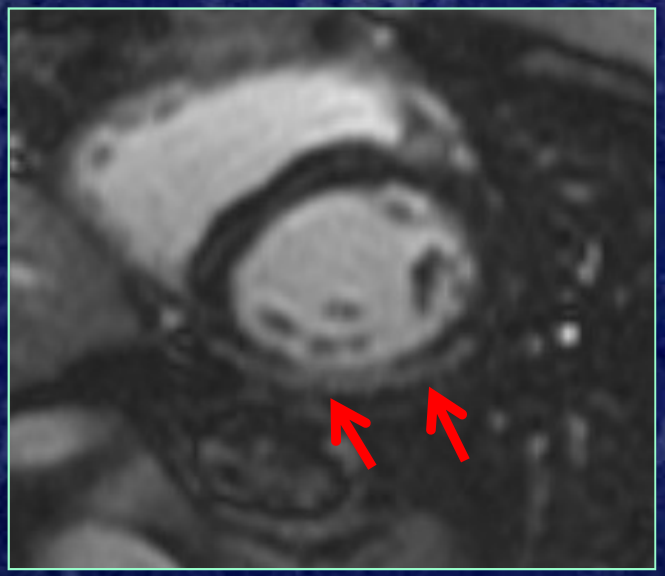
Clinical Presentations



- Myopericarditis/MINOCA
- Sudden Death
- Acute Dilated Cardiomyopathy
- Chronic Dilated Cardiomyopathy

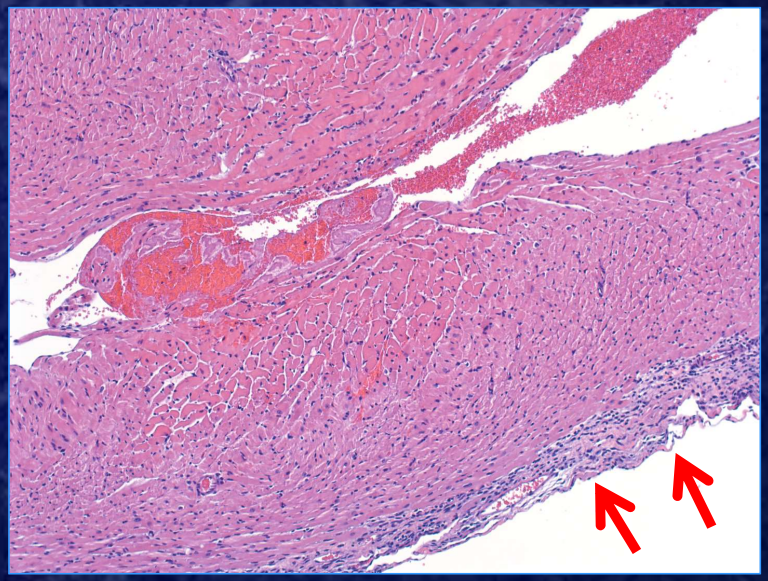
Myopericarditis MRI and Histology

Epicardial-Mid Wall



Marholdt, H, etal. Circulation 2004

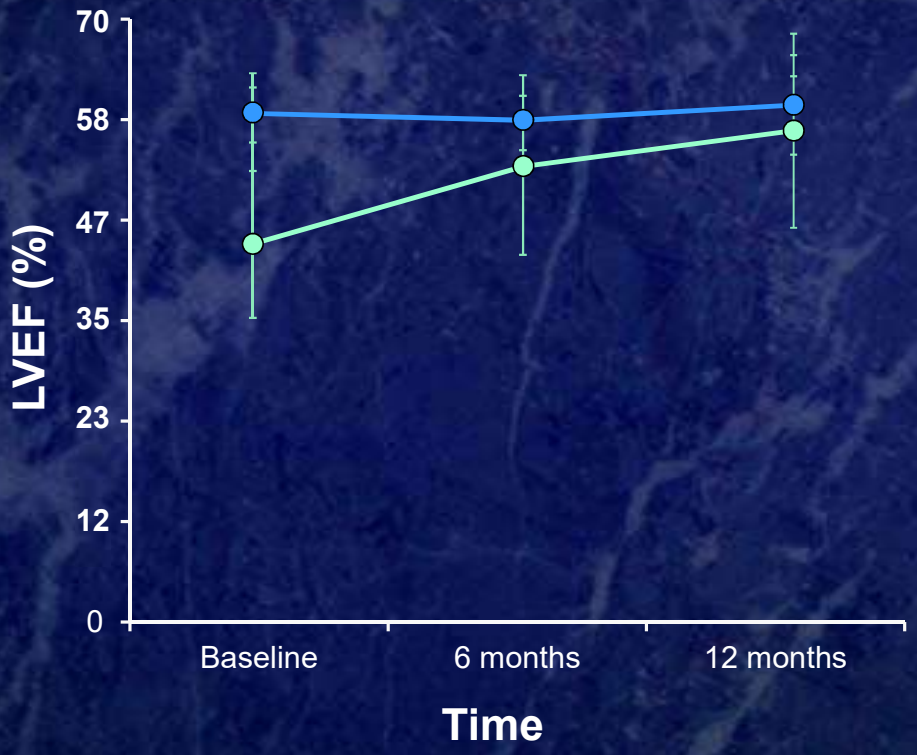
Mouse model of CVB Myocarditis



Fairweather, DL, Cooper, LT, et al

Good Prognosis for Pericarditis With and Without Myocardial Involvement

Results From a Multicenter, Prospective Cohort Study



N= 486

No Deaths

10.5% risk of recurrence

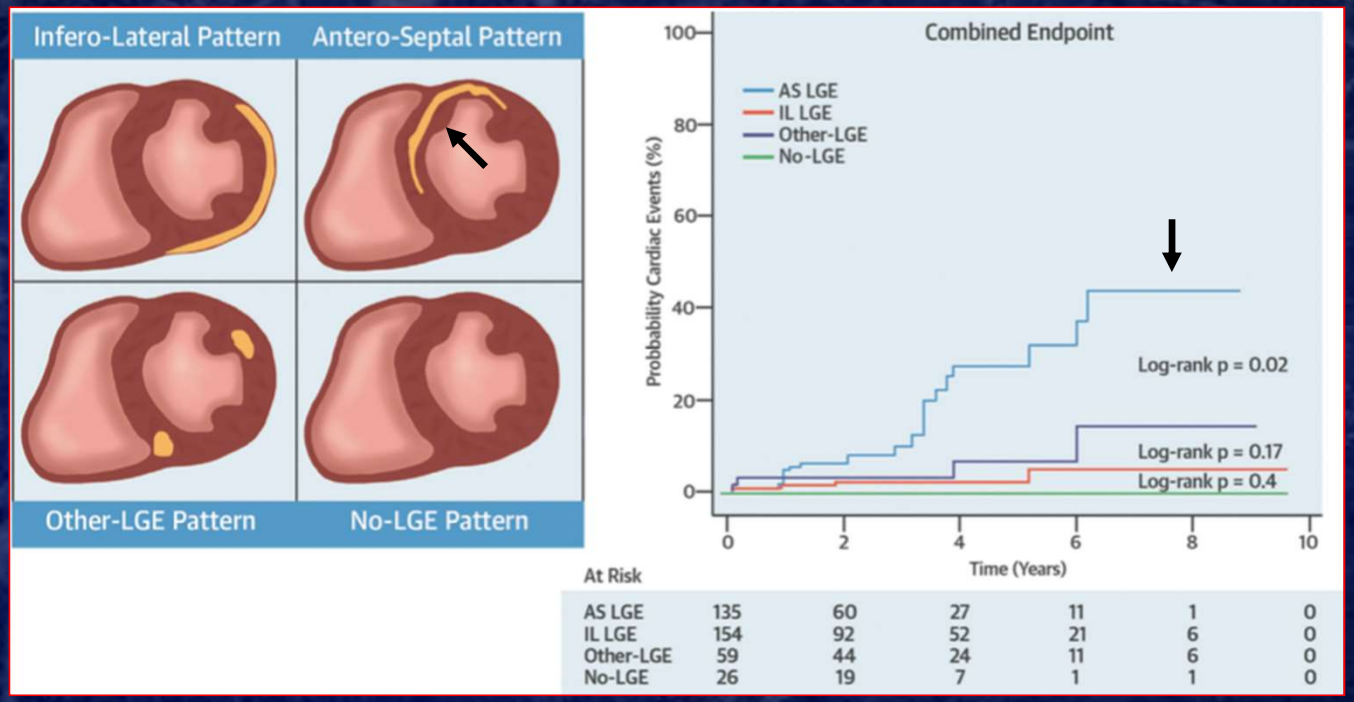
Imazio, M. et al. Circ 2013

ITAMY Study
Ten Center Italian Registry
2006-2013

- 374 patients with suspected myocarditis
- Chest pain 95%
- Age 35, 73% male; LVEF 62%
- Median FU 4.3 years
- Events: 26/374.

