Noninvasive evaluation of the patient with angina

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No disclosures
Objectives

1. Give an overview of the different diagnostic testing options in patients with angina

2. Discuss practical and technical considerations of noninvasive cardiac tests

2. Discuss sensitivities/specificities and cost effectiveness of noninvasive cardiac tests
Case

• 32 yo AAF with no PMH presents to ED with left-sided CP lasting 5 minutes at a time. Occurs with rest. No SOB/DOE. She has associated nausea and diaphoresis.

• Nonsmoker, no drugs

• Dad had MI at age 66

• BP 132/88mmHg, HR 76, RR 14, O₂ sats 99% RA
Normal EKG
Troponins x 2 WNL
CXR WNL
CT PE Protocol was normal
What test should the ED order next to evaluate this patient’s chest pain?

1. Treadmill stress test
2. Coronary CT angiogram
3. Stress echocardiogram
4. Nuclear stress test (SPECT)
5. Other test or none
Pretest probability of CAD

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Gender</th>
<th>Typical/Definite Angina Pectoris</th>
<th>Atypical/Probable Angina Pectoris</th>
<th>Nona Chest</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–39</td>
<td>Men</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td><strong>Very low</strong></td>
<td>Very</td>
</tr>
<tr>
<td>40–49</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very</td>
</tr>
<tr>
<td>50–59</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td>60–69</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

- High indicates >90%; intermediate, 10–90%; low, <10%; and very low, <5%.

- 1 No data exist for patients <30 or >69 y, but it can be assumed that prevalence of coronary artery disease increases with age. In a few cases, patients with ages at the extremes of the decades listed may have probabilities slightly outside the high or low range.

ACC/AHA Guidelines for Exercise Testing
Important factors for choosing a cardiac test

- Need/indication
- Test availability and local expertise
- Diagnostic accuracy
- Body habitus
- Side effects of medications
- Cost
• “The tests usually aren’t necessary before low-risk surgery.”
• “Heart imaging tests can pose risks.”
• “Imaging tests can cost a lot.”

ACP’s Choice of 5 Overused Items for “Choosing Wisely” Campaign

- Screening exercise ECG in asymptomatic individuals at low risk for coronary heart disease
- Imaging studies in patients with non-specific low back pain
- Brain imaging studies (CT or MRI) for simple syncope and a normal neurological examination
- CT pulmonary angiogram as the first study in patients with low pretest probability of venous thromboembolism, rather than D-dimer
- Preoperative chest radiography in the absence of a clinical suspicion for intrathoracic pathology
<table>
<thead>
<tr>
<th>Functional:</th>
<th>Anatomic:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear perfusion</td>
<td>CT angiogram</td>
</tr>
<tr>
<td>MR perfusion</td>
<td>Cardiac MRI</td>
</tr>
<tr>
<td>Stress EKG</td>
<td>Echo</td>
</tr>
<tr>
<td>PET</td>
<td></td>
</tr>
<tr>
<td>Echo</td>
<td></td>
</tr>
</tbody>
</table>
Stress Testing

• In general, if patients can exercise, exercise is preferred over pharmacologic testing

• Exercise can be performed with either treadmill or bicycle

• Bruce protocol is most commonly used: monitor EKG, symptoms, BP and HR during graded exercise
Exercise Stress - Bruce Protocol

• Reports exercise capacity in metabolic equivalents (METS)

• METs reflect resting volume oxygen consumption per minute \( (\text{VO}_2) \) for a 70kg, 40 yo man

• 1 MET = 3.5mL/min/kg of body weight

• Stage 1 is 1.7 mph at 10% grade= 5 METS
• Stage 2 is 2.5 mph at 12% grade= 7 METS
• Stage 3 is 3.4 mph at 14% grade= 9 METS
• Each stage goes for 3 minute intervals
Contraindications to exercise stress

**Absolute**

- Recent MI (within 2 days)
- Recent significant change in resting ECG
- High risk unstable angina
- Uncontrolled arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe AS
- Acute aortic dissection
- Acute PE
- Acute myo/pericarditis
- Uncontrolled symptomatic heart failure
Practical considerations for exercise stress

1. Can the patient adequately exercise?

2. Does the patient have an interpretable EKG?
   - LBBB
   - Pacing
   - Pre-excitation (WPW)
   - Digoxin
   - LVH
Exercise stress

- ECG’s at rest, each exercise stage, peak exercise, and every 1-2 minutes in recovery for at least 5 minutes

- Also record HR, BP, patient’s perceived exertion, symptoms

- Completed when patient attains 85% of age-predicted maximum HR: $220 - \text{age}$ or because of symptoms
Duke Treadmill Score

