Advanced Cardiac Imaging for the Internist
(with a focus on Cardiac Magnetic Resonance)

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Objectives

• Discuss cases where advanced cardiac imaging may help with diagnosis or therapy (focus on cardiomyopathies)

• Discuss indications and contraindications for cardiac imaging tests including cardiac magnetic resonance (CMR), coronary CT, echo strain and nuclear imaging.
Case 1: 38 yo BM with HTN and new onset HF and LV EF 20% with LVH and global hypokinesis. No angina, normal EKG. He is started on GDMT for acute systolic HF (ACEI, BB, MRA). Which of the following advanced cardiac imaging tests are reasonable for evaluation of etiology of his HF?

A. Invasive coronary angiography
B. SPECT myocardial perfusion imaging
C. Cardiac MRI (CMR)
D. Coronary computed tomography (CTA)
E. All of the above may be reasonable first steps
Nuclear Stress (SPECT and PET)
- well validated
- SPECT available at most centers
- functional (perfusion) and scar
- no contrast
- highest radiation dose (esp SPECT)

Computed Tomography (CT)
- fast
- excellent resolution (anatomic data)
- requires iodinated contrast and radiation
- cost
- near 100% negative predictive value for CAD

Cardiac Magnetic Resonance (CMR)
- excellent physiologic and anatomic data
- no iodinated contrast or ionizing radiation
- only available at specialized centers
- cost
- not as affected by obesity
Indications for cardiac MRI

- Quantifying LV/RV volumes or function
- Cardiomyopathy etiology evaluation
  - Cardiomyopathy/heart failure (ARVD, LV noncompaction, sarcoidosis, hemachromatosis, amyloidosis, myocarditis)
- Defining cardiac anatomy
  - Constrictive pericarditis, cardiac masses, thrombus, congenital heart disease, ASD/PFO/VSD
- Myocardial perfusion/stress testing
- Quantifying blood flow
  - Valvular disease (MR, AI, AS, PR)
  - Quantifying shunts (Qp:Qs)
- Assessing myocardial viability/scar
- Angiography
  - Coarctation, anomalous coronaries, pulmonary veins
Special considerations for CMR

• Inability to obtain adequate echo windows (CMR can slice through any tissue plane)

• Poor nuclear candidates (ie large breasts, obese, small size women)

• When you need accurate quantification (ie those receiving chemotherapy)

• When you want a comprehensive test rather than multiple tests (provides anatomic and physiologic data)
MRI Safety

MR safe or conditional = coronary and vascular stents, most prosthetic heart valves, prosthetic joints, most IVC filters, loop recorders

MR unsafe = most pacemakers, insulin pumps, most ICD’s, metallic foreign bodies
Nephrogenic systemic fibrosis (NSF)

- Thought to be related to toxic effects of gadolinium ions
- Causes fibrosis of skin, joints, eyes, and internal organs
- Most gadolinium contraindicated for GFR < 30
- If absolutely necessary in patients with severe renal failure, consider hemodialysis within 2 hours
- No cases of NSF reported in patients with normal renal function
Late gadolinium enhancement (LGE) can characterize myocardial infarction, inflammation or infiltrative disease.

Gadolinium contrast stays in the extracellular space and can be imaged on delayed (late) imaging.

Four chamber LGE image showing transmural apical infarction.
Late gadolinium enhancement (LGE) patterns can help distinguish cardiomyopathy etiology

TD Karamitsos et al. *JACC*, 2009
Ischemic cardiomyopathy with subendocardial and transmural LGE

Four chamber cine

Four chamber LGE
Case 2: 44 yo female with substernal chest pain, elevated troponin and ST elevation involving the inferior and lateral leads. She recently had an URI.

Emergent LHC/angiography revealed angiographically normal coronaries
Which of the following imaging findings would be less likely given her clinical presentation?

A. Segmental wall motion abnormalities
B. Diffuse midwall late gadolinium enhancement on CMR
C. Pericardial effusion
D. Reduced LV systolic function
E. Inferior wall subendocardial late enhancement on CMR
Myocarditis (rather than nonischemic CMP)
A “patchy” LGE pattern was associated with ~ 3-fold increase risk for MACE (death, HF hospitalization), heart transplant, sustained VT.
Midwall LGE involving the anteroseptal segments is associated with worse prognosis in patients with normal EF.