Aquaro, et al JACC 2017

Anteroseptal Pattern on MRI
Increased risk of MACE



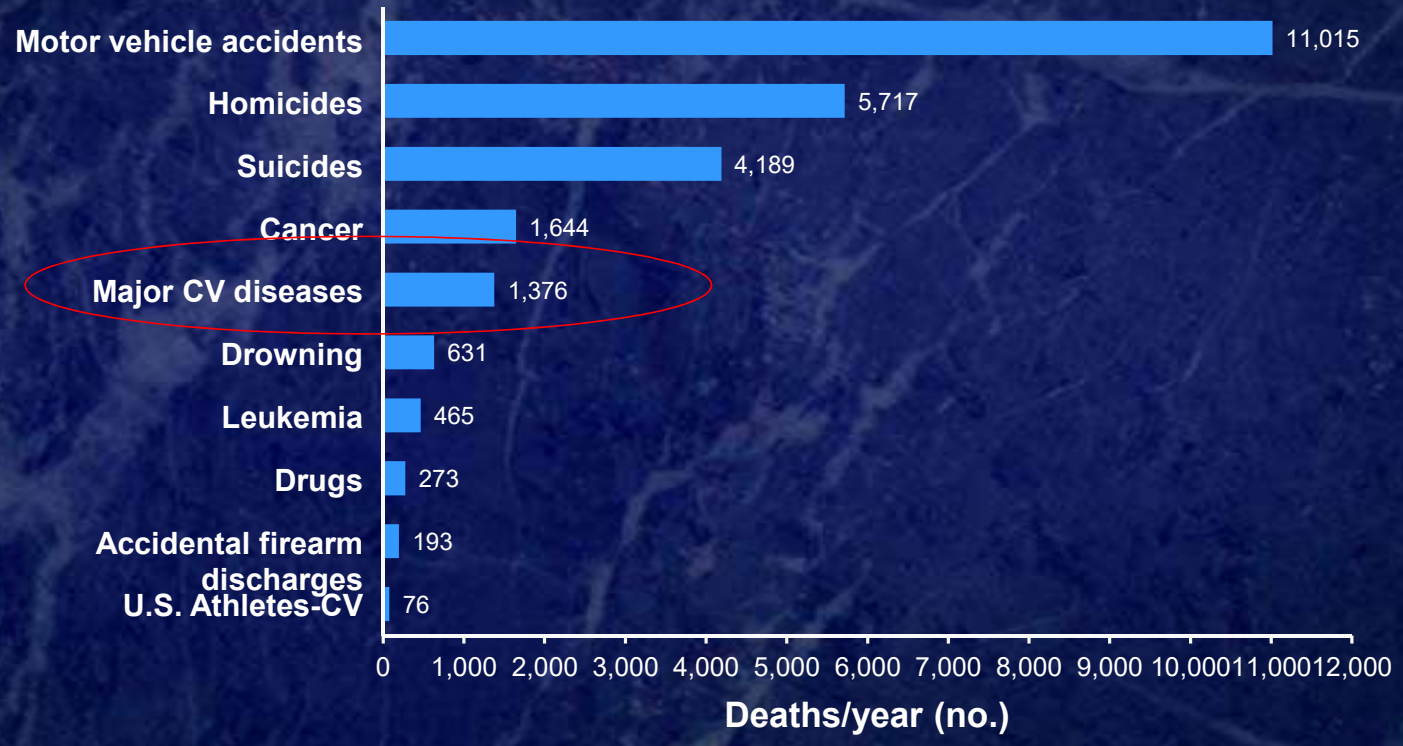
5 yr event probability 0.36 in AS group

Aquaro, et al JACC 2017

The Rojas Family and Elysa

Denver Rapids website

Comparative Frequencies of Death Attributable to All Causes in Individuals Aged <25 Years



Maron et al: Circulation 130:1303, 2014

Myocarditis and Sudden Death

- ≈2% of infant CV sudden deaths
- ≈5% of childhood CV sudden deaths
- ≈4-20% of CV sudden deaths in athletes less than age 35-40
- Males > Females

Maron, BJ…Cooper, LT et al. Revised 36th Bethesda Conference
Circulation, December 2015

Sudden Death Risk in Myocarditis

AHA/ACC Scientific Statement

Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 3: Hypertrophic Cardiomyopathy, Arrhythmogenic Right Ventricular Cardiomyopathy and Other Cardiomyopathies, and Myocarditis

A Scientific Statement From the American Heart Association and American College of Cardiology

- Avoid Competitive Sports for 3-6 months
- ETT, Echo, Holter before clearance
- Role of CMR in risk stratification is uncertain

