Diagnosis of Coronary Artery Disease: Which Stress Test for Which patient?

- Akash Ghai, MD, FACC
- February 27, 2015

No Disclosures
Epidemiology of CAD
Question: Which population has the highest incidence of myocardial infarction in the United State?

- A. White men 65–74 years
- B. Black women 65–74 years
- C. Black men 55–64 years
- D. Black men 65–74 years
- E. White men 55–64 years
Epidemiology of CAD

- 17,600,000 people with CVD (Prevalence 7.9%)
  - 12.1% of Whites
  - 10.2% of African-Americans
  - 8.1% Hispanics
  - 5.2% of Asians (almost 2x in Asian Indians)
- 8,500,000 people with MI (Prevalence 3.6%)
- Cardiovascular disease account for 1 in 2.9 deaths
  - 380,000 deaths per year from ischemic heart disease
  - Leading cause of death in men and women
Prevalence of CAD Increases with Age

CAD Prevalence as a Percent of the Population

Lloyd-Jones et al; Circulation 2010:121:e46
Incidence of MI by Age, Race and Gender

Per 1000 Person Years

Age Group

35–44  45–54  55–64  65–74

White Men  Black Men  White Women  Black Women

Lloyd-Jones et al; Circulation 2010:121:e46)
Mortality from CVD in the US Is Declining

Lloyd-Jones et al; Circulation 2010:121:e46)
Question: Which of the following features are classified as high-risk in a patient with unstable angina?

- A. Previous history of cardiovascular disease
- B. Prolonged rest pain (> 20 minutes) that has resolved
- C. Age > 70 years
- D. ST depression > 1 mm
- E. None of the above
How to diagnose

- Majority of patients with CAD are diagnosed with provocative test which attempt create and then visualize supply–demand myocardial oxygen mismatch.
Confirmatory Stress Tests

- Exercise treadmill stress test
- Stress Echo
- Myocardial Nuclear Perfusion Imaging
- Stress MRI
The Stress in Stress Testing

1. **Exercise**
   - Achieves higher level of physiologic stress and thus preferred
   - Exercise capacity alone is also a strong prognostic indicator of long-term risk

2. **Dobutamine**: increases heart rate and contractility

3. **Vasodilators**: increase blood flow to normal arteries and decrease perfusion to stenotic vessels
Nuts & Bolts of Exercise Stress Testing

- Target HR: 85% age-predicted HR (220−age)
- Sensitivity 68%; specificity 77%
- ST depression does not localize ischemia; ST elevation does
- Prognostic factors
  - ECG: max ST depression, # leads ST depression, time ST shift, recovery time, ventricular arrhythmia
  - Hemodynamics: peak HR (chronotropic incompetence), BP (exercise induced hypotension), rate pressure product
  - Duration: time, METS, workload

Angina
## Exercise Stress Testing: Clinical Contraindications

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
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<tbody>
<tr>
<td>Acute MI (&lt; 2 days)</td>
<td>LMCA stenosis</td>
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<tr>
<td>Acute PE or pulmonary infarct</td>
<td>Moderate valvular stenosis</td>
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<td>Acute myocarditis or pericarditis</td>
<td>Electrolyte abnormalities</td>
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<td>Acute aortic dissection</td>
<td>Severe HTN</td>
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<td>Unstable angina</td>
<td>Tachy or bradyarrhythmia</td>
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<td>Symptomatic arrhythmia</td>
<td>High degree AV block</td>
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<td>Severe symptomatic AS</td>
<td>HOCM</td>
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<tr>
<td>Decompensated CHF</td>
<td>Mental/physical inability</td>
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# Exercise Stress Testing: Reasons to Terminate Test

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
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<tbody>
<tr>
<td>Ischemia and drop of SBP &gt; 10 mm Hg</td>
<td>No ischemia, drop of SBP &gt; 10 mm Hg</td>
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<tr>
<td>Moderate to severe angina</td>
<td>ST depression &gt; 2 mm or marked axis shift</td>
</tr>
<tr>
<td>CNS symptoms (ataxia, dizziness, presyncope)</td>
<td>Multifocal PVC’s, PVC triplets, SVT, heart block or bradyarrhythmia</td>
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<tr>
<td>Poor perfusion (cyanosis or pallor)</td>
<td>Fatigue, SOB, wheezing, leg cramps or claudication</td>
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<tr>
<td>Patient requests to stop</td>
<td>IVCD or BBB similar to VT</td>
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<tr>
<td>Sustained VT</td>
<td>Increasing chest pain</td>
</tr>
<tr>
<td>&gt; 1 mm ST elevation in a non-Q wave lead (except V1 or AVR)</td>
<td>Hypertensive response (SBP &gt; 250/DBP &gt; 115)</td>
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</table>
Exercise Stress Testing: Conditions Obscuring ST Changes

