Cardiac Stress Testing in Nuclear Cardiology

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Learning Objectives:

- Indications for stress testing
- Contraindication for stress testing
- Basic concepts of myocardial perfusion imaging (MPI)
- Various modalities for cardiac stress testing (Exercise vs Pharmacological)
- What agent to choose for a pharmacological stress test (Lexiscan, Adenosine, Dipyridamole, Dobutamine)
- Pros and Cons of each pharmacological agent

Indications for Stress Testing

- Symptoms suggesting coronary artery disease: chest pain, SOB, Syncope
- Determine prognosis and degree of coronary artery disease
- Evaluation of arrhythmia
- Evaluation of functional capacity
- Patients with CHF, valvular heart disease, cardiomyopathy, or planned non-cardiac surgery may be candidates for stress testing
Contraindications for Stress Testing

Patients with:
- Acute MI
- Acute myocarditis or pericarditis
- Unstable progressive angina
- Rapid ventricular and atrial arrhythmias
- 2nd and 3rd degree AV block
- Acutely ill patient ie with infection, hyperthyroidism or severe anemia

Approach to Choosing the Optimal Stress Test

- Clinical factors to consider:
  1. Can the patient exercise to reach an adequate work load?
     - Adequate level of exercise = ≥85% of maximum predicted heart rate (220-age)
  2. Abnormalities in the baseline EKG that can make the EKG nondiagnostic (>1mm ST segment depression pre-stress, LBBB, or paced rhythm). These patients should have a pharmacologic stress test (not dobutamine).*  
     - LBBB & V-Pacing: false positive reversible defects in the septal wall or LAD appear with exercise in the absence of CAD

Types of Cardiac Stress Tests

- Exercise stress is preferred in patients who can exercise adequately & achieve an adequate cardiac workload because it provides valuable prognostic information of exercise capacity, heart rate and blood pressure responses, and symptoms, as well as ST-segment response, that can be useful in clinical decision making.

- Pharmacologic Stress Test is typically performed when the patient cannot adequately exercise or if they have a LBBB or are being paced:
  - Performed using a vasodilator or a drug that has positive inotropic/chronotropic effect.

Bonow et al, Braunwald's Heart Disease (2012);1: 312-315.
Myocardial Perfusion Imaging (MPI)

- **EKG-Gated single emission computed tomography (SPECT)** obtains images from different parts of the cardiac cycle allowing measurement of the ejection fraction and identifying wall motion abnormalities (Fig. 1).
- An intravenously injected radiotracer distributes to the cardiac muscle in proportion to myocardial perfusion with resulting images displayed in a series of slices in the short axis, vertical long axis, and horizontal long axis orientation (Fig. 2).

![Image](image1)

Hurst’s et al, The Heart (2015);1:563-569.

Myocardial Perfusion Imaging (MPI)

- **Positron Emission Tomography (PET)** uses radiotracers rubidium-82 or ammonia to measure myocardial perfusion.
- Emission data are displayed similar to the SPECT display in the horizontal and vertical long-axis and short-axis views.
- Some advantages of PET imaging vs SPECT include: higher spatial resolution, improved scattered corrections and attenuation, and potential for quantifying regional blood flow thereby improving detection of CAD.
  - Ex: Patients with multivessel CAD may have uniform decrease in flow on SPECT, failing to detect this balanced ischemia.
  - However, an important limitation of PET perfusion imaging is that it is isolated to pharmacological stress test only due to the relatively short half-lives of radiotracers.


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Exercise Stress Test

![Image](image2)

"It's not looking good! We pulse is up to 200 just from getting out of the chair and another 30 on the treadmill."
Exercise Stress Test

• SPECT MPI is commonly performed with exercise stress testing to induce coronary hyperemia, and is best for patients who have exertional symptoms, as this allows us to link symptoms to the location and severity of abnormal perfusion patterns.

• All exercise stress tests should be symptom-limited, the patient has to be able to achieve the desired maximum predicted HR (220-age) of ≥85% and exercise for a minimum of 4-5 minutes on the protocol.

• Radioactive tracer injected at maximal stress & exercise is continued for 1-min to allow the tracer to be taken up by the myocardium.

• CAD can be detected when the radioactive tracer does not accumulate in areas of reduced myocardial perfusion due to a severely stenosed vessel.

The EKG: ST-Segment Displacement

• With myocardial ischemia ST-segment can take on different patterns: Horizontal & down-sloping depression most typical.

• ST segment becomes more horizontal or flattens as severity of the ischemic response worsens.