Circulation 2015

2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

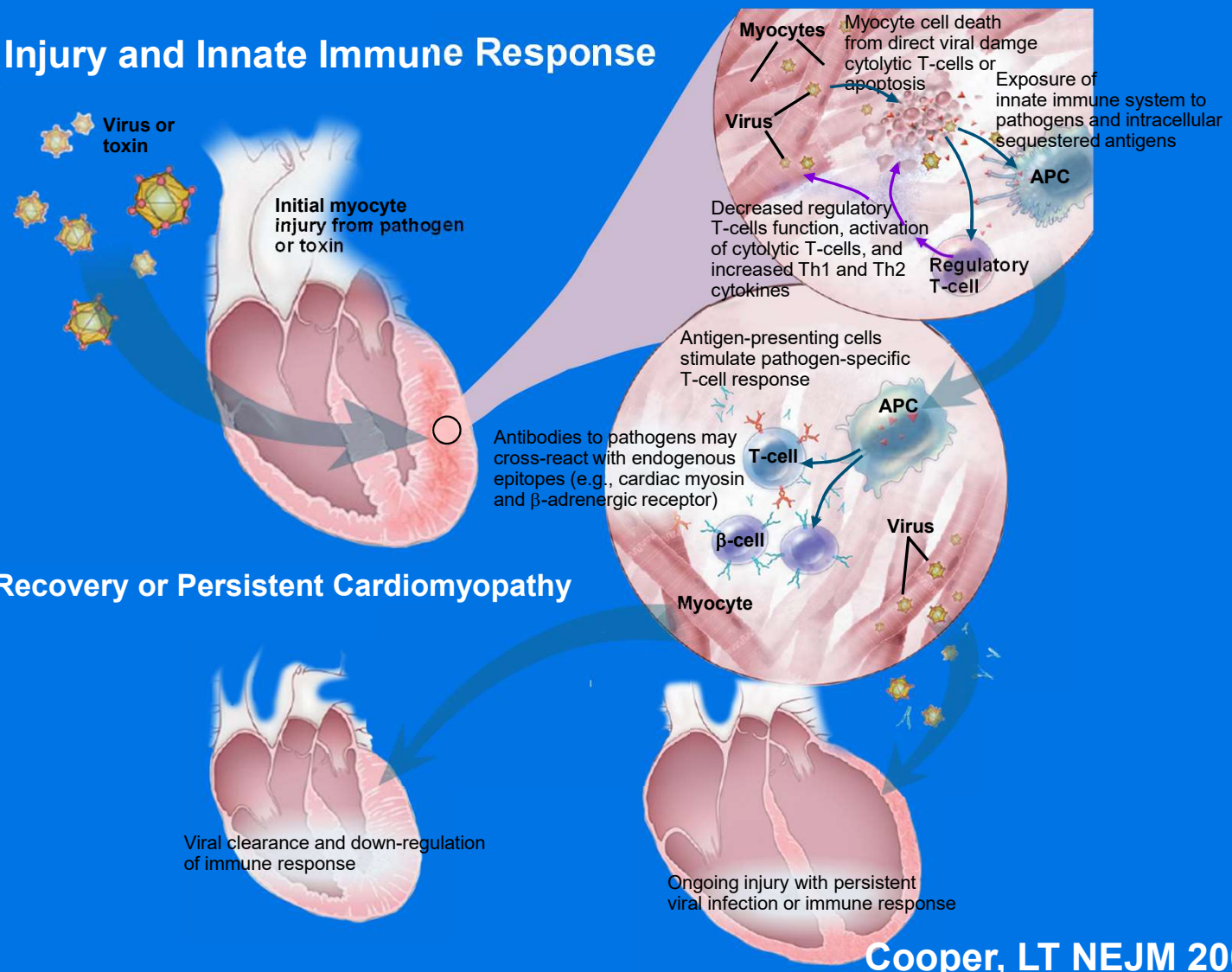
Recommendations for Myocarditis

References that support the recommendations are summarized in Online Data Supplement 32.

COR	LOE	Recommendations
I	C-LD	1. In patients with life-threatening VT or VF associated with confirmed or clinically suspected myocarditis, referral to centers with mechanical hemodynamic support and advanced arrhythmia management is recommended (1).
IIb	C-LD	2. In patients with giant cell myocarditis with VF or hemodynamically unstable VT treated according to GDMT, an ICD and/or an antiarrhythmic medication may be considered if meaningful survival of greater than 1 year is expected (2-4).

JACC, October 2017

Injury and Innate Immune Response



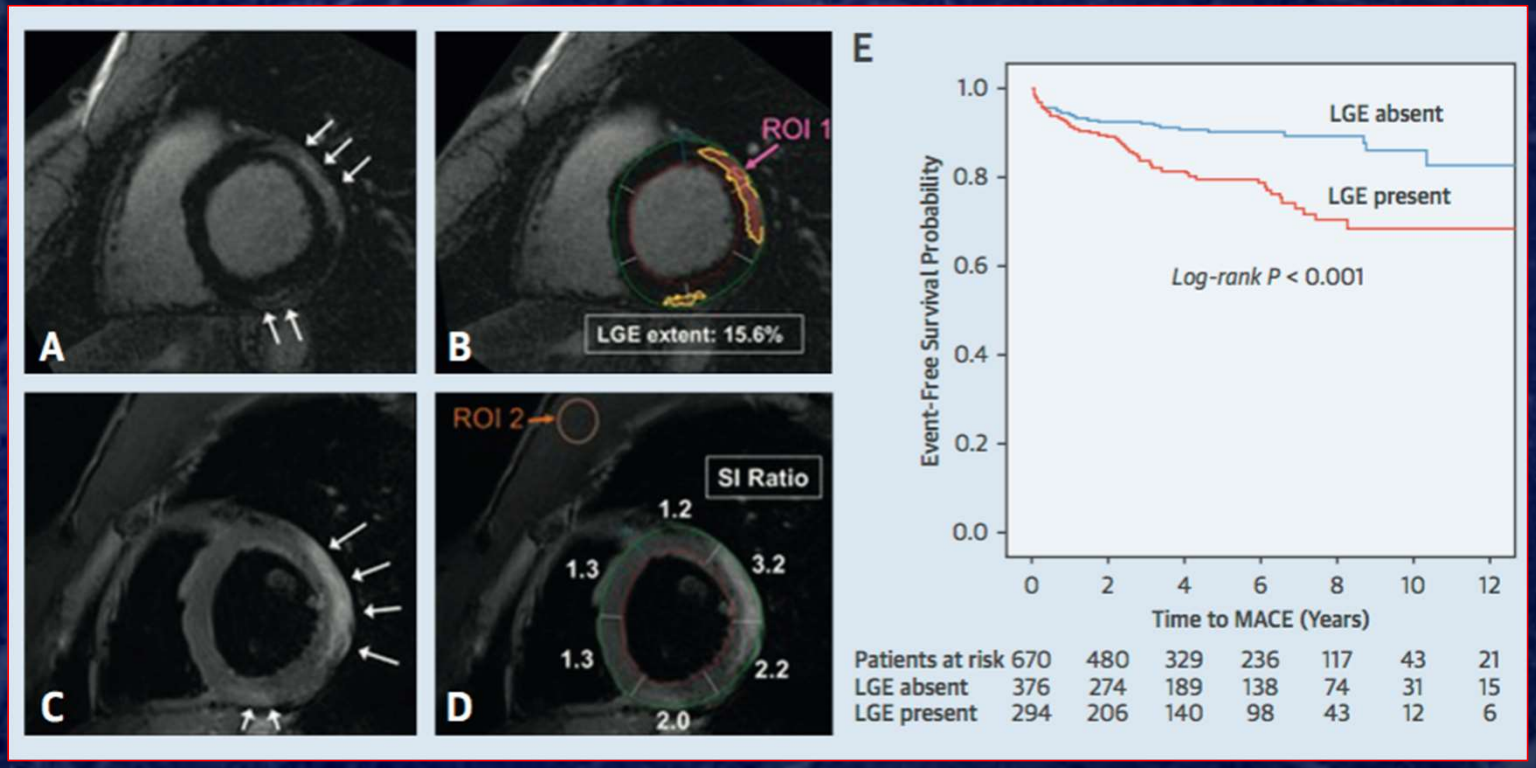
Cooper, LT NEJM 2009

Brigham and Women's Hospital MRI Case Series 2002-2015

- 670 patients with suspected myocarditis
- Chest pain 52% (LV dysfunction/ dyspnea 30%; Rhythm problems 18%)
- Age 47, 59% male; 13% QRS>120 ms
- All had MRI -294 with DGE
- Median FU 4.7 years

