Objectives

- Review indications for stress testing and anatomic evaluation for coronary artery disease
- Recognize traditional and less traditional risk factors for CAD
- Review the ACC/AHA 2013 ASCVD calculator
Exercise Treadmill Test (ETT)

- Most frequent indication for ETT is to aid in establishing the diagnosis of CAD
- ETT can provide valuable functional and prognostic information
- Post-test probability of CAD is related to the pretest risk and sensitivity/specificity of the test
ETT – the higher the pre-test probability the better the test

- Pooled sensitivity of 68% and specificity of 77% for the detection of CAD

- Confounders are resting ST segment depression, digoxin use, LV hypertrophy which reduce specificity

- Ideal patient is intermediate pre-test risk and is able to exercise with an interpretable resting EKG

Define abnormal ST segment displacement with exercise

- Down sloping ST segment depression is normal with exercise

- In patients with myocardial ischemia the ST segment becomes more horizontal as the severity of the ischemic response worsens

- 0.10 mV or more from the PQ junction as the baseline, 80ms after the J point in 3 consecutive beats

ST segment depression and extent of ischemia on SPECT

ST elevation in lead avR

Figure 1. Bayesian Analysis of STE in Lead aVR for the Prediction LMCA or Ostial LAD Stenosis

J Am Coll Cardiol Img. 2011
Rapidity of Recovery of ST segment changes

*J Am Coll Cardiol.* 2014; 63(13):1264-1274
Take away points: ST segment changes

- Learn to recognize abnormal vs. normal ST changes with exercise
- Severity of ST changes correlates to extent of ischemia
- Time to recovery an important prognostic indicator
Metabolic equivalent = unit of oxygen uptake

1 MET = 3.5 ml O$_2$/kg/min of body weight

Standardizes exercise workloads and performance with different protocols

3-5 METS = raking leaves, golf, walking
5-7 METS = singles tennis
9 METS = running 6 to 7 mph
Predicted versus Expected METS

- Predicted METs = 14.7 - (0.13 \times \text{age})
Cumulative 20 yr survival rates in normal men versus exercise capacity

Circulation. 2008;117: 614-622
Duration of Exercise and % ischemia on SPECT

Predictors of > 10% Ischemia of the LV

### Table 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chi-Square</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 METs exercise capacity</td>
<td>8.9</td>
<td>10.1</td>
<td>2.2–46.0</td>
<td>0.003</td>
</tr>
<tr>
<td>ST-segment depression ≥1 mm on exercise ECG</td>
<td>18.8</td>
<td>7.1</td>
<td>2.9–17.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest pain during stress</td>
<td>6.1</td>
<td>3.2</td>
<td>1.3–8.0</td>
<td>0.014</td>
</tr>
<tr>
<td>Male sex</td>
<td>4.6</td>
<td>3.0</td>
<td>1.1–8.2</td>
<td>0.033</td>
</tr>
<tr>
<td>Ejection fraction (↓ by 5%)</td>
<td>3.9</td>
<td>1.3</td>
<td>1.0–1.7</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Take Away Points: Duration of Exercise

- Regardless of the result, exercise duration provides invaluable prognostic information.

- When able, and there are no contraindications, preferred modality is always exercise.
How did your patient feel while exercising?

- Treadmill-induced typical angina increases the sensitivity for the diagnosis of CAD

- Risk of events is higher when symptoms are induced at a lower workload

Am J Cardiol 1978;41:227–32.
Duke Treadmill Score
Combining several factors

- 2800 patients with chest pain underwent both an ETT and cardiac catheterization

- ST segment deviation was the strongest predictor of both cardiac death and non fatal MI, but exercise duration and angina index also important

Duke Treadmill Score

\[
\text{Duke Treadmill Score} = \text{Exercise Duration (min)} - 5 \left( \frac{\text{ST Deviation (mm)}}{5} \right) - 4 \left( \text{Angina Index} \right)
\]

**Angina Index**
0 – none, 1 – typical angina, 2 – angina causing test cessation

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk Group</th>
<th>Stenosis ≥ 75%</th>
<th>Multivessel Disease</th>
<th>1-Year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 5</td>
<td>Low</td>
<td>40.1%</td>
<td>23.7%</td>
<td>0.25%</td>
</tr>
<tr>
<td>-10 to 4</td>
<td>Intermediate</td>
<td>67.3%</td>
<td>55.0%</td>
<td>1.25%</td>
</tr>
<tr>
<td>≤ -11</td>
<td>High</td>
<td>99.6%</td>
<td>93.7%</td>
<td>5.25%</td>
</tr>
</tbody>
</table>

Duke Treadmill Score

All cause mortality

Myocardial Infarction

In this regard, our scores (treadmill scores pro-

11, 13, 14). Conclusions of treadmill variables

score and to arbitrarily

14. Thus, a patient

risk (annual mortality rate,

treadmill results (no ST de-
exercise duration of 5 minutes

treadmill results (1-mm ST

depression) but without angina and with an exercise du-

ration of at least 10 minutes (Patient 2). At the other end

of the spectrum, a patient with “early-positive” treadmill

results (2-mm ST depression at 6 minutes, for example)

would be at high risk (annual mortality rate, ≥ 5%) if

he or she stopped exercising because of angina (Patient 5:
treadmill score, −12) or at moderate risk (annual mor-

tality rate, 2% to 3%) if no angina occurred during exer-

cise (Patient 4: treadmill score, −4).