- Pre-excitation (WPW syndrome)
- Electronically paced ventricular rhythm
- Resting ST depression > 1 mm
- Complete LBBB
- Left ventricular hypertrophy
- Digoxin
Analyze ST–segment depression > 80 msec after the J–point compared to PQ segment, in any lead except V1 or AVR.
Exercise Stress Testing: EKG Interpretation

- If ST segment isoelectric at baseline
  - Positive: > 1 mm horizontal or down sloping ST segment

- If ST segment depression < 1 mm at baseline
  - Positive: > 2 mm additional horizontal or down sloping ST segment
  - Nondiagnostic: 1–2 mm additional horizontal or down sloping ST segments

- ST elevation (0.1%): Transmural ischemia induced by coronary spasm or myocardial injury
  - ST elevation in aVR associated with left main or multivessel disease
Quite common but non-specific and should not be read to interpret ischemia!
Duke Treadmill Score and Mortality

- DTS: exercise time in minutes – 5 x max ST depression – 4 x angina index
  - Angina index: 0 (no CP), 1 (CP), 2 (chest pain stops exercise)

<table>
<thead>
<tr>
<th>Risk</th>
<th>Score</th>
<th>1 year mortality</th>
<th>5 year CV mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&gt; 5</td>
<td>1%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>+4 to -10</td>
<td>1-3%</td>
<td>9.5%</td>
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<tr>
<td>High</td>
<td>&lt; -11</td>
<td>&gt; 3%</td>
<td>35%</td>
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Exercise Testing: Other Variables Associated with Poor Prognosis

- Chronotropic Incompetence
  - Impaired heart rate response to exercise
  - Defined as failure to achieve 85% of age-predicted maximum heart rate
  - Associated with mortality

- Heart rate recovery
  - Variable defined but generally < 12 to < 18 beats at home minute
  - Associated with increased mortality

- Ventricular ectopy (> 7 VPB/minute, bigeminy/trigeminy, VT)
  - During exercise is associated with decreased LVEF
  - During recovery is associated with decreased LVEF and increased mortality
Stress Test with Imaging
Question: A 55 y.o. male is referred for a stress test for chest pain while walking. He has a history of HTN, HLD, COPD, prior TIA and recent R. hip replacement for OA. He currently ambulated with a walker. His resting ECG is WNL. His medications include Aggrenox, theophylline, lisinopril, metformin and atorvastatin. Which of the following modalities is most appropriate?

A. Exercise echocardiography
B. Adenosine sestamibi
C. Dobutamine stress echocardiography
D. Persantine thallium
E. Exercise sestamibi
Stress Testing with Imaging: Basic Principles

- Addition of imaging (echo/nuclear) to EKG stress testing improves sensitivity and specificity.
- Stress nuclear and echo have similar sensitivity for diagnosis of CAD, but stress echo has higher specificity (i.e., fewer false positives).

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Exercise ECG</td>
<td>68%</td>
<td>77%</td>
</tr>
<tr>
<td>Stress Echo</td>
<td>80%</td>
<td>86%</td>
</tr>
<tr>
<td>Stress Nuclear</td>
<td>84%</td>
<td>77%</td>
</tr>
</tbody>
</table>
Stress Testing with Imaging Indications

- Inability to exercise
- Uninterpretable ECG – LBBB, LVH, WPW
- Intermediate/high risk Duke Treadmill score
- Pre-op vascular surgery, > 1 clinical risk factor for CAD, poor functional capacity (< 4 METS)
- Intermediate coronary stenosis (60–70% lesion)
- Ischemic equivalent post PCI/CABG
- Myocardial viability
- Ventricular tachycardia
Stress Echocardiography
Nuts & Bolts of Dobutamine Stress Echo

- Mechanism: direct $\beta_1$ and $\beta_2$ stimulation $\rightarrow$ increase in HR, BP, contractility. Coronary stenosis $\rightarrow$ minimal increase flow (subepicardial $>$ subendocardial)

- Goal is 85% of age predicted heart rate
  - Starting dose 5 to 10 mcg/kg/min, increased at 3 minute intervals to 20, 30, and 40 mcg/kg/min
  - Add Atropine if goal HR not achieved at peak dose: 0.25 mg IV, q 2–3 min, max dose 1–2 mg