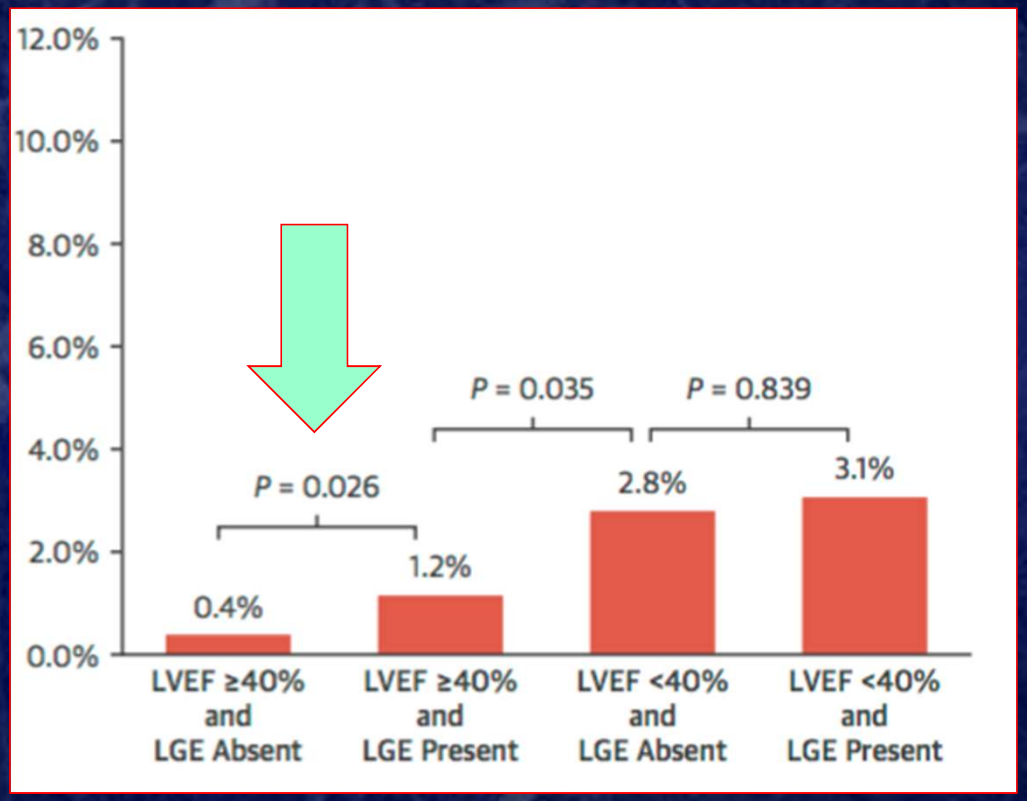
Grani, C et al JACC 2017

DGE on CMR associated with greater risk of MACE



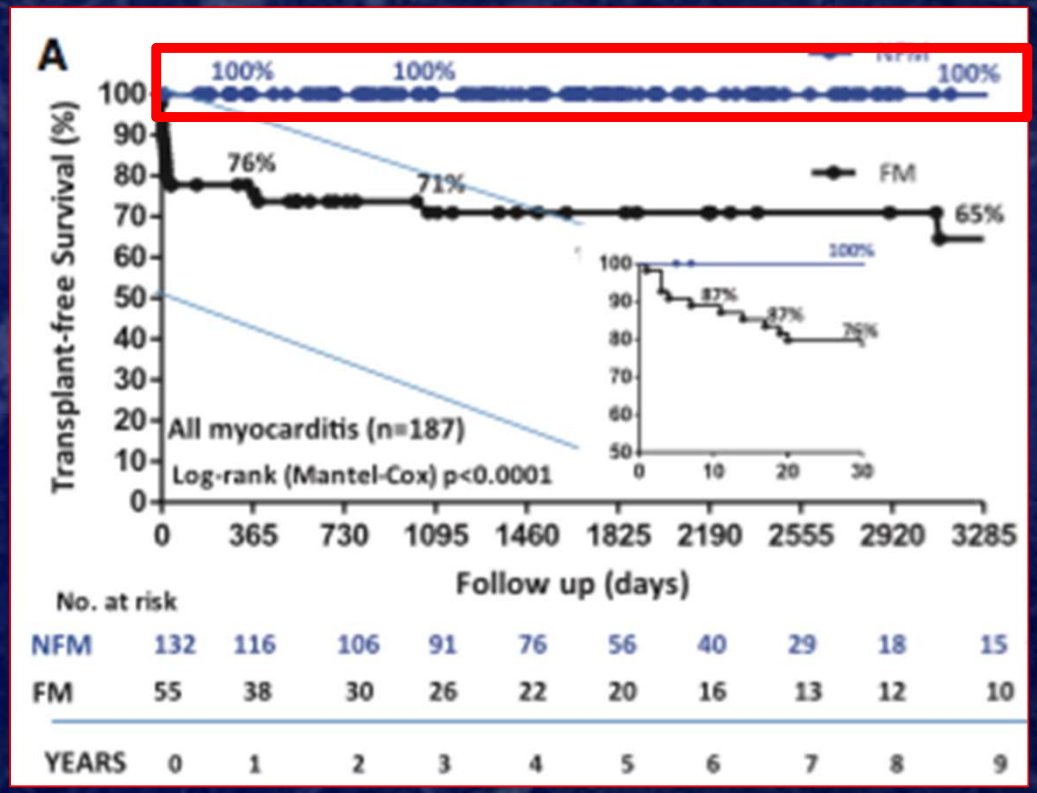
Grani, C et al JACC 2017

Annualized Risk of Death varies with LVEF and DGE



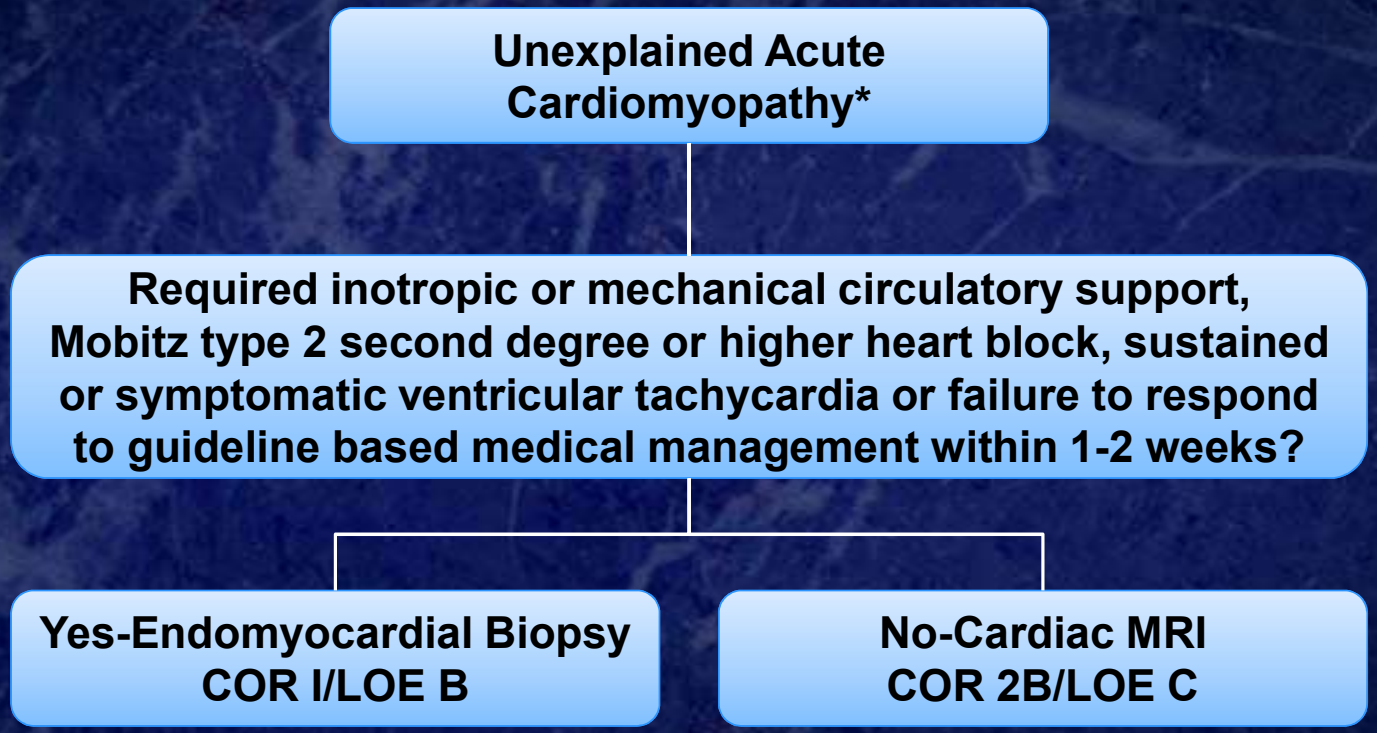
Grani, C et al JACC 2017

Survival in Fulminant Versus Nonfulminant Acute Myocarditis n=187



Enrico Ammirati, Circulation August 2017

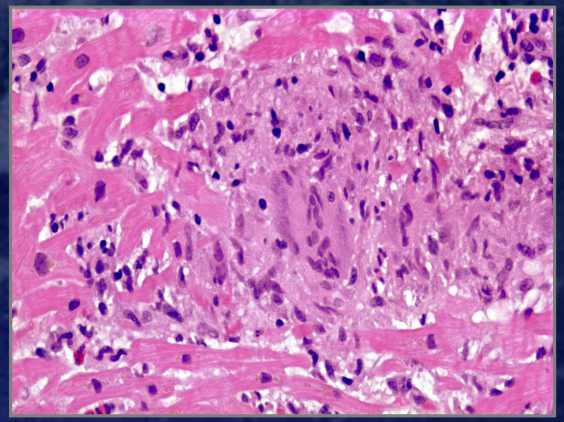
Algorithm for the Evaluation of Suspected Myocarditis in the Setting of Unexplained Acute DCM

