DIAGNOSTIC TESTING IN PATIENTS WITH STABLE CHEST PAIN

JOSHUA MESKIN, MD, FACC
-Medical College of Wisconsin
-Associate Professor of Medicine
-Director of Froedtert Health Echo Labs
-Director of Froedtert Cardiology Clinics

OBJECTIVES
- Prognosis & diagnosis
- Available modalities
- Choosing modalities

GUIDEINE-BASED CARE

PURPOSE OF A CARDIAC STRESS TEST
- Diagnostic
  - Does the patient have occlusive coronary artery disease
- Prognostic
  - What is the likelihood of the patient suffering a myocardial infarction or dying in the near future

CORONARY BLOOD FLOW RELATED TO DEGREE OF STENOSIS

How much stenosis in large coronary artery is needed to produce physiologically important obstruction?

ISCHEMIC CASCADE

1. Myocardial perfusion by nuclear or CMRI
2. Symptoms
3. ECG changes
4. Intracoronary abnormalities
5. Flushing

NONINVASIVE ASSESSMENT
CHOOSING AN APPROACH

INITIAL STEP: RISK STRATIFICATION
- Chest pain description
  - Stable versus unstable
- Left ventricular systolic function
  - Normal LVEF versus undifferentiated cardiomyopathy
- Coronary anatomy
  - Known CAD or coronary artery calcifications
- Arhythmia
  - Presence of ventricular arrhythmias
- Resting ECG
  - Normal versus ST-T abnormalities or Q waves
- CAD risk factors
- Clinical assessment

PRETEST LIKELIHOOD OF CAD
(COMBINED DIAMOND/FORRESTER AND CASS DATA)

DIAGNOSTIC MODALITIES
- Clinical
  - Response to optimal medical therapy
- Increase myocardial oxygen demand to provoke ischemia
  - Treadmill ECG
  - Exercise echocardiographic stress
  - Treadmill
  - Bicycle
  - Pharmacologic echocardiographic stress
  - Dobutamine/atropine

DIAGNOSTIC MODALITIES
- Create perfusion disparities by increasing flow through coronary arteries
  - Regadenoson (Lexiscan) / dipyridamole (Persantine) / adenosine
  - Nuclear imaging (SPECT (single photon emission computer tomography))
  - Cardiac MRI
  - PET scan
- Anatomic assessment
  - CT coronary arteries
  - Additional functional information with FFR
CLINICAL SCENARIO

A 49-year-old woman is evaluated for intermittent sharp, nonradiating, substernal chest pain for the past 2 weeks. The pain occurs more frequently in the morning and is not associated with meals or exertion but may be initiated with emotional stress. The pain often lasts for 10 minutes and subsides spontaneously.

- She has hyperlipidemia treated with pravastatin.
- Her mother had a myocardial infarction and heart failure starting at the age of 52 years.

WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE DIAGNOSTIC TEST TO PERFORM NEXT?

A. Diagnostic coronary angiography
B. Exercise electrocardiography
C. Exercise nuclear perfusion study
D. Pharmacologic nuclear perfusion study
WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE DIAGNOSTIC TEST TO PERFORM NEXT?

A. Diagnostic coronary angiography
B. Exercise electrocardiography
C. Exercise nuclear perfusion study
D. Pharmacologic nuclear perfusion study

PRETEST LIKELIHOOD OF CAD (COMBINED DIAMOND/FORESTER AND CASS DATA)

<table>
<thead>
<tr>
<th>Nonanginal</th>
<th>Atypical Angina</th>
<th>Typical Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>30-39</td>
<td>4</td>
<td>34</td>
</tr>
<tr>
<td>40-49</td>
<td>13</td>
<td>51</td>
</tr>
<tr>
<td>50-59</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>60-69</td>
<td>7</td>
<td>61</td>
</tr>
</tbody>
</table>

CONTRAINDICATIONS TO STRESS TESTING:
- Patient able to exercise?
- Previous coronary revascularization?
- Resting ECG interpretable?

