DIAGNOSIS OF CORONARY ARTERY DISEASE: WHICH STRESS TEST FOR WHICH PATIENT?

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QUESTION 1

Which segment of the population has the highest incidence of myocardial infarction in the United States?
ANSWERS

- 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

Lloyd-Jones et al; Circulation 2010:121:e46
MORTALITY FROM CVD IN THE US IS DECLINING

Lloyd-Jones et al; Circulation 2010:121:e46
Which of the following is considered the worst prognostic factor in a patient who has unstable angina?
A. Previous history of cardiovascular disease
B. Prolonged rest pain (> 20 min) that has resolved
C. Age > 70 years
D. ST depression > 1 mm
E. Delayed heart rate recovery time
Majority of patients with coronary artery disease are diagnosed with a provocative test which attempts to create and then visualize a supply-demand myocardial oxygen mismatch.
CONFIRMATORY STRESS TESTS

- Exercise treadmill stress test
- Stress Echo
- Myocardial Nuclear Perfusion Imaging (SPECT or PET)
- Stress MRI
Approximately 600,000 stress tests are performed on adults each year.

Frequency of stress tests has increased 3% per year.

Use of SPECT has decreased by 15% over the past 10 years.

Use of stress echo has increased 27% over the same time period.

Use of PET and Stress MRI has increased 65%!
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:
   - Increases blood flow more to normal coronary arteries relative to diseased arteries creating flow heterogeneity
NUTS & BOLTS OF EXERCISE STRESS TESTING

- Target HR: 85% age-predicted HR \((220-\text{age}) \times 0.85\)
- Sensitivity 68%; specificity 77%
- ST depression does not localize ischemia (PW)
- 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

#### Absolute
- Acute MI (< 2 days)
- Acute PE
- Acute myocarditis or pericarditis
- Acute aortic dissection
- Unstable angina
- Symptomatic arrhythmia
- Severe symptomatic AS
- Decompensated CHF

#### Relative
- LMCA stenosis
- Moderate valvular stenosis
- Electrolyte abnormalities
- Severe HTN
- Tachy or bradyarrhythmia
- High degree AV block
- HOCM
- Mental/physical inability
EXERCISE STRESS TESTING: REASONS TO TERMINATE TEST

**Absolute**
- Ischemia and a drop of SBP > 10 mm Hg
- Moderate to severe angina
- CNS symptoms (ataxia, dizziness, pre-syncope)
- Poor perfusion (cyanosis or pallor)
- Patient requests to stop
- Sustained VT
- > 1 mm ST elevation in a non-Q wave lead (except V1 or AVR)

**Relative**
- No ischemia, drop of SBP > 10 mm Hg
- ST depression > 2 mm or marked axis shift
- Multifocal PVC’s, PVC triplets, SVT, heart block or bradyarrhythmias
- Fatigue, SOB, wheezing, leg cramps or claudication
- IVCD or BBB similar to VT
- Increasing chest pain
- Hypertensive response (SBP > 250/DBP > 115 mm Hg)
EXERCISE STRESS TESTING: CONDITIONS OBSCURING ST CHANGES

- Pre-excitation (WPW syndrome – Delta wave)
- Digoxin effect – Scooped ST segment
- Electronically paced ventricular rhythm
- Resting ST depression > 1 mm
- Complete LBBB
- Left ventricular hypertrophy
EXERCISE STRESS TESTING: EKG INTERPRETATION

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
  - Non-diagnostic: 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>
</tr>
<tr>
<td>High</td>
<td>&lt; -11</td>
<td>&gt; 3%</td>
<td>35%</td>
</tr>
</tbody>
</table>
EXERCISE TESTING: OTHER VARIABLES ASSOCIATED WITH POOR PROGNOSIS

- **Chronotropic Incompetance**
  - Failure to achieve age-predicted maximum HR during exercise.
  - (Healthy 208-0.7xage - Tanaka; CAD pts 164-0.7xage - Brawner)
  - Due to reduced or insensitive B-receptors
  - Independent predictor of MACE (1/3 HF pts)

- **Heart rate recovery**
  - Variable defined but generally < 12 bpm in the first minute
  - Associated with a 4 x increase risk of mortality!
  - Marker of dysfunction of vagal reactivation

- **Ventricular ectopy (> 7 VPC/minute)**
  - During exercise is associated with decreased LVEF
  - During recovery is associated with decreased LVEF and increased mortality!