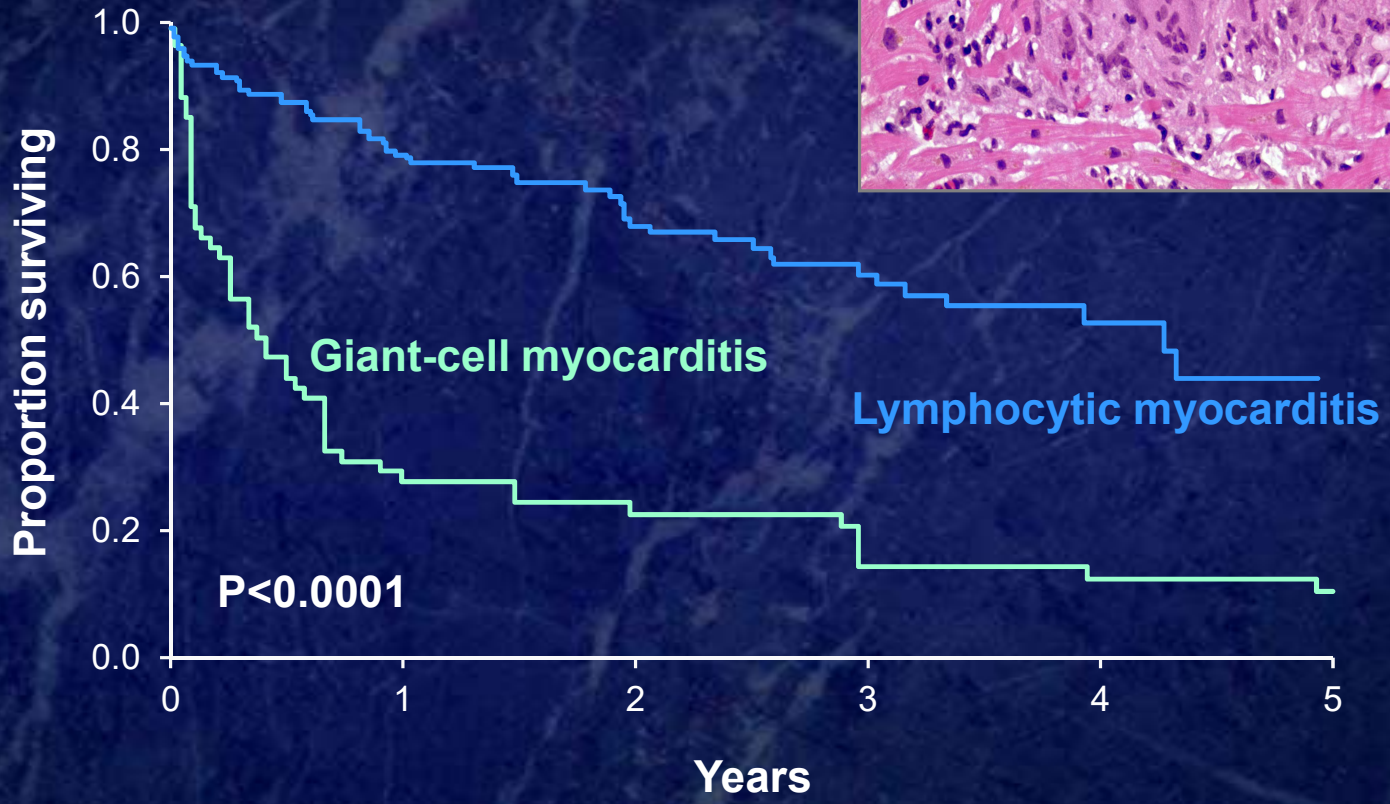


*Usually a dilated cardiomyopathy. Fulminant myocarditis may have normal end diastolic diameter with mildly thickened walls. Excluded ischemic, hemodynamic (valvular, hypertensive), metabolic, and toxic causes of cardiomyopathy as indicated clinically.