LOW OR INTERMEDIATE LIKELIHOOD OF OBSTRUCTIVE CAD:
- Standard exercise ECG
- MPI or Echo w/ exercise or pharm CMR

INTERMEDIATE TO HIGH LIKELIHOOD OF OBSTRUCTIVE CAD:
- CCTA
- Initiate Guideline-Directed Medical Therapy

NONINVASIVE ASSESSMENT
CHOOSING AN IMAGING MODALITY

CORONARY CT ANGIOGRAPHY
- Accurately excludes presence of CAD
- Very high negative predictive value
- Defines anatomy of CAD
  - Single vessel versus multivessel
  - Proximal disease versus distal disease
- Prognostic implications including coronary calcium score
- Determination of physiologic significance possible with FFR

FRACTIONAL FLOW RESERVE (FFR)
- Ratio of maximal blood flow achievable in stenotic coronary artery relative to maximal flow in the same vessel if it were normal
- FFR = Pa/Pd
  - [abnormal if <0.8]
Diagnostic performance of stress myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis

Maurice C. de Jong, Tessa J. A. Grobbee, Ruttel van Nieuwenhuijze, Arjan Buitelaar, W. G. M. van den Bemdt

* MRI: 2,970 patients from 28 studies
* ECHO: 795 patients from 10 studies
* SPECT: 1,323 patients from 13 studies

**DIAGNOSTIC PERFORMANCE OF EACH MODALITY**

**CHOICE OF IMAGING MODALITY**

- Specificity versus sensitivity
- Local expertise and interpretation style
- Availability
- Body habitus
- Patient preference
- Level of concern for radiation exposure

---

SPECT

MRI

ECHO

Obstructive CAD Based on Anatomy from Invasive Angiography

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress ECG</td>
<td>59 (46-70)</td>
<td>82 (75-89)</td>
</tr>
<tr>
<td>Stress echo</td>
<td>89 (80-95)</td>
<td>70 (62-78)</td>
</tr>
<tr>
<td>CCTA</td>
<td>97 (92-99)</td>
<td>70 (52-84)</td>
</tr>
<tr>
<td>SPECT</td>
<td>67 (60-75)</td>
<td>85 (75-95)</td>
</tr>
<tr>
<td>PET</td>
<td>66 (59-74)</td>
<td>85 (75-95)</td>
</tr>
<tr>
<td>Stress CMR</td>
<td>96 (92-99)</td>
<td>85 (75-95)</td>
</tr>
</tbody>
</table>

Obstructive CAD Based on Invasive Angiography with Invasive Flow Assessment

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>68 (60-75)</td>
<td>75 (55-85)</td>
</tr>
<tr>
<td>CCTA</td>
<td>90 (84-96)</td>
<td>73 (67-80)</td>
</tr>
<tr>
<td>SPECT</td>
<td>72 (66-78)</td>
<td>68 (59-78)</td>
</tr>
<tr>
<td>PET</td>
<td>89 (82-95)</td>
<td>85 (75-95)</td>
</tr>
<tr>
<td>Stress CMR</td>
<td>89 (82-95)</td>
<td>85 (75-95)</td>
</tr>
</tbody>
</table>

---

**Obstructive CAD Based on Invasive Angiography with Invasive Flow Assessment**
LOCAL INTERPRETATION STYLES FOR INFLUENCE SENSITIVITY AND SPECIFICITY

Sensitivity (%) vs. Specificity (%)

- Lack of hyperkinesis
- 1 segment new WMA
- >1 segment new WMA
- Extensive new WMA
- LV dilation

Sensitivity (%)

Specificity (%)

LOCAL PRACTICES FOR INFLUENCE SENSITIVITY AND SPECIFICITY

Echo Contrast Usage Results in Enhanced Confidence & Image Quality

NONINVASIVE ASSESSMENT CHOOSING A STRESS AGENT

CHOICE OF STRESS AGENT

- Exercise preferred
  - Provides additional prognostic information
  - Correlation of symptoms with findings
- Pharmacologic stress
  - Used if unable to exercise
  - Regadenoson (Lexiscan)/adenosine/ dipyridamole (Persantine)
  - Nuclear imaging
  - CMR
  - Dobutamine
  - Echo
  - Nuclear imaging (not commonly used)