DTS = Exercise Time – (5 x Max ST) – (4 X Angina Index)

Angina Index:
- 0 = no angina during exercise
- 1 = non-limiting angina
- 2 = Exercise limited angina

Risk:
- ≥ +5 = low risk
- +4 to -10 = Moderate Risk
- ≤ -11 = High Risk

***Patients with a “low risk” exercise EKG incur ≤ 1% per year cardiac mortality.

Mark DB et al. *NEJM* 1991
Shaw LJ et al. *Circulation* 1998
Exercise capacity is strongly predictive of mortality

Each 1-MET increase in exercise capacity conferred a 12% improvement in survival

• The use of imaging in low pretest probability patients is inappropriate if patients can exercise and have an interpretable EKG

(2006 Appropriate Use Criteria Guidelines for cardiac CT and MRI, JACC; 2003 Echo Updated Guidelines, JASE)

• The sensitivity and specificity of ETT are lower than noninvasive imaging (68% and 77% respectively)

(Meta-analysis of 24000 patients; Gianrossi et al. Circulation, 1989)

• Some patients (ie those at intermediate to high risk in addition to those that cannot exercise or have an interpretable EKG) may benefit from imaging
You’ve decided a patient needs pharmacologic stress testing with imaging due to inability to exercise. Which patient should NOT receive adenosine or regadenoson (Lexiscan)?

1. Patient admitted with CHF
2. 39 yo obese female
3. Patient with mild aortic stenosis
4. **Patient admitted with COPD exacerbation**
5. Patient with acute renal failure
Vasodilators (Adenosine, regadenoson)—preferred for assessment of myocardial perfusion

- Contraindications: asthma, severe hypotension, bradyarrhythmias
- Withhold caffeine for 12 hours
• **Dobutamine** - inotrope; preferred agent when the test is based on assessment of regional wall motion (stress echo or stress MRI) or if vasodilator is contraindicated.

**End points**: reaching target HR (85% of age-predicted max HR), new or worsened wall motion abnormality, significant arrhythmias, hypotension, intolerable symptoms
Stress Imaging (and CT)

• In general, exercise stress with EKG is the preferred initial test in patients who can adequately exercise and have an interpretable EKG.

• Imaging does increase the sensitivity and specificity of stress testing.

• Patients who require pharmacologic stress require imaging due to the low sensitivity of pharmacologic stress EKG alone.
Stress ECHO (exercise or dobutamine)

• Grade myocardial wall segments using 17 segment model at rest and at stress

Each segment is graded as:
1. Normal or hyperdynamic
2. Hypokinetic
3. Akinetic
4. Dyskinetic
5. Aneurysmal

Both wall motion and perfusion are highly accurate (more accurate than EKG changes) for detection of CAD.

However, wall motion is more specific and requires ischemia. Perfusion images are typically more sensitive.
Stress echo

• Normal results: normal LV wall motion/thickening at rest and stress

• Abnormal:
  – Fixed wall motion abnormality- abnormal at rest and stress- suggests previous MI
  – New or worsened wall motion abnormalities suggest ischemia

***Variables associated with adverse outcomes are extensive ischemia (WMAs), poor EF% response, low ischemic threshold (early abnormalities), location of WMA in LAD territory

Inducible inferior wall motion abnormality

Baseline

Target HR
Other indications for stress echo

• Myocardial viability
• Evaluation of mitral valve disease
  – Evaluate exercise PA systolic pressures
    (>60mmHg is indication for MV surgery)
• Evaluation of aortic valve disease
  – Low gradient aortic stenosis
Stress echo

- Sensitivity 79%, Specificity 87% (wall motion abnormalities require ischemia)
- Sensitivity is reduced in people with poor acoustic windows (obesity, COPD, large breasts)
  
  (Heijenbrok-Kal et al. *Am Heart J*, 2007)

- A normal stress echo is associated with excellent prognosis: 1-year cardiac event-free survival of 99% and 3-year survival of 97%

  (McCully RB et al. *JACC*, 1998)
Nuclear (SPECT) Stress Test

- Radioactive tracer (Technetium-99) is administered

- Tracer decays spontaneously and emits energy (photons)

- Photons leave the body and are captured with a gamma camera

- During stress, metabolic changes drive agent into the cell
Normal Myocardial Perfusion
Myocardial Ischemia
SPECT

Pros:

• Sensitive for ischemia (70-90%)
• No need for contrast dye
• Safe in patients with ICDs/PCMs
• Widely available
• Well validated

Cons:

• Image quality in obesity, women (attenuation artifacts)
• Limited anatomic info
• Radiation dose (equivalent to >500 CXRs)
• Availability of technetium

***In 21,000 patients with a normal SPECT and 2-year follow-up, annual hard cardiac event rate was 0.7%***

Cardiac MRI

No Field  |  $B_0$ Field Applied

$B_0$  |  $B_1$ out of the slide

Craig Hamilton, PhD, Biomedical Engineering, Wake Forest
Which of the following patients is safe for a stress cardiac MRI?