Bozkurt, et al. Circulation, 2016

Prognosis in Myocarditis Varies by Histology

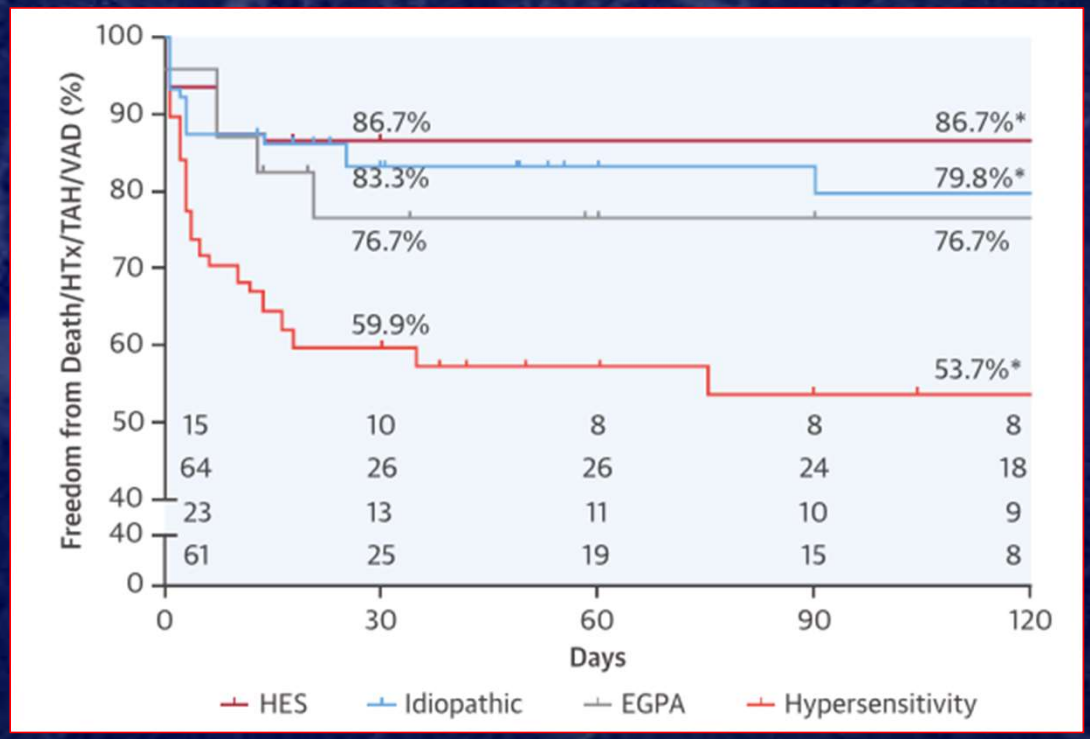




Cooper, et al: N Engl J Med 1997 336:1860-66

Eosinophilc Myocarditis

Outcome



Brambatti, et al. JACC Nov 7th 2017

Mechanical Circulatory Support Outcomes vary by Histology

- **Lymphocytic Myocarditis**
  75% bridge to recovery –

  Boehmer JP. J Card Fail 2012

- **EMB performed in only 26% of FM-**

  Lorusso, et al Ann Thor Surg 2016

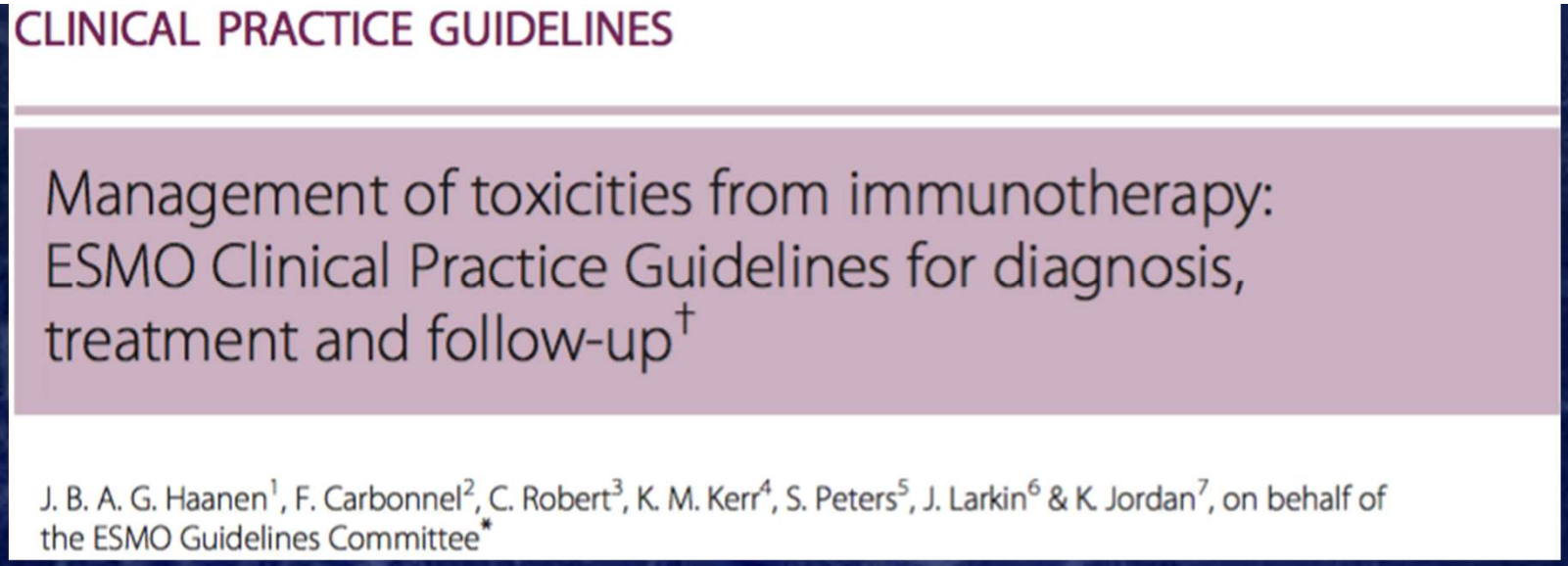
- **Giant Cell Myocarditis**
  80-100% rate of death/transplant-ECMO

  Montero, Int J Cardiol 2018

Checkpoint Inhibitor Myocarditis
8 Centers; n=35

- Prevalence of Myocarditis 1.14%
- Median time from treatment 34 days
- CHB 3; CV shock 3; CV arrest 4 cases
- Overall 46% MACE rate over 102 days
- Higher dose steroids associated with lower troponin and MACE rates

Mahmood, SS JACC 2018



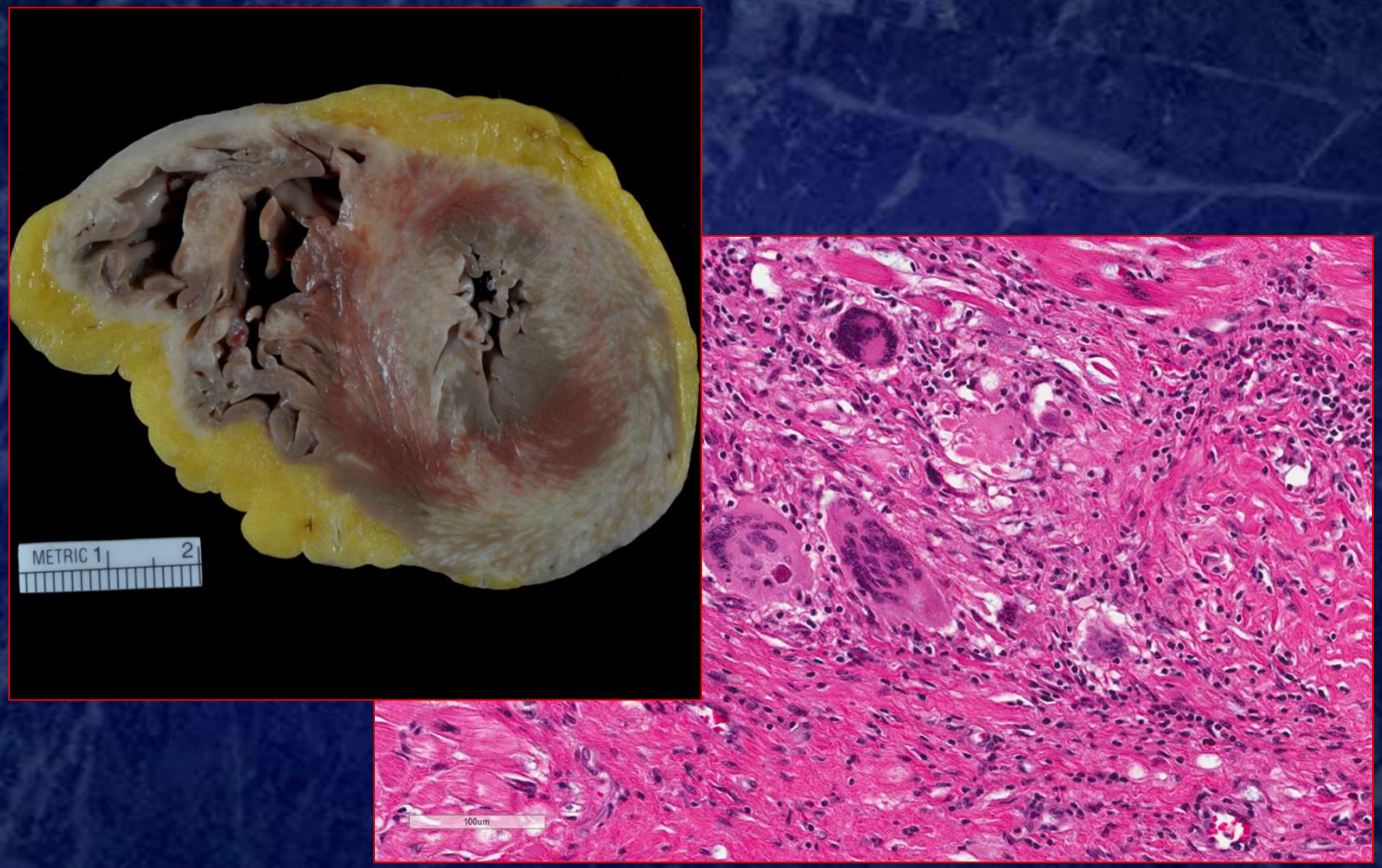
- Cardiotoxicity usually presents within 2 months with CHF or ventricular arrhythmias
- Start methylprednisolone 1-2 mg/kg.
- If deterioration, consider adding MMF or tacrolimus
- Heart Biopsy?