• With progressive exercise, the depth of ST segment depression may increase, involve more leads, and the patient may develop angina.

• Horizontal or down-sloping ST changes of 1mm or more are considered signs of ischemia.
Cont...

- As the ischemia in the subendocardium spreads to the epicardium and involves the full thickness of the myocardium, ST segment elevation is noted indicating an acute MI.

- Hours or days later after an acute MI, pathological Q waves develop, ST segment is back to baseline and the T waves invert.

Pharmacological Stress Test

- The most widely used pharmacological stress agents include:

  - Coronary vasodilators
    - regadenoson (Lexiscan),
    - Adenosine,
    - Dipyridamole

  - Adrenergic agents such as
    - Dobutamine.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Duration</th>
<th>Isotope Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regadenoson</td>
<td>0.4 mg IV injection over 10 sec followed by 5 ml NS flush</td>
<td>Bolus</td>
<td>10-20 sec after NS flush</td>
</tr>
<tr>
<td>Adenosine</td>
<td>140 mcg/kg/min</td>
<td>6-min infusion</td>
<td>At 3 minutes into infusion</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>142 mcg/kg/min</td>
<td>4-min infusion</td>
<td>3 min after completion of infusion</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>5-40 mcg/kg/min</td>
<td>Until achieved 85% of predicted HR</td>
<td>At achievement of predicted HR</td>
</tr>
</tbody>
</table>
Pharmacological: 
Vasodilator Stress
Adenosine, regadenoson, dipyridamole

• MOA: Stimulation of A2A receptors
  • Increasing arteriolar vasodilation, thereby increasing coronary blood flow 4-5 times its norm.
  • Methylxanthines= caffeine and theophylline are competitive inhibitors of this effect
  • Hold prior to testing to allow the reversal of the effect with aminophylline when clinically indicated.

• Hemodynamic Effects
  • Drop in systolic and diastolic BP by 8-10 mm Hg
  • Reflex increase in HR

Regadenoson VS Adenosine

Pros:
  • Low affinity agonist for A2A adenosine receptor
  • Short half-life of <10 sec
    • S/E resolve in few sec (flushing, CP, dyspnea, dizziness, N, drop in BP)
    • Aminophylline rarely required

Cons:
  • Activation of A1, A2b, and A3 receptors may cause:
    • AV Block (A1 receptor)=7.6% of patients
    • Peripheral vasodilation (A2b)
    • Bronchospasms (A2b & A3)

Vasodilator Stress With Low-Level Exercise

• Dipyridamole: Low-level exercise starts after the end of infusion.
• Adenosine: Exercise performed during infusion.
• Lexiscan: Exercise starts before injection, allowing the vasodilator and tracer to be injected with increased exercise.

Benefits:
  • Even low level exercise facilitates early post-infusion imaging (as early as 10-15 min following injection) compared to the 1-hr delay required when no exercise is performed.
  • Marked reduction in the frequency and severity of side effects from the vasodilator agent.
  • Even low-level exercise provides additional prognostic information.
Pharmacological: Dobutamine Stress Test

- **MOA**: Inotropic reaction (broad adrenergic receptor agonist)
  - Increases the force of cardiac muscle contraction
  - Necessary achievement of predicted HR ≥85%

- **Pros**:
  - Reserved for patients w/ asthma, COPD, or those who ingested caffeine
  - S/E’s resolve within few minutes (can be aborted w/ IV BB)

- **Cons**:
  - S/E’s are frequent & bothersome: palpitations, CP
  - Adverse reaction: ventricular irritability more common than with vasodilator stress (PVCs, NSVT)
  - Myocardial blood flow less than vasodilator stress
    - Therefore, degree of heterogeneity of coronary flow with a coronary stenosis is also less

Bonow et al, Braunwald’s heart disease (2012) 9:1 314-316

Summary of Key Points:

- **Exercise stress** is preferred in patients who can exercise adequately & achieve an adequate cardiac workload.
- **Pharmacologic Stress Test** is typically performed when the patient cannot adequately exercise or if they have a LBBB or are being paced. Consider the pros and cons of each vasodilator stress agent when choosing the agent.
- **All exercise stress tests should be symptom-limited**, the patient has to be able to achieve the desired maximum predicted HR (220-age) of ≥85% and exercise for a minimum of 4-5 minutes on the protocol.
- Even low level exercise facilitates early post-infusion imaging (as early as 10-15 min following injection) compared to the 1-hr delay required when no exercise is performed.

Thank you for your attention