In a population of patients with acute myocarditis (AM) and preserved ejection fraction (EF), we identified 4 main patterns of distribution of late gadolinium enhancement (LGE) (left). The anteroseptal pattern of late gadolinium enhancement was associated with a worse prognosis than the other patterns (right). AS = anteroseptal; IL = inferolateral.
Myocarditis Treatment

- Standard medical therapy including ACEI, beta blocker (if compensated) and MRA
- Myocardial biopsy?
- Corticosteroids (eosinophilic or Giant Cell)?
- Avoidance of exercise
CASE 3: 56 yo male with HTN and DM presents with several week history SOB/DOE. Echo revealed severely reduced LV systolic function with global hypokinesis and inferior wall akinesis. Cath showed 2V CAD including severe stenosis of the proximal RCA and a 90% discrete proximal LAD lesion.
>50% LGE in a myocardial segment is associated with nonviability

Two chamber cine showing **inferior akinesis**

Two chamber LGE
Case 4: 40 female with palpitations and syncope with NSVT on Holter

- Physical exam and laboratory examinations were normal

- EKG was normal (normal QTc), no ST-T changes

- + Uncle who died of SCD

- Echo interpreted as normal: Normal LVEF, no valve abnormalities, no pericardial effusion
Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) with RV wall motion abnormality

Four chamber cine

Short axis cine stack
• ARVC prevalence is estimated 1 in 2000-5000
• 2 x more common in women
• Average onset of age is 29
• Inherited in autosomal dominant and recessive patterns
• SCD is 3rd most common presentation (behind syncope and palpitations) but is initial symptom in 23%

Peters M et al. RIV abstract, May 2013
Imaging is a major component of ARVC

Diagnostic Criteria

1. Global or regional dysfunction and structural alterations
   1. Major: RV akinesis or dyskinesis and 1 of the following:
      A. $\text{RVEDVi} \geq 110 \text{ml/m}^2$ (male) or $\geq 100 \text{ml/m}^2$ (female)
      B. $\text{RVEF} \leq 40\%$
   2. Minor: RV akinesis/dyskinesis and 1 of the following:
      A. $\text{RVEDVi} \geq 100 \text{ml/m}^2$ to $< 110$ (male) or $\geq 90$ to $< 100 \text{ml/m}^2$ (female)
      B. $\text{RVEF} 40$ to $\leq 45\%$

2. Tissue characterization of wall (Histologic): % of residual myocytes (<60% for major) with fibrofatty replacement of RV free wall

3. Repolarization abnormalities- Major: Inverted T waves in right precordial leads (V1-V3) in those older than 14 in absence of complete RBBB

4. Depolarization/conduction abnormalities: Epsilon wave

5. Arrhythmias:
   A. Major: NSVT or sustained VT with LBBB and superior axis
   B. Minor: NSVT or sustained VT with RV outflow configuration, LBBB with inferior axis or of unknown axis with $> 500$ PVCs/24 hour on Holter

6. Family history
   A. Major: ARVC confirmed in 1st degree relative, pathologically confirmed, or positive mutation in the patient under evaluation
   B. Minor: History of ARVC in 1st degree relative whom it is not possible to confirm, SCD (<35 years old) due to suspected ARVC in 1st degree relative, ARVC confirmed in 2nd degree relative

Marcus FL et al. *Eur Heart J.* 2010
Case 5

• 51 yo WF with HTN formerly morbidly obese s/p gastric bypass surgery

• Had echo at OSH (estimated PASP~50mmHg), Normal LV systolic function, LVH, diastolic dysfunction. Also noted LAE.
  
  “Echo findings due to previous obesity”

• Referred by pulmonologist for RHC to eval for pulmonary HTN due to SOB/DOE
Low voltage despite LVH
My patient’s CMR

4C cine

4C LGE
Characteristic myocardial “speckling”
Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis.

Phelan D¹, Collier P, Thavendiranathan P, Popović ZB, Hanna M, Plana JC, Marwick TH, Thomas JD. Heart 2012;98(19)

AMYLOID (N=55) VS HCM (N=15) VS AORTIC STENOSIS (N=15) LVH (+)

RELATIVE APICAL LONGITUDINAL STRAIN (1.0) = AVERAGE APICAL LS/AVERAGE BASAL + MID LS
SENSITIVITY 93%, SPECIFICITY 82% TO DETECT AMYLOID

