Current Status of Endomyocardial Biopsy

24th Annual Heart Failure 2020: an Update on Therapy
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DISCLOSURE

Relevant Financial Relationship(s)
None

Off Label Usage
None
1. Use EMB in clinical scenarios in which the tissue diagnosis will meaningfully impact prognosis or therapy at acceptable risk
2. No safer alternative test exists
Disorders that can be diagnosed by Heart Biopsy

- Infiltrative Disorders: Amyloidosis
- Inflammatory Disorders: Sarcoid, Myocarditis
- Infectious Diseases: Viral, Chagas
- Adverse Drug Reactions: non-inflammatory, e.g. Hydroxychloriquine; doxarubacinc
Original Konno Bioptome
Role of EMB for Suspected Amyloidosis

• “Bulls Eye” strain pattern on echo strain- preserved apical motion

Agha, et al JACC 2018
Algorithm for Diagnosis of Cardiac Amyloidosis

1. Careful physical exam seeking other potential organ involvement, e.g., proteinuria, periorbital purpura
2. Biopsy of selected cardiac or noncardiac tissue
3. Biopsy positive: Amyloidosis confirmed

Where feasible, special stains such as immunogold
- Amyloid type confirmed
  - TTR
    - Genetic testing for mutant TTR
      - Positive: Familial amyloidosis
        - Supportive therapy
        - Assess for liver transplant and need for cardiac transplant
      - Negative: SSA
        - Supportive therapy
  - AL amyloidosis
    - Quantify light chains (as baseline for follow-up) and exclude concomitant myeloma
      - Positive: AL amyloidosis
      - Negative: Familial amyloidosis
        - Supportive therapy
        - Chemotherapy and supportive therapy

Special stains unavailable
- Serum and urine IFE, FLC assay, bone marrow biopsy
- One or (usually) more positive
  - AL amyloidosis
  - Genetic testing for mutant TTR or ApoA1
    - Positive: Familial amyloidosis
    - Negative: Probably SSA
      - Supportive therapy
53 yo woman with complete heart block 3 years ago now with symptomatic NSVT
Apical Core: Cardiac Sarcoidosis
Distribution of Cardiac Sarcoidosis at Autopsy

Kandolin 2015
Electrogram Guidance

A Method to Increase the Precision and Diagnostic Yield of Endomyocardial Biopsy for Suspected Cardiac Sarcoidosis and Myocarditis

• Electrogram voltage $<5$ mV: 100% specificity and PPV
  Sensitivity 70%; 62% NPV

• Voltage $>5$ mV signified normal myocardium with no significant diagnostic yield.
RV Voltage Map in Suspected Cardiac Sarcoidosis

Left Anterior Oblique

Right Lateral

Fractionated Signals

His Bundle

Fractionated Signals

eMAP Trial- Randomized, crossover to map vs no map Biopsy
Normal

Surface ECG

Abnormal

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

Unexplained Acute Cardiomyopathy*

Required inotropic or mechanical circulatory support, Mobitz type 2 second degree or higher heart block, sustained or symptomatic ventricular tachycardia or failure to respond to guideline based medical management within 1-2 weeks?

Yes-Endomyocardial Biopsy
COR I/LOE B

No-Cardiac MRI
COR 2B/LOE C

*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.

Histologic “Dallas” Criteria

Sampling error, Variation in interpretation, Low sensitivity, Lack of correlation with outcome

Baughman, K, Circulation 2006
Giant Cell Myocarditis
Prognosis in Myocarditis Varies by Histology

Eosinophilic Myocarditis Outcome

Brambatti, et al. JACC Nov 7th 2017
Drug-Related Hypersensitivity Myocarditis
45 year old woman with DRESS syndrome
• 10% of acute DCM + myocarditis
• 50% idiopathic.
• Other ways to identify myocarditis…
Myopericarditis MRI and Histology

Epicardial-Mid Wall

Marholdt, H, etal. Circulation 2004

Mouse model of CVB Myocarditis

Fairweather, DL, Cooper, LT, et al
Immuostains for the Diagnosis of Myocarditis

CD3  CD68  CD163

Nakayama et al EJHF 2017
Meta-analysis of Immunohistology and Histology to Diagnosis Inflammatory CMP

- n=61 publications with 10,491 patients
- IHC-detection rate of DCMi was 50.8% (95% CI: 47.7–53.8%; range: 18.4 – 91.7%)
- Dallas criteria 8.04% (95%-CI: 5.08–12.5%; subset of n=3,274 patients in n=30 publications)
- 13 different IHC protocols - need for standardization

Noutsias, M. Eur J Heart Fail. 2017 May;19 Suppl 1:88
Predictors of Outcome in Patients with Acute Myocarditis

**Immunohistology Results**
- Positive
- Negative

**Histopathological Results According to DALLAS Criteria**
- DALLAS negative
- DALLAS positive

**Freedom from cardiac death and HTx**

- P<0.001
- P=0.192

Number of CD3 or CD68 Inflammatory Cells Predicts Outcome in Myocarditis

Nakayama et al EJHF 2017
Transcriptomic Biomarkers for the Accurate Diagnosis of Myocarditis

Bettina Heidecker, MD; Michelle M. Kittleson, MD, PhD; Edward K. Kasper, MD; Ilan S. Wittstein, MD; Hunter C. Champion, MD, PhD; Stuart D. Russell, MD; Ralph H. Hruban, MD; E. Rene Rodriguez, MD; Kenneth L. Baughman, MD†; Joshua M. Hare, MD

RT-PCR from EMB: TLR1, TLR2, TL7, and CD14 overexpressed In LM vs DCM
Future Directions: EAM Clinical Trial

- eMAP – electrogram vs unguided biopsy
- U Penn; Mayo
- About 24/40 enrolled
- Use of CMR and PET with EAM
Cardiac Sarcoidosis