Cardiac Imaging: Role of imaging in the detection and management of Coronary artery disease and heart failure
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Assistant Professor of Medicine, Section on Cardiology
Objectives

• Review the role of stress testing in the assessment of coronary artery disease
  • Diagnosis
  • Prognosis
  • Guiding revascularization therapies
• Which modality to choose?
• Review imaging assessment of heart failure
• Newer techniques in the assessment of heart failure
Diagnosis of CAD

- Asymptomatic
- Symptomatic
Asymptomatic patient
Asymptomatic patient

- Coronary calcium scoring in moderate to high risk patients
- Powerful risk stratification tool
- Might result in aggressive risk factor modification
### Symptomatic patient

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Typical/Definite Angina Pectoris</th>
<th>Atypical/Probable Angina Pectoris</th>
<th>Nonanginal Chest Pain</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;39</td>
<td>Men</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate, Low</td>
<td></td>
<td>Very low</td>
</tr>
<tr>
<td>40–49</td>
<td>Men</td>
<td>High</td>
<td>Intermediate, Low</td>
<td>Intermediate, Low</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate, Low</td>
<td></td>
<td>Very low</td>
</tr>
<tr>
<td>50–59</td>
<td>Men</td>
<td>High</td>
<td>Intermediate, Low</td>
<td>Intermediate, Low</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate, Low</td>
<td></td>
<td>Very low</td>
</tr>
<tr>
<td>&gt;60</td>
<td>Men</td>
<td>High</td>
<td>Intermediate, Low</td>
<td>Intermediate, Low</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>High</td>
<td>Intermediate, Low</td>
<td></td>
<td>Low</td>
</tr>
</tbody>
</table>

- **High**: $>90\%$ pretest probability; **Intermediate**: between 10\% and 90\% pretest probability; **Low**: between 5\% and 10\% pretest probability; and **very low**: $<5\%$ pretest probability.

- Modified from Gibbons et al\(^9\) to reflect all age ranges.
High pretest probability

High risk features during acute episode

- ST-T changes suggestive of acute injury or ischemia/infarction
- Positive biomarkers
- Evidence of heart failure
- Ventricular arrhythmias
Low and Intermediate probability patients

• ECG interpretable
• Able to exercise
• Physiologic stress testing with imaging
Why add an imaging component?

- Reduced sensitivity of stress testing, particularly in women

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>With referral bias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>68%</td>
<td>77%</td>
</tr>
<tr>
<td>3 vessel disease</td>
<td>86%</td>
<td>53%</td>
</tr>
<tr>
<td>1 vessel disease</td>
<td>25-71%</td>
<td></td>
</tr>
<tr>
<td>Without referral bias</td>
<td>45%</td>
<td>85%</td>
</tr>
</tbody>
</table>

- 30-67% of false positive EKGs in women
When to choose a pharmacological stress study?

• ECG un-interpretable
• Unable to exercise
Which imaging modality

- Echocardiography
- Cardiac MRI
- Coronary CTA
- Nuclear stress testing
Ischemic cascade

- Perfusion defect
- Metabolic disorders
- Diastolic dysfunction
- Systolic dysfunction
- ECG changes
- Chest pain
- Myocardial infarction


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Physiology (Perfusion studies) vs. Anatomy (Coronary CTA)

• Two multicenter NIH funded studies are ongoing to answer that question
• Excellent negative predictive value >95%
• Poor specificity noted in studies depending on disease prevalence
• Need oral beta blockers
• Caveat: Significantly elevated calcium score >400
Appropriateness Criteria Coronary CTA

• Low to intermediate pretest probability with non-acute symptoms

• ER evaluation of Low to intermediate probability with chest pain and negative biomarkers/ EKG/equivocal stress
Coronary CTA at Wake Forest Baptist Hospital

- Low dose CTA supervised by physicians
- Individualized patient scan
- Stratification by calcium score
Physiological studies

- Dobutamine echocardiography
- Adenosine CMR
- Adenosine Nuclear study
**Dobutamine echocardiography**

- Sensitivity 72-86%, Specificity 77-95%
- Accuracy 76-89%
- Sensitivity limited in patients with LVH

<table>
<thead>
<tr>
<th>LVH</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (RWT &lt;0.45)</td>
<td>90%</td>
<td>88%</td>
</tr>
<tr>
<td>Yes (RWT&gt; 0.45)</td>
<td>63%</td>
<td>73%</td>
</tr>
</tbody>
</table>