DIAGNOSTIC ACCURACY BASED ON STRESS AGENT


CHOICE OF PHARMACOLOGIC AGENT

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dobutamine</th>
<th>Vasodilator (regadenoson, adenosine, etc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchospasm</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>2nd or 3rd degree heart block</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Significant elevation in blood pressure</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Large aortic aneurysm</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>✗</td>
<td>✔</td>
</tr>
</tbody>
</table>
PROGNOSIS BASED ON TESTING

PROGNOSIS BASED ON TESTING

BEYOND CORRELATION WITH CORONARY ARTERY STENOSIS

- Prognostic value of stress testing to predict clinical outcomes
  - Death
  - Myocardial infarction
  - Need for revascularization

PROGNOSTIC VARIABLES DURING STRESS TEST

- Exercise duration
- Strongest prognostic value
- Coronary Artery Surgery Study (CASS)
  - Three-vessel CAD and preserved left ventricular function
    - 100% 4 year survival in those who exercised more than 12 minutes
- Duke treadmill score
  - Exercise time - (5 x ST deviation) - (4 x anginal index)
  - Anginal index: 0 = none; 1 = nonlimiting; 2 = stopped test
  - Predicts CV mortality per year
  - Low-risk (>4): < 1%
  - Intermediate-risk (-10 to +4): 1% to 3%
  - High-risk (< -10): > 5%

PROMISE TRIAL

Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE)
March 14, 2015

Composite End Point
Death, MI, unstable angina, major procedural complication

Comparative Value of a Treadmill Exercise Score in Outpatients with Suspected Coronary Artery Disease
Prognostic Value of a Treadmill Exercise Score in Outpatients with Suspected Coronary Artery Disease

- Duke treadmill score
  - Exercise time - (5 x ST deviation) - (4 x anginal index)
  - Anginal index: 0 = none; 1 = nonlimiting; 2 = stopped test
  - Predicts CV mortality per year
  - Low-risk (>4): < 1%
  - Intermediate-risk (-10 to +4): 1% to 3%
  - High-risk (< -10): > 5%

The Prognostic Value of Normal Exercise Myocardial Perfusion Imaging and Exercise Echocardiography
A Meta-Analysis
Louise D. Mihal, MD, Mary Huston, MD, Robert Hoss, MD, Eric F. Rudberg, MD, Michael G. Tchekmedyian, MD, PhD

- Total of 11,000 patients
  - CV death, MI, unstable angina & revascularization
- Normal stress yields annual risk of 0.4-0.9%
- NPV for MI and cardiac death
  - MPI: 98.8% over 36 months of follow-up
  - Echo: 98.4% over 33 months of follow-up
- Corresponding annualized event rates
  - MPI: 0.45% per year
  - Echo: 0.54% per year

The Prognostic Value of a Treadmill Exercise Score in Outpatients with Suspected Coronary Artery Disease
Prognostic Value of a Treadmill Exercise Score in Outpatients with Suspected Coronary Artery Disease

- Duke treadmill score
  - Exercise time - (5 x ST deviation) - (4 x anginal index)
  - Anginal index: 0 = none; 1 = nonlimiting; 2 = stopped test
  - Predicts CV mortality per year
  - Low-risk (>4): < 1%
  - Intermediate-risk (-10 to +4): 1% to 3%
  - High-risk (< -10): > 5%
**TAKE HOME POINTS**

1. Exercise ECG testing is recommended as the initial test of choice in patients with a normal baseline ECG and an intermediate pretest probability of coronary artery disease based on age, sex, and symptoms.

2. Results of stress testing should be used to determine both prognosis and diagnosis.

3. Modality of stress testing should be based on ability to exercise, local expertise and risk of adverse reaction from stress agent.

**QUESTIONS**

---

**EXAMPLES OF IMAGING MODALITIES**

**NUCLEAR PERFUSION STUDY**
REFERENCES

- Nesto RW, Kowalchuk GJ. The ischemic cascade: temporal sequence of hemodynamic, electrocardiographic and symptomatic expressions of myocardial ischemia. Am J Cardiol 1987; 59: 23C-30C.