Annals of Oncology 2017
Johnson, DB NEJM 2016

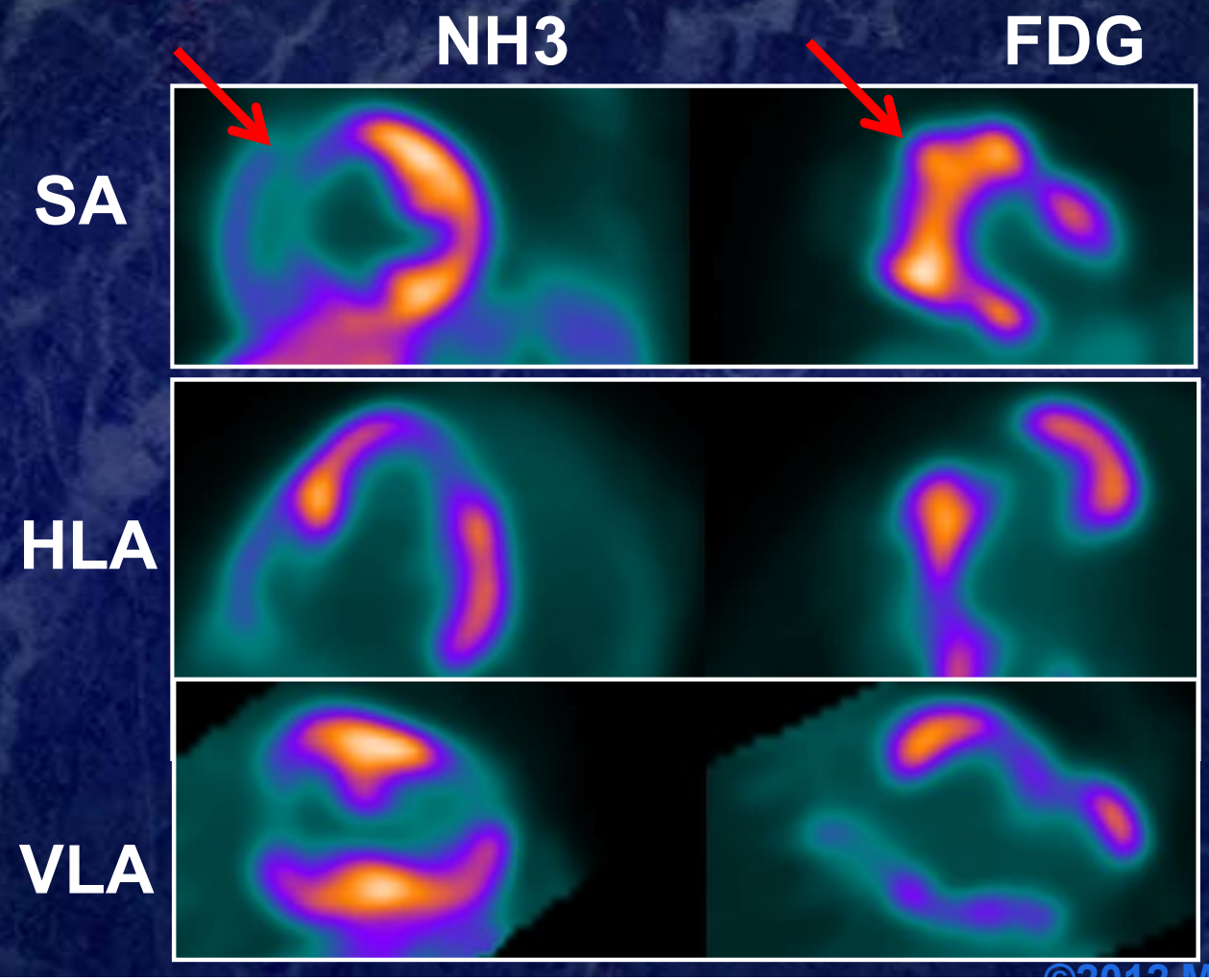
2019 Summary of Management of Acute/Fulminant Myocarditis

- **All**- GDMC and Hemodynamic support- unloading if possible
- **GCM**- Immunosuppression including cyclosporine or tacrolimus
- **Checkpoint Inhibitor**- Corticosteroids
- **Eosinophilic**- Immunosuppression

Cardiac Sarcoidosis



^{13}N-NH3 defects and matched ^{18}F-FDG uptake associated with Cardiac Sarcoidosis



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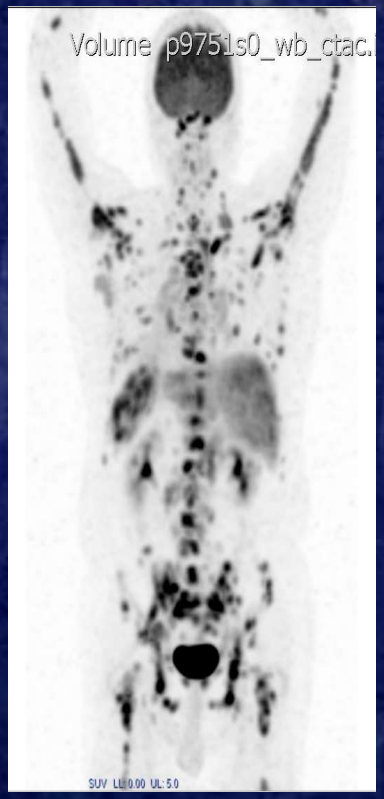
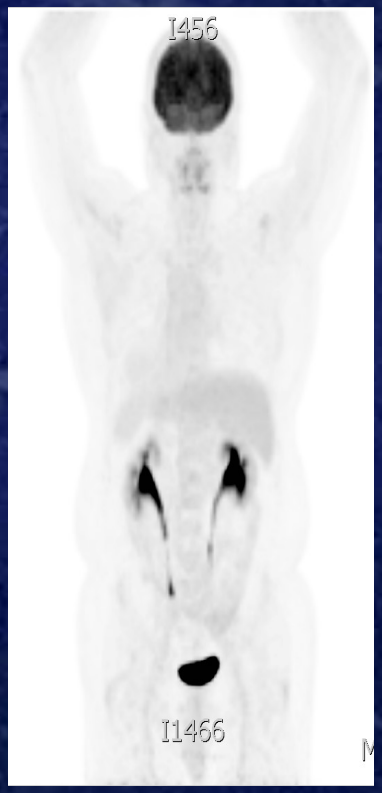
FDG PET to follow Response to Treatment