- Half-life 2 minutes

- Side effects (75% patients)
  - Palpitations, chest pain, headaches, flushing, dyspnea, SVT, VT, ischemic ST shift
  - Treat with short acting IV beta-blockers
## Dobutamine Stress Testing: Contraindications

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
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</thead>
<tbody>
<tr>
<td>Symptomatic severe AS</td>
<td>Hypokalemia</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>LV thrombus</td>
</tr>
<tr>
<td>HOCM</td>
<td>Intracranial arterial aneurysm</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Abdominal aortic aneurysm</td>
</tr>
<tr>
<td>Unstable coronary syndrome</td>
<td>Severe ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>High degree AV block</td>
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<tr>
<td></td>
<td>Uncontrolled HTN (BP &gt; 200/110)</td>
</tr>
<tr>
<td></td>
<td>Uncontrolled AF</td>
</tr>
</tbody>
</table>

Geleijnse et al. Circulation 2010;121:1756
Dobutamine Stress Echo: Termination of Study

- Achievement of target heart rate
- Achievement of peak dose
- Intolerable symptoms
- Severe HTN (BP > 240/120 mm Hg)
- Hypotension (decrease in SBP > 20 mm Hg)
- Serious ventricular arrhythmia
- WMA > 3 segments
Complications of Dobutamine Stress Testing

- **Mortality:** < 0.01%
- **Cardiac rupture:** < 0.01%
  - Akinetic or dyskinetic inferior wall, MI within past 4–14 days
- **Myocardial infarction:** 0.02%
  - Dobutamine induced platelet aggregation, $\alpha-1$ mediated vasoconstriction, increased shear forces
- **Stroke:** < 0.01%
- **Asystole:** < 0.01%
  - Sinus node deceleration
- **Sustained VT:** 0.15%
- **VF:** 0.04%
  - Impaired LV function + ischemia
Complications of Dobutamine Stress Testing

- SVT: 1.3%
- AF: 0.9%
- Coronary spasm: 0.14%
  - $\alpha - 1$ receptor medicated vasoconstriction
- Hypotension: 1.7%
  - Inadequate increase in CO to compensate for a decline in SVR
  - Can be due to: inadequate contractile reserve, severe ischemic LV dysfunction, fixed/dynamic obstructive left sided disease
- HTN: 1.3%
## Stress Echo: Risk Stratification

<table>
<thead>
<tr>
<th>Very Low (&lt;1%/y cardiac death/MI)</th>
<th>Low (&lt;2%/y)</th>
<th>Increasing Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal exercise echo with good exercise capacity</td>
<td>Normal dobutamine stress with low to intermediate pretest probability</td>
<td>Ischemic stress EKG</td>
<td>Extensive rest WMA (4–5 segments)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resting WMA</td>
<td>Baseline EF &lt;40%</td>
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<tr>
<td></td>
<td></td>
<td>No change/increase in ESV</td>
<td>4–5 ischemic segments</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No change/decrease in EF</td>
<td>Low ischemic threshold</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Worsening WMA with stress</td>
<td>Ischemic WMA with no change or decrease in EF</td>
</tr>
</tbody>
</table>

Pellikka et al. JASE 2007;20:1021
Exercise stress testing

- Always preferred over pharmacologic
- ASE does not prefer treadmill over bicycle,
- Advantage of supine bicycle protocol is that imaging can be performed during exercise
In 2005 ASE recommended the 16 or 17 segment model for interpretation.

Function in each segment is graded at rest and with stress as normal or hyperdynamic, akinetic, dyskinetic or aneurysmal.

Function from low stages of dobutamine should also be assessed.
Image Interpretation

Coronary Artery Territories

Left Ventricular Segmentation in Standard Echocardiographic Views
Hypokinesis – defined as delay in the velocity, onset of contraction or reduction of the maximum amplitude of contraction.

Differences in the onset of contraction and relaxation between segments may range from 50 to more than 100 ms.

What is an abnormal study?
- Fixed wall motion abnormality
- New or worsening abnormality indicative of ischemia
A way to quantify the degree of ischemia during a stress echo

1. Low risk patient
1.1 – 1.7 – intermediate risk patient
> 1.7 – high risk patient

Figure 1. Cardiac event rate per year as a function of wall motion score index (WMSI). The number of patients within each WMSI category is shown below each column. Statistical significance increases as a function of the WMSI result.
Stress Echo Results Predict Survival

**Figure 3.** Cumulative survival as a function of wall motion score index (WMSI) using cardiac events as an end point.
Normal Stress Echo
Normal Stress Echo
Abnormal Stress Echo
Stress Nuclear
Question: Which of the following patients would be appropriate for an adenosine nuclear stress test?