1. Patient with pacemaker
2. Patient with coronary stents
3. Patient on hemodialysis
4. Patient with gastric pacemaker
MRI Safety

MR safe

MR conditional= most metallic heart valves, Stents, prosthetic joints, dentures

MR unsafe= most pacemakers, insulin pumps, Most ICD’s, metallic foreign bodies
Nephrogenic Systemic Fibrosis (NSF)

- Rare, but serious complication thought to be related to toxic effect of gadolinium ions in patients with advanced renal failure/ESRD
- Causes fibrosis of skin, joints, eyes, internal organs
- Gadolinium contraindicated with GFR<30
- **No cases of NSF reported in patients with normal renal function**
Requirements

• Hemodynamically stable

• Can breath-hold

• Can lie flat

• Can’t be claustrophobic
Special considerations for CMR

- Inability to obtain adequate echo windows (CMR can slice through any tissue plane)
- Poor nuclear candidates (i.e., large breasts, obese, small size women)
- When you need accurate quantification of LV or RV function (i.e., those receiving chemotherapy)
- When you want a comprehensive test rather than multiple tests (provides anatomic and physiologic data)
CMR is the gold standard for quantitating LV and RV volumes and ejection fraction.

Get volume of each slice x slice thickness = EDV or ESV
CMR Adenosine Stress Test

Adenosine 140mcg/kg/min
(3-6 minutes)

- Scout images
- Cine Images
- Stress Perfusion
- Additional Images
- Rest Perfusion
- Delayed Enhancement

Time (mins)

Gad

Gad
Adenosine stress CMR

Rest Perfusion

Stress Perfusion
Dobutamine stress CMR

Peak dose dobutamine

Stress perfusion
Principles of late (delayed) gadolinium enhancement

Gadolinium is an inert biological tracer that distributes in extracellular water and cannot cross an intact cell membrane. Therefore, expanded extracellular space (i.e., fibrosis or scar) causes a relative accumulation of gadolinium relative to normal myocardium.
Late gadolinium enhancement patterns

Mesocardial
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Pulmonary hypertension

Patchy
- Sarcoid
- Amyloid
- Myocarditis

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

Transmural
- Infarction (*most common*)
- Myocarditis, severe
- Sarcoid, chronic

Subepicardial
- Myocarditis (*most common*)
- Sarcoid

Hundley et al. 2006 ACC/AHA Cardiac MRI Guidelines
Myocardial infarction
CMR detects infarcts missed by SPECT

Wagner et al. Lancet. 2003
Stress CMR is more sensitive than SPECT for detection of significant CAD

NPV 91% for CMR vs 79% for SPECT

CMR is more sensitive than SPECT in both sexes


Stress CMR strategy in the ED chest pain unit reduces health care expenditures in intermediate-risk patients

- Randomized 109 intermediate to high risk participants to CPU observation vs inpatient care
- No difference in rate of cardiac events at 1 year
- Costs (including index visit) were lower in the CMR group compared to inpatient care ($3101 vs $4,742, p=0.004)

Mean cumulative cost after hospital discharge

Miller CD et al. *JACC Imaging*, 2011
Myocardial Viability

> 50% delayed enhancement in a myocardial segment is associated with lower likelihood of viability
Aneurysm with layering thrombus
Microvascular ischemia
Myocarditis

T2 (water) image showing myocardial edema
Takotsubo CMP
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
- Requires breath holding
- Can be obscured in patients with highly calcified vessels
Coronary calcium scoring

- Usually acquired before contrasted angiogram

- Excessive calcium (CAC score >400 can cause overestimation of stenoses

- Good prognostic marker of future cardiac events

- Not as useful in acute chest pain settings- does not rule out ACS
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
Prospective ECG gating reduces radiation exposure

CTA can be routinely performed with < 4mSv

Patients with angina and no or minimal CAD on CTA may be able to be safely discharged home from the ED

- No events (MI or UA after 6 months f/u), Sensitivity and NPV: 100%

- CT strategy reduced time to diagnosis (3.4 hrs vs 15 hrs, p<0.001)

- CT strategy reduced costs ($1586 vs $1872, p<0.001)

- CT resulted in fewer repeat evaluations for recurrent CP (2% vs 7%, p=0.01)