Baseline



Following Infliximab



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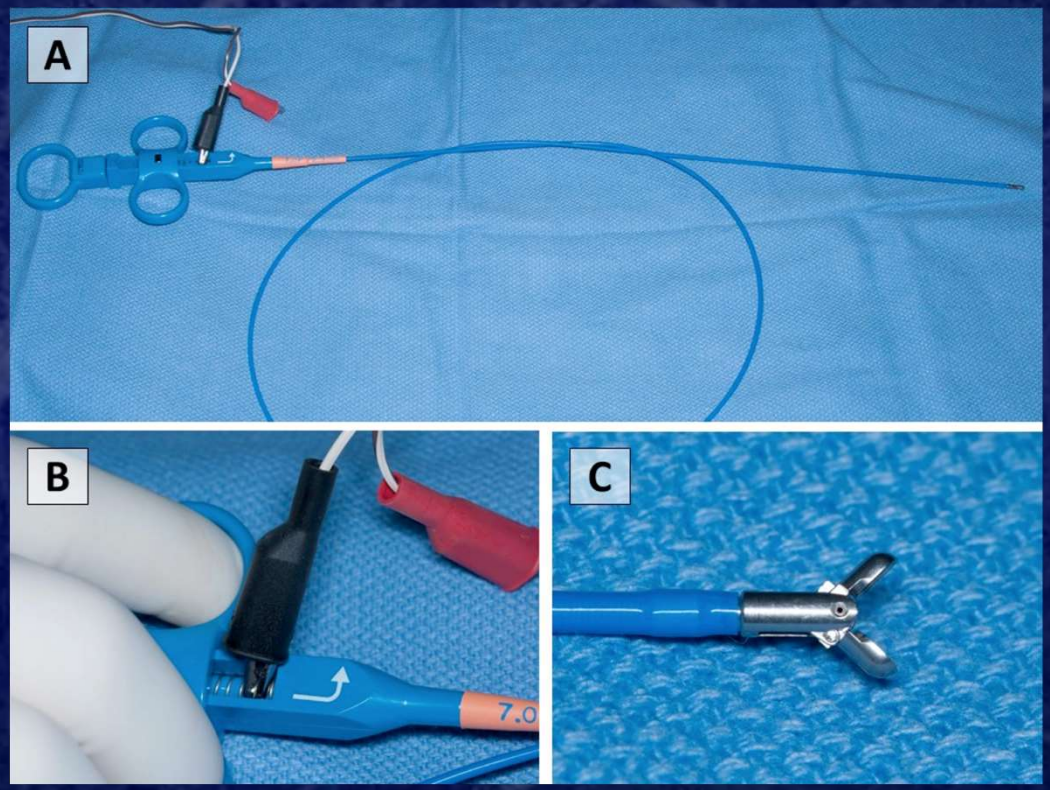
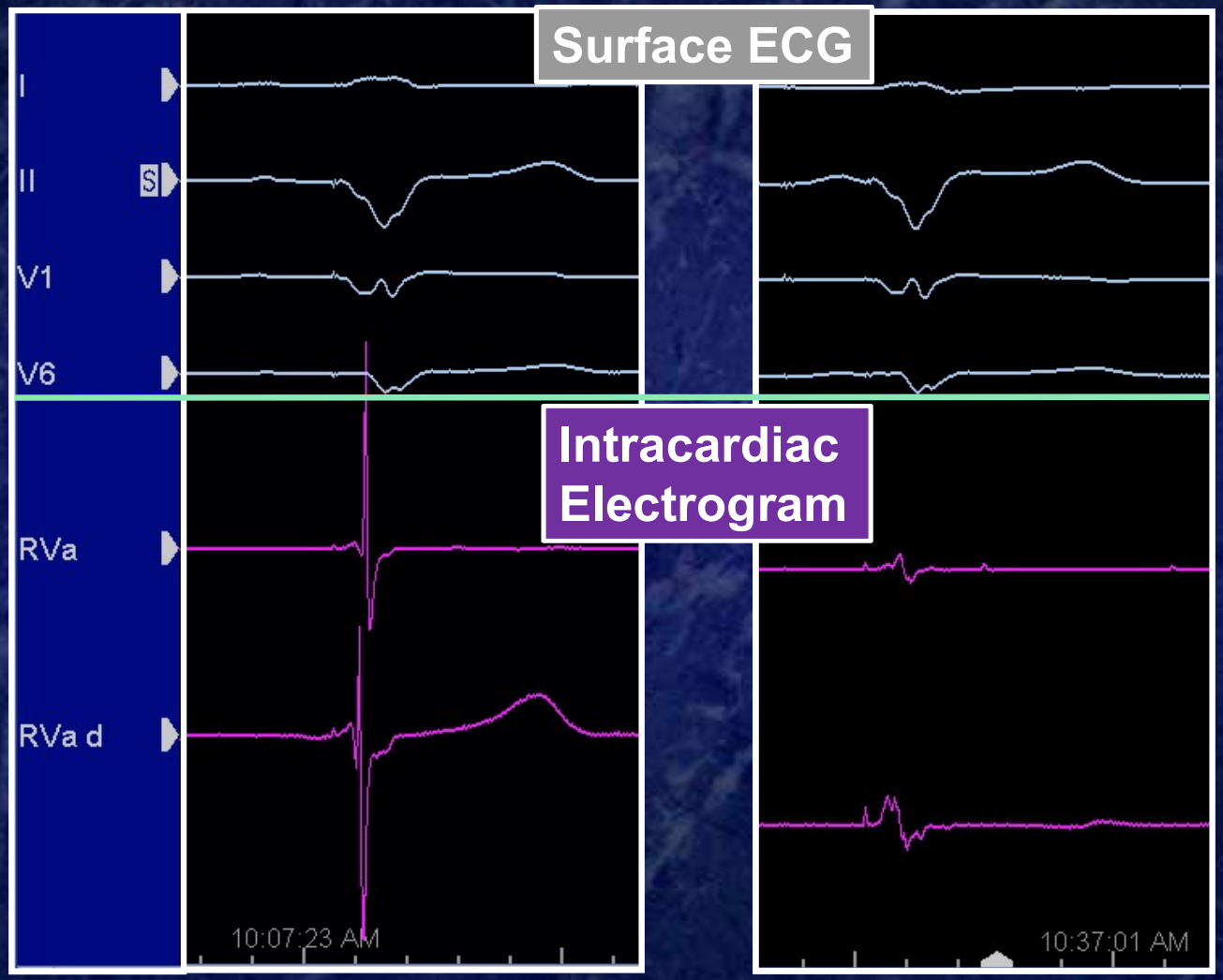
Courtesy of Jukka Lehtonen

Connection of the EA mapping system to a Cordis bioptome



Konecny , et al Ther Adv CV Dis 2015



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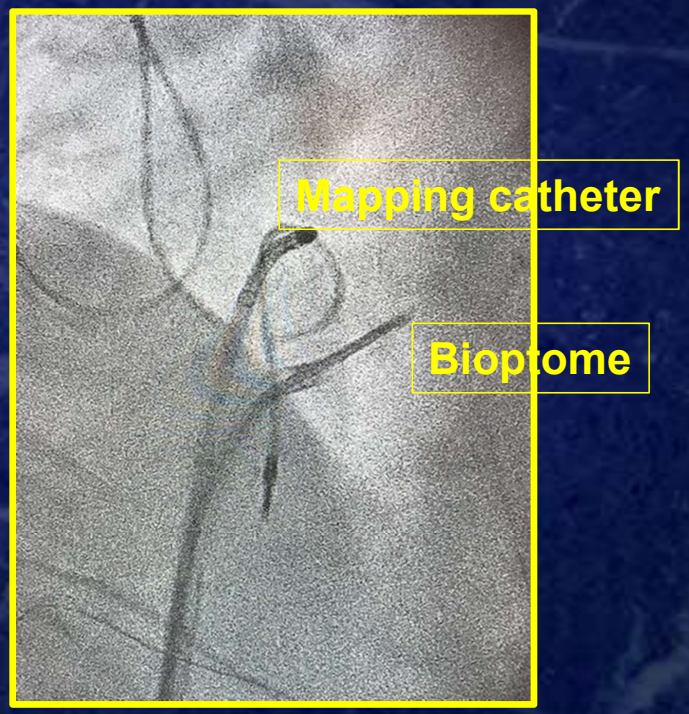
Safety and Diagnostic Yield of Electrogram-guided Biopsy for Suspected Sarcoidosis

- Two femoral artery pseudoaneurysms and 1 stroke out of 59 patients with EGM-guided EMB.
- No Tamponade.
- 70% yield of diagnostic findings



Future Directions: Clinical Trials

- IVIG for PVB19 + Chronic DCM NCT 000659386
- Secukinumab for Acute myocarditis (DZHK)
- CASTT- Canadian Sarcoidosis Tx Trial (CHASM-CS; CHIR IRSC)
- eMAP -electrogram biopsy(U Penn; Mayo)

New MRI Imaging Sequences Increase Sensitivity for Acute Myocarditis

- **Standard:** T2 STIR (Body coil-edema/water)
- **Standard:** Post-Gadolinium T1 early and late
- **New:** Native T1 Mapping
- **New:** Native T2 Mapping

Ferreire, M et al. J Am Coll Cardiol Img 2013
MyoRacer JACC 2016

NEW Gene Variations Associated with Myocarditis

Heterozygous variations with MAF <0.01%			
Cardiomyopathy-associated genes	**Acute Myocarditis (n = 42)**	**1000 Genomes (n = 1,164)**	**In-house (n = 2,324)**
Number of carriers	18 (42.9)	539 (46.3)	996 (42.9)
Myocarditis vs. other cohorts p Value		2.23E-01	9.47E-01
Homozygous variations with MAF <1%			
Cardiomyopathy-associated genes	**Acute Myocarditis (n = 42)**	**1000 Genomes (n = 1,164)**	**In-house (n = 2,324)**
Number of carriers	5 (12)	10 (0.9)	29 (1.2)
Myocarditis vs. other cohorts p Value		2.22E-03	1.08E-04

Genes: BAG3,DSP,PKP2,RYR2,SCNA5,TNNI3

Belkaya, S et al. JACC 2017; 69(13):1653-65

Myocarditis 2020

- **Checkpoint inhibitors-new cause of FM**
- **Biopsy +/- EG guide to define specific histology in high risk cohorts**
- **Mechanical unloading may improve inflammation and accelerate recovery**
- **Bridge to recovery is common in lymphocytic; less likely in GCM.**
- **AHA Statement –Fulminant Myocarditis; ESC/HFSA/JCS Biopsy Statement**

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