Adenosine MRI: Study components

<table>
<thead>
<tr>
<th>TIME [minutes]</th>
<th>CMR TECHNIQUE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>CINE</td>
<td>Includes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cardiac function, volumes, mass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Valvular morphology, stenosis, regurgitation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pericardium</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Optional</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Dark and bright blood tomographic imaging of heart &amp; great vessels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- T2 weighted imaging of acute injury</td>
</tr>
<tr>
<td>13</td>
<td>MORMHLOGY</td>
<td>Performe in appropriate patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Post MI risk stratification</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Ischemia evaluation</td>
</tr>
<tr>
<td>16</td>
<td>STRESS PERFUSION</td>
<td>10 min interval between stress/rest perfusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Velocity/Flow imaging for valvular disease and cardiac output</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Whole heart coronary MRA (may be performed prior to contrast)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Additional cine imaging</td>
</tr>
<tr>
<td>25</td>
<td>ADDITIONAL IMAGING</td>
<td>Performed in appropriate patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Improves specificity of stress perfusion imaging</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Quantification of myocardial blood flow reserve</td>
</tr>
<tr>
<td>32</td>
<td>REST PERFUSION</td>
<td>Typical Sequence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- 2D or 3D, Segmented (high resolution and high SNR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Useful Additional Sequences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Single 5s (rapid, no breath hold required, resistant to arrhythmias)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Long inversion time (~800 ms)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(useful for thrombus detection and “no-reflow” regions in acute MI)</td>
</tr>
<tr>
<td>36</td>
<td>DELAYED ENHANCEMENT</td>
<td>5 minute delay</td>
</tr>
</tbody>
</table>

Edema imaging: differentiate between acute and chronic MI, non-ACS causes of Troponin elevation
Mechanism of delayed enhancement

Normal myocardium

Intact cell membrane

Collagen matrix

Scar

Wake Forest Baptist Health
Excellent correlation between LGE-MRI and histopathology: Gold standard

Figure 5. Left, Comparison of ex vivo MR images with TTC-stained slices in 1 animal at 3 days after infarct. Slices are arranged from base to apex starting in upper left and advancing left to right, then top to bottom. Right, Magnified view.

Diagnostic accuracy >90% in acute and chronic MRI

**Figure 3** Sensitivity of DE-CMR for Acute and Chronic MI

The diagnostic sensitivity of detecting MI is summarized according to gadoversetamide dose group and imaging time point. Numbers in parentheses are 95% confidence intervals. Modified, with permission, from Kim et al. (12). Abbreviations as in Figures 1 and 2.
# Perfusion studies Stress MR

<table>
<thead>
<tr>
<th></th>
<th>Cardiac MRI</th>
<th>Nuclear perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>0.89 (0.88-0.91)</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>0.80 (0.78-0.83)</td>
<td>0.90</td>
</tr>
<tr>
<td><strong>Ability to detect small MIs</strong></td>
<td>As little as 1 gm of infarct</td>
<td>No</td>
</tr>
<tr>
<td><strong>Ischemia and viability</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

- **Referral bias**, only the positive patients sent for coronary angiography

<table>
<thead>
<tr>
<th><strong>N = 752, 40% disease prevalence</strong></th>
<th>Cardiac MRI</th>
<th>Nuclear perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>86·5% (81·8–90·1)</td>
<td>66·5% (60·4–72·1)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>83·4% (79·5–86·7)</td>
<td>82·6% (78·5–86·1)</td>
</tr>
</tbody>
</table>

- **No referral bias** All patients underwent coronary angiography

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Hamon et al. *Journal of Cardiovascular Magnetic Resonance* 2010, 12:29  
First pass perfusion
Infarct assessment: Relative to how much is alive myocardium
Higher detection of subendocardial MI with LGE-MRI

Figure 3: Comparison of SPECT, contrast-enhanced CMR, and histology in a dog with a nearly transmural infarct.

Figure 4: Short axis views from three dogs with subendocardial infarcts.

Figure 5: Imaging of infarcts by SPECT and CMR in patients. Results are shown on a segmental (A, B) and an individual basis (C).
Is it clinically relevant to detect small myocardial infarcts?

- Strongest predictor of MACE, cardiac mortality independent of clinical and angiographic variables

**TABLE 4. Best Overall Multivariable Cox Proportional-Hazards Regression Models for All MACE and Cardiac Mortality, When All Variables Were Considered**

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MACE (LR χ² for model=33.74)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of LGE</td>
<td>5.98 (2.68-13.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Angiographically significant coronary stenosis at study completion*</td>
<td>2.43 (1.11-5.32)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Cardiac mortality (LR χ² for model=21.15)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of LGE</td>
<td>9.43 (3.15-28.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MI by noninvasive stress imaging*</td>
<td>3.00 (0.91-9.90)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Diagnosed before or after CMR during the study period.

Threshold effect- Small amount of LGE associated with >7 fold MACE

Figure 5. LGE% and WMS% in tertiles and HR for MACE.

Identifying infarct irrespective of wall motion abnormalities

Figure 3. Left, Similar results in 3 additional animals. Right, Wall thickening and image intensities for all animals.