A1-A4: CARDIAC AMYLOID

A1-A4: CARDIAC AMYLOID

B1 B2

B1 B2

C1 C2

C1 C2

SIPTAL HYPERTROPHY CARDIOMYOPATHY

AORTIC STENOSIS
Systemic manifestations of amyloidosis

AL amyloidosis

Macroglossia

Nail Dystrophy

**ATTR (wild-type or familial) vs AL Amyloid**

**Transthyretin Amyloidosis (ATTR)**
- Better prognosis (3-5 years)
- 90% have transmural LGE
- Greater LV mass compared with AL
- More base-apex LGE gradient
- TX: ? Heart-Liver TX, novel drugs

**Cardiac Light Chain Amyloid (AL)**
- Worse prognosis (<12 months)
- Diffuse subendocardial LGE
- TX: stem cell transplant, Cybor-D

Dungu JN et al. *JACC Imaging*, 2014
In patients with AL amyloid, LGE pattern is associated with prognosis.

**Figure 3: Survival by Visual LGE Pattern**

- None (n = 20)
- Focal Patchy (n = 24)
- Global (n = 32)

Log Rank p < 0.001

- Global
- Global- “can’t null”
- Focal, “patchy”
- Normal

Case 6: 65 yo Indian woman with chronic LBBB- told she had septal MI but never had coronary angiography

Due to LBBB and dyskinetic septal wall segment she underwent coronary angiography which was normal
My patient’s CMR shows septal aneurysm but no LGE (no infarct)
Cardiac Sarcoidosis

- Myocardial involvement in ~25% of sarcoid patients at autopsy
- Can be difficult to diagnose by biopsy due to patchy nature of disease

Usually subepicardial LGE in the basal anteroseptal or inferolateral segments

Can manifest with focal aneurysms

Karamitsos R, *JACC*, 2009
Clinical Features of Sarcoidosis

Cardiac Manifestations

- LV dilation
- Cardiac dysfunction/heart failure
- Heart block
- Ventricular arrhythmias
### Spectrum of Echocardiographic findings

<table>
<thead>
<tr>
<th>Normal</th>
<th>Focal aneurysms</th>
<th>Dilated Cardiomyopathy</th>
</tr>
</thead>
</table>

![Echocardiographic images](image1)

### Spectrum of Late Gadolinium Enhancement

<table>
<thead>
<tr>
<th>Normal</th>
<th>Focal</th>
<th>Multi Focal</th>
<th>Extensive LGE</th>
</tr>
</thead>
</table>

![Late Gadolinium Enhancement images](image2)

CMR is the most sensitive and specific cardiac test for detection of cardiac sarcoid.

**Note:** echo has low sensitivity for detection of myocardial sarcoid (27%).

**TABLE 1** Sensitivity, Specificity, PPV, NPP, and AUC of the Baseline Diagnostic Modalities in Isolation and in Various Combinations

<table>
<thead>
<tr>
<th>Diagnostic tests</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPP, % (95% CI)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac symptoms</td>
<td>64.6 (54.2-74.1)</td>
<td>56.9 (50.1-63.5)</td>
<td>39.0 (31.4-47.0)</td>
<td>79.0 (71.9-85.0)</td>
<td>0.607</td>
</tr>
<tr>
<td>ECG</td>
<td>20.8 (13.3-30.3)</td>
<td>80.9 (75.1-85.8)</td>
<td>31.8 (20.6-44.7)</td>
<td>70.5 (64.6-76.6)</td>
<td>0.509</td>
</tr>
<tr>
<td>Holter monitoring</td>
<td>59.4 (48.9-69.3)</td>
<td>57.8 (51.0-64.3)</td>
<td>37.5 (29.8-45.7)</td>
<td>76.9 (69.8-83.1)</td>
<td>0.586</td>
</tr>
<tr>
<td>IPE</td>
<td>71.4 (61.2-77.6)</td>
<td>57.0 (43.2-69.9)</td>
<td>39.4 (26.3-54.6)</td>
<td>75.0 (69.5-80.7)</td>
<td>0.621</td>
</tr>
<tr>
<td>CMR</td>
<td>96.9 (91.1-99.4)</td>
<td>100 (98.4-100.0)</td>
<td>100.0 (98.1-100.0)</td>
<td>98.7 (96.2-99.7)</td>
<td>0.984</td>
</tr>
</tbody>
</table>

Receiver-operating characteristic (ROC) curve testing various combinations of available diagnostic tests (electrocardiogram [ECG], Holter, echocardiography, cardiac magnetic resonance [CMR]) for the diagnosis of cardiac sarcoidosis based on Heart Rhythm Society (HRS) criteria. Echo = echocardiogram; JMHW = Japanese Ministry of Health and Welfare.