Goldstein JA et al. JACC, 2007
ROMICAT II: Coronary CTA improves efficiency of clinical decision making in ED patients with acute chest pain

- Randomized study of 1000 patients with suspected CAD in ED to standard care and normal EKG and negative troponins
- Only 8% of screened patients actually had ACS
- Average time to diagnosis for CTA group was 10.4 hrs vs 18.7 in SOC group
- CTA approach reduced mean hospital LOS from 31 hrs to 23 hrs (p=0.0002)
- Almost 50% of patients in CTA group were discharged within 9 hrs
- No missed ACS in either group (within 30 days)
- However, CTA patients underwent more coronary angiography
- No significant difference in cost between groups

Hoffman U et al. *NEJM*, 2012
Functional CT is coming

CT Fractional Flow Reserve

CT stress perfusion and delayed enhancement


Conclusions

- Noninvasive cardiac testing can help answer the questions “Is significant CAD present?”, and if so, “what is the patient’s prognosis?”

- In general, if a patient can exercise and has an interpretable EKG, consider exercise stress testing.

- The choice of imaging modality to identify functional significance of CAD should be based on test availability, patient body habitus, local expertise, cost-effectiveness.

- Perfusion imaging can also guide which patients may benefit from revascularization strategies (those with >10% of ischemic myocardium).

Dowsley T et al. *Canadian Journal of Cardiology*, 2013
Thanks
American College of Cardiology
Five Things Physicians and Patients Should Question

1. Don’t perform stress cardiac imaging or advanced non-invasive imaging in the initial evaluation of patients without cardiac symptoms unless high-risk markers are present.

2. Don’t perform annual stress cardiac imaging or advanced non-invasive imaging as part of routine follow-up in asymptomatic patients.

3. Don’t perform stress cardiac imaging or advanced non-invasive imaging as a pre-operative assessment in patients scheduled to undergo low-risk non-cardiac surgery.
Diagnostic Imaging Studies in Patients in Large Integrated Health Care Systems: 1996-2010

### Table 1.1. Symptomatic

Refer to pages 16 and 17 for relevant definitions, in particular Table A and text for age, sex, symptom presentation, and risk factors relevant to each pre-test probability category.

<table>
<thead>
<tr>
<th>Indication Text</th>
<th>Exercise ECG</th>
<th>Stress RNI</th>
<th>Stress Echo</th>
<th>Stress CMR</th>
<th>Calcium Scoring</th>
<th>CCTA</th>
<th>Invasive Coronary Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Low pre-test probability of CAD&lt;br&gt;ECG interpretable AND able to exercise</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>2. Low pre-test probability of CAD&lt;br&gt;ECG uninterpretable OR unable to exercise</td>
<td></td>
<td>A</td>
<td>A</td>
<td>M</td>
<td>R</td>
<td>M</td>
<td>R</td>
</tr>
<tr>
<td>3. Intermediate pre-test probability of CAD&lt;br&gt;ECG interpretable AND able to exercise</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>M</td>
<td>R</td>
<td>M</td>
<td>R</td>
</tr>
<tr>
<td>4. Intermediate pre-test probability of CAD&lt;br&gt;ECG uninterpretable OR unable to exercise</td>
<td></td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>A</td>
</tr>
<tr>
<td>5. High pre-test probability of CAD&lt;br&gt;ECG interpretable AND able to exercise</td>
<td>M</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>A</td>
</tr>
<tr>
<td>6. High pre-test probability of CAD&lt;br&gt;ECG uninterpretable OR unable to exercise</td>
<td></td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>A</td>
</tr>
</tbody>
</table>

Appropriate Use Key: A = Appropriate; M = May Be Appropriate; R = Rarely Appropriate.
A = Appropriate; CAD = coronary artery disease; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; Echo = echocardiography; M = May Be Appropriate; R = Rarely Appropriate; RNI = radionuclide imaging.

### Table 1.2. Asymptomatic (Without Symptoms or Ischemic Equivalent)

Refer to pages 17 and 18 for relevant definitions.

<table>
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<th>CCTA</th>
<th>Invasive Coronary Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Low global CHD risk&lt;br&gt;Regardless of ECG interpretability and ability to exercise</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>8. Intermediate global CHD risk&lt;br&gt;ECG interpretable and able to exercise</td>
<td>M</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>M</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>9. Intermediate global CHD risk&lt;br&gt;ECG uninterpretable OR unable to exercise</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>R</td>
<td>M</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>10. High global CAD Risk&lt;br&gt;ECG interpretable and able to exercise</td>
<td>A</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>11. High global CAD Risk&lt;br&gt;ECG uninterpretable OR unable to exercise</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>R</td>
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