Transmural extent of LGE predicts functional recovery

Change in EF and Wall motion score with increasing proportion of viable myocardium

Why wall motion is insufficient?
Case studies: Ischemia and infarction

- 62 year old male hypertensive h/o CAD, LAD disease diagnosed 10 years prior managed medically presents with worsening angina.
  - Angina occurs with minimal exertion
  - No evidence of HF on physical exam
  - Depressed LV systolic function
3 Chamber
4 Chamber
2 Chamber
Short axis
Short axis
Ischemia with normal LV systolic function

- 51 year old male with hypertension and angina for 6 months.
- Underwent stress echocardiogram. At 5 minutes, found to have akinesia of the apical septum.
- Underwent cardiac stress MRI to locate extent of perfusion defects.
3 Chamber
4 Chamber
2 Chamber
Short axis images
Stress perfusion
Stress Perfusion
Delayed enhancement images
SPECT
LAD
Prognostic significance of Ischemia

Kwong RY et al: (Circulation. 2009;120:1390-1400.)
Association preserved in patients with no history of CAD

Kwong RY et al: (Circulation. 2009;120:1390-1400.)
Normal Adenosine CMR has excellent prognosis

Table 2. Diagnostic Performance of Individual CMR Components in Detecting Future Adverse Cardiac Outcome

<table>
<thead>
<tr>
<th></th>
<th>Resting RWM (n = 19)</th>
<th>Adenosine Perfusion (n = 28)</th>
<th>Delayed Enhancement (n = 14)</th>
<th>Any Abnormality (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>70</td>
<td>100</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>96</td>
<td>93</td>
<td>97</td>
<td>91</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>74</td>
<td>71</td>
<td>79</td>
<td>67</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>95</td>
<td>100</td>
<td>93</td>
<td>100</td>
</tr>
</tbody>
</table>

CMR = cardiac magnetic resonance; NPV = negative predictive value; PPV = positive predictive value; RWM = regional wall motion.

Figure 2. Kaplan-Meier survival distributions based on presence or absence of any abnormality on the cardiac magnetic resonance (CMR) and ≤3 versus >3 total cardiac risk factors (TLCRF). Although the separation is statistically significant for each curve, note that a normal adenosine perfusion has 100% event-free survival (100% negative predictive value) whereas 35% of subjects with ≤3 TLCRF missed 35% of patients with an outcome dropping event-free survival in that group. CAD = coronary artery disease.

Figure 3. Estimated receiver operating characteristic curve for total number of cardiac risk factors (TLCRF) (triangles) and receiver operating characteristic curve for total number of abnormalities on adenosine cardiac magnetic resonance (TLCMR) as a predictors of adverse cardiac outcome (circles).

Assessment of heart failure

- Pattern of myocardial fibrosis helps determine the etiology of cardiomyopathy

Mesocardial
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Pulmonary hypertension

Subendocardial
- Vascular
  - Infarction
- Non-vascular
  - Amyloid
  - Hypereosinophilic syndrome
  - Histiocytoid cardiomyopathy
  - Cardiac transplant

Patchy
- Sarcoid
- Amyloid
- Myocarditis

Subepicardial
- Myocarditis (most common)
- Sarcoid

Transmural
- Infarction (most common)
- Myocarditis, severe
- Sarcoid, chronic
53 year-old male presents with 2 week history of chest pain, shortness of breath and lower extremity edema.

- Weight gain of approximately 18 pounds
- He had recent upper respiratory infection

Past Medical History:
- Hypertension
- Asthma

Family History: no early coronary artery disease
History and Physical

• Physical Exam:
  • BP: 151/105, HR: 90
  • Lungs: decreased breath sounds at bases
  • Cardiac: normal rate, reg rhythm, no murmurs.

• Presented to emergency department:
  • BNP: >2000, troponin: 0.13
  • Emergent echo: EF 10-15% with RV dysfunction
3 Chamber
4 Chamber
2 Chamber
Short Axis Late Gadolinium Enhancement
Long Axis Late Gadolinium Enhancement
Short axis post revascularization
3 Chamber post revascularization
4 Chamber post revascularization
2 Chamber post revascularization
Identifying the etiology of Troponin elevation

• 37 year old female with lupus and cocaine use.
• Presented with chest pain, and found to have Troponin of 100.
3 Chamber
4 Chamber
2 Chamber
Short axis images
Short axis images
Beyond wall motion : Thrombus/aneurysm
Serial delayed enhancement: Mural thrombus

1 minute DE

3 minute DE
Serial delayed enhancement: Mural thrombus

5 minute DE

7 minute DE
Long axis delayed enhancement
Assessment of microvascular obstruction: Acute MI

- Occurs during embolization of thrombus and edema of microvasculature
- Occurs most often during late presentation of MI
- Associated with persistent chest pain after PCI, ST elevation and poor recovery of wall motion
Microvascular obstruction - 1 minute
3 minutes
5 minutes
10 minutes
Beyond wall motion: assessment of systolic strain using echocardiography

- More sensitive than assessing wall motion
- Currently used in most of the heart failure patients in our institution
- Used to assess improvement in systolic strain with medical therapy and post transplant.
Systolic strain displayed as bull’s eye plot of the myocardium
Conclusions

• State of the art diagnostic modalities with interpreting expertise available at Wake Forest University Baptist Medical Center
• Need to characterize myocardial substrate and accurately identify extent of infarction beyond wall motion.
• Appropriate utilization of these modalities will enable improved care and control of health care costs.
Conclusions

- State of the art imaging technology and expertise is available
- Appropriate use of imaging techniques in a cost effective manner