Brubaker et al; Circulation 2011:1010-1020
A 55 year old male is referred for a stress test for chest pain while walking. He has a history of HTN, HLD, COPD, prior TIA and recent right hip replacement for OA. He is currently ambulating with a walker.

His resting ECG is WNL. His medications include Aggrenox, Theophylline, Lisinopril, Metformin and Atorvastatin.

Which of the following stress tests is the most appropriate for this patient?
ANSWERS

- A. Exercise echocardiography
- B. Adenosine sestamibi
- C. Dobutamine stress echocardiography
- D. Persantine thallium
- E. Exercise sestamibi
The addition of imaging to EKG stress testing improves the sensitivity and specificity for CAD detection.

Stress nuclear and echo have similar sensitivities but stress echo has higher specificity (i.e., fewer false positives)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<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 with CP syndrome
- Uninterpretable ECG – LBBB, LVH, WPW
- Intermediate risk Duke Treadmill score without angina
- Pre-op vascular surgery or immediate risk surgery and > 1 CAD RF and poor functional capacity (< 4 METS)
Intermediate coronary stenosis detected by cath or cardiac CTA

Ischemic symptoms and prior PCI/CABG

Asymptomatic prior to revascularization and > 3 years post PCI and > 5 years post CABG

Ventricular tachycardia
Mechanism: direct $\beta_1$ and $\beta_2$ stimulation -> increase in HR, BP, contractility.

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 – thus monitor patient 10 minutes post dobutamine infusion termination

Side effects (75% patients)
- Palpitations, chest pain, headaches, flushing, dyspnea, SVT, VT.
- Treat with short acting IV beta-blockers
DOBUTAMINE STRESS TESTING: CONTRAINDICATIONS

**Absolute**
- Symptomatic severe AS
- Acute aortic dissection
- HOCM
- Hypersensitivity
- Unstable coronary syndrome

**Relative**
- Hypokalemia
- LV thrombus
- Intracranial arterial aneurysm
- Abdominal aortic aneurysm
- Severe ventricular arrhythmias
- High degree AV block
- Uncontrolled HTN (BP > 200/110)
- Uncontrolled AF

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, α-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%
<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>
</tr>
<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
Recent abstract from Yang et al. presented at ACC 2016 showed stress echo done as an outpatient for low risk chest pains is safe and cost effective.

- 198 pts. 98 admitted, 98 discharged
- Discharged pts had stress echo within 5 days.
- 94/98 outpatient had negative stress echo (none had MI or death during 30 day f/u)
- 92/98 inpatient had negative stress echo (none had MI death during 30 day f/u)
- Total cost for 98 inpatients was $397,164.5
- Total cost for 98 outpatients was $65,954!

Yang DC et al, In: ACC 2016 April 2; Session 1132: Abstract #7.
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.
- **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
Which of the following patients would be the best candidate 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.

E. Patient with intermittent Wenckebach on resting EKG
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

Increase in the flow of stenosed artery, in comparison to normal artery, is thus attenuated (i.e. relative flow heterogeneity.)
Myocardial ischemia is 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 - 2 to 3 min

Hyperemia within 30 seconds

Radiotracer thus injected 10-20 seconds after regadenoson
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
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

REGADENOSON STRESS TESTING: TERMINATION OF STUDY
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

Event rate (%)

Sum Stress Score

Normal (SSS < 4)  SSS 4-8  SSS 9-13  SSS > 13

Cardiac Death
MI

Hachamovitz et al., Circulation 1998;97:535
MYOCARDIAL PERFUSION

Diagram showing myocardial perfusion images under different conditions (Exercise and Rest) for comparison.
TRANSIENT ISCHEMIC DILATATION

a)

Stress
Rest
TID 1.30

b)

Stress
Rest
TID 1.23
INCREASED LUNG UPTAKE

Increased lung-heart ratio > 0.5 is abnormal, and conveys poor prognosis (Normal ratio < 0.42 for Tc)

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- 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)

Can patient exercise?

Exercise Treadmill Test?

Unable to exercise

Able to exercise

Stress cardiac Imaging

Examine for contraindications

Pharmacologic Nuclear

Dobutamine Stress echo

Exercise Echo (if no WMA)

Exercise Nuclear

No LBBB
THANK YOU!