- A. Patient with BP of 188/90 mm Hg on presentation
- B. Asthmatic
- C. Patient taking Aggrenox
- D. Patient who drank a cup of regular coffee earlier this morning.
Mechanism: Agonist of the A2A receptor on vascular smooth muscle cells, results in coronary arteriolar vasodilation through increased cAMP
- 4-fold increase in myocardial blood flow

Increased in the flow of stenosed artery, in comparison to normal artery, is thus attenuated (i.e. relative flow heterogeneity.)

Myocardial ischemia rare, as myocardial blood flow increases to variable degree in all vascular beds.

Greater HR increase than adenosine, similar BP effects

Dosing 0.4 mg IV bolus, t1/2 0 2.2 to 3 min

Hyperemia within 30 seconds
- Radiotracer thus injected 10–20 seconds after regadenoson
Myocardial perfusion imaging protocols

**Rest**
- Inject rest dose
- Imaging
- 0 → 30-60 mins

**Exercise**
- Inject stress dose
- Imaging
- 0 → 10-20 mins

*Figure 5.* Tc-99m imaging protocols: One-day rest/exercise stress.
Side effects of Regadenoson

- Side effects:
  - A1 receptors: AV block (8% – transient, 2nd degree 4%, 3rd degree < 1%)
  - A2B (much less than adenosine): peripheral vasodilation and bronchospasm
  - A3,A4 receptors: bronchospasm – mast cell degranulation

- Minor (> 80% cases)
  - Higher risk of headaches and GI effects than adenosine due to rapid bolus
  - Most common side effect is dyspnea

- ST depression: 5–7% (unclear of significance)
Regadenoson Stress Testing: Contraindications

- **Absolute**
  - Asthma
  - Second or third degree AV block
  - Sick sinus syndrome
  - SBP < 90 mm Hg
  - Recent oral dipyridamole (including Aggrenox)
  - Aminophylline or caffeine within 12 hours
  - Known hypersensitivity
  - AMI or unstable ACS

- **Relative**
  - HR < 40 bpm
  - Symptomatic carotid stenosis
Regadenoson Stress Testing: Termination of Study

- Severe hypotension (SBP < 80 mm Hg)
- Development of symptomatic, persistent 2\textsuperscript{nd} or 3\textsuperscript{rd} degree heart block
- Wheezing
- Severe CP associated with > 2 mm ST depression
- Poor perfusion (pallor, cyanosis, and cold skin)
- Patient’s request to stop
Stress Nuclear and Prognosis

- Normal nuclear associated with very low cardiac event rate (<1%/year)
  - This effect persists for patient with strongly positive exercise EKG or angiographic stenosis

- High-risk features include
  - > 20% of LV ischemic
  - Increased lung to heart ratio or trace uptake
  - Fixed LV dilatation
  - Transient LV dilatation (TID): misnomer, actually due to diffuse subendocardial ischemia
  - Increase RV uptake

Stress Nuclear and Prognosis

Hachamovitz et al., Circulation 1998;97:535
Myocardial perfusion

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Rest</th>
<th>Exercise</th>
<th>Rest</th>
<th>Exercise</th>
<th>Rest</th>
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Transient Ischemic Dilatation
Increased lung–heart ratio > 0.5 is abnormal, and conveys poor prognosis (Normal ratio < 0.42 for Tc)
Increased RV Uptake

- Normally < 50% LV counts
- Increased RV uptake due to higher RV mass from pulmonary hypertension or reduced LV counts from ischemia.
GATED SPECT

Helps to increase specificity – soft tissue attenuation vs. artifact
Stress Test Algorithm

ECG Abnormalities
(LVH with strain, LBBB, PM, Digitalis effect, WPW)

- **Yes**
  - Stress cardiac Imaging

- **No**
  - Can patient exercise?
    - **Yes**
      - Exercise Treadmill Test?
        - **Yes**
          - Assess for contraindications
            - Pharmacologic Nuclear
        - **No**
          - Assess for contraindications
            - Dobutamine Stress echo
    - **No**
      - Exercise Echocardiogram (if no WMA)

**Unable to exercise**

**Able to exercise**

No LBBB