Kouranos et al, *JACC Card Imaging*, 2017
After follow-up of ~12 years, LGE was an independent predictor of all-cause mortality, sustained VT or HF

*Other predictors of events were age and baseline NSVT

Kouranos et al, *JACC Card Imaging*, 2017
T2 imaging (edema) can help evaluate acuity and/or response to therapy.
PET can be useful for sarcoidosis diagnosis or monitoring response to therapy

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Uptake Pattern</th>
<th>Perfusion</th>
<th>Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Perfusion: Normal</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td>Metabolism: No FDG Uptake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild or Early Disease</td>
<td>“Focal Mismatch Pattern”</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td>Perfusion: No or mild defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolism: FDG uptake in area of defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or Progressive</td>
<td>“Focal Mismatch Pattern”</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>Disease</td>
<td>Perfusion: Moderate defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe or Fibrous Disease</td>
<td>Perfusion: Severe defect</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td>Metabolism: No or minimal FDG uptake</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cardiac imaging plays an important early role in detection (and monitoring) of infiltrative myocardial diseases.
Case 7: 31 yo M with recurrent syncope and ?aborted SCD

- Presented with troponin 1.2 and nonspecific ST-T changes
- Echo shows mildly reduced LV systolic function (LVEF 40%) with mild global hypokinesis. Prominent apical trabeculations are noted
- Coronary angiography was normal
CMR Findings
LV Noncompaction

- Noncompacted to compacted ratio >2.3:1 on end-diastolic image (4C, 3C and 2C)
- Noncompacted/compact ed 2:1 on end-systolic images
- Noncompacted myocardium LV mass>20%
Dysmorphic facial features such as prominent forehead, bilateral strabismus, low set ears, and micrognathia.

Chin et al. *Circulation* 1990
Embryology of noncompaction

Gati e al.  JACC Cardiovascular Imaging, 2014
My case

• Due to no witnessed arrhythmia or documented SCD and LVEF 40% he did not meet standard criteria for ICD

• Due to the LGE pattern we felt he was higher risk and elected to place an ICD

• He later had appropriate ICD therapy for sustained VT which was aborted
Case 8: 43 yo WM smoker with HTN presents to the ED with substernal CP and SOB. Troponins x 3 are WNL. EKG shows nonspecific ST-T changes. Patient cannot exercise due to knee pain. What imaging test would be reasonable to r/o significant CAD?

A. Dobutamine stress echo
B. Regadenoson CMR stress
C. Regadenoson nuclear stress
D. Coronary CTA
PROMISE TRIAL: In symptomatic patients with suspected CAD who required noninvasive testing, an initial strategy of CTA was similar to functional testing (exercise EKG, nuclear stress or stress echo)

However, coronary CTA provides better prognostic information in patients at risk with nonobstructive disease

Compared with functional testing, CTA was associated with reduced incident myocardial infarction.

CTA patients were also more likely to receive a new diagnosis of CAD and initiated on ASA and statins.

Foy AJ et al. *JAMA Internal Med*, 2017
Coronary CT angiography

- Highly sensitive for detection of CAD (near 100%)

- Negative predictive value ~99% makes this an ideal tool for acute chest pain setting

- Rapid test (<10 minutes)

- Can visualize coronary plaque characteristics

High-risk plaques

- Low attenuation plaques
- Predominantly non-calcified
- Positive remodeling

Motoyama S et al. JACC, 2009
Coronary CT angiography

- Requires radiation and iodinated contrast (~120ml’s)
- Optimal with low and stable (<65 bpm) heart rate—use ECG gating; often need beta blockers
- Image quality/diagnostic accuracy reduced with obesity (BMI cutoff ~38 kg/m²)
- Requires breath holding
- Can be obscured in patients with highly calcified vessels
Thanks!

Questions?
Case 9: 66 yo obese woman with HTN and DM and recently diagnosed breast cancer. Oncology plans on treating with anthracycline. Baseline echo shows “borderline” LV systolic function with LVEF ~50%
Cancer Therapy-Related Cardiac Dysfunction and Heart Failure: Prevention, Treatment, Guidelines and Future Directions

Hamo CE, Butler J. Circ Heart Fail, 2016
Options for serial measures of LV function

- Standard echo
- Echo Strain
- MUGA (nuclear)
- CMR

More quantitative