The development of a prognostic treadmill score ex-

Blood Pressure Response With Exercise

- Normal exercise response is to increase SBP with increasing workload
- Diastolic blood pressure should not change significantly
Excessive BP response is a poor prognostic marker

Am J Cardiol. 2008 Jun 1;101(11):1614-20
Failure to augment blood pressure with exercise is also a poor prognostic marker

- Failure to increase SBP beyond 120mmHg
- Sustained decrease greater than 10mmHg repeatable within 15s
- Fall in SBP beyond resting values
Heart Rate Recovery

- Abnormal HR recover refers to a slow deceleration of HR following exercise cessation
- Reflects decreased vagal tone
- A value of 12 beats/min or less is abnormal if upright exercise
Contraindications to Exercise

- Acute MI within 2d
- High-risk unstable angina
- Decompensated CHF
- Uncontrolled cardiac arrhythmias
- Advanced AV block
- Severe symptomatic AS or HCM
- Uncontrolled hypertension
- Aortic Dissection
- Left Bundle Branch Block
ETT – Consider reporting more than just “positive or negative”

- What is your patient’s exercise capacity?
- Was there ST segment depression or elevation?
- If ECG changes, how long in recovery did they persist?
- What was blood pressure response?
- What was heart rate recovery?
- Did the patient report angina?
- What is the Duke Treadmill Score?
ETT in Special Populations
ETT in Women

- Pooled sensitivity in 3,700 women from 19 studies only 61% and specificity was 70%.

- Decreased specificity of ST-segment depression is thought to be due to increased prevalence of baseline ST-T changes.

Am J Cardiol 1999; 83:660–6
What Is the Optimal Method for Ischemia Evaluation in Women trial
Single-Photon Emission Computed tomography (SPECT) Stress testing

- Exercise or pharmacologic
- Involves injection of a radiotracer
- Radiotracer is extracted from the blood by viable myocytes and retained for a period of time
SPECT Stress Testing

- Photons are emitted from the myocardium and is proportional to uptake

- Standard camera captures the photons and converts the information into digital data

- Allows comparison between “rest” and “stress”
In patients who can exercise, does SPECT imaging provide incremental value?

SPECT imaging predicts cardiac death

Circulation. 1998;97:535-543
Indications for Pharmacologic SPECT Stress Testing

- Patients who cannot exercise
- Left Bundle Branch Block
- Ventricular Paced Rhythm
Pharmacologic SPECT Stress testing

Dipyridamole

Metabolized by ADA

Adenosine

Adenosine $A_{2a}$ receptor

Vasodilation

Coronary Arteriole

↓Arteriolar resistance

↑MBF
Adenosine

- Non-selective

- 140 ug/kg/min induces max coronary hyperemia

- After infusion, max flow occurs at an average of 84s

- Side effects are AV block, flushing

- Reverse with aminophylline
Regadenoson

- Selective $A_{2A}$ receptor agonist
- 0.4mg injected over 10 seconds
- Hyperemia with onset in < 30s
- Effects last for 2 to 5 min
- Not approved for use in hemodialysis patients
Coronary Flow Reserve

- The magnitude of blood flow increase relative to resting flow values is termed coronary blood flow reserve.

- It is the ability to increase flow above resting values in response to pharmacologic vasodilation.

- Coronary blood flow increases during exercise by decreasing resistance at the coronary arteriolar level.
Effect of Coronary Stenosis on Coronary Blood Flow Reserve

A

- P normal
- R2 normal
- Rest flow normal

B

- P ↓
- R2 ↓
- Rest flow normal

Compared to rest
- P slight ↑
- R2 ↓↓↓
- Stress flow ↑↑↑

- P +/- ↑
- R2 +/- ↓
- Stress flow +/- ↑
Contraindications to vasodilator stress testing

- Active bronchospastic airway disease
- Significant hypotension
- Sick sinus syndrome or high degree AV block
Stress Echocardiography

- Can be exercise or pharmacologic

- If able to exercise then options are treadmill or supine bike depending on echo lab protocol

- If pharmacologic, majority of studies are done with IV dobutamine
Stress Echocardiography

- Baseline echo images in multiple views
- Sequential echo images at intermediate, peak, and in recovery
- Comparison of rest and exercise images for wall motion abnormalities
Incremental Value of Exercise Stress Echocardiography

Circulation. 2001;103:2566-2571
Incremental Value of Stress echo with exercise

![Graph showing the incremental value of stress echo with exercise](image)

- Clinical
- Clin+Rest LV
- Clin+Rest LV+Stress test

- Global chisquare
  - P<0.001
  - P<0.001

- Statistical significance between groups

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**References**

Dobutamine Stress Echocardiography

- Stimulates B1, B2, and A1 receptors
- 5 μg/kg/min increased every 3 min to max dose of 40 μg/kg/min
- Palpitations, NSVT, Hypotension are common side effects
Indications for Dobutamine Stress Echocardiography

- Patients unable to exercise
- Reactive airway disease that precludes use of vasodilators
Coronary Artery Calcium Scoring
Coronary Artery Calcium Scoring

- Non contrast, limited chest CT acquired with a 3-5s breath hold
- The presence of CAC is quantified through the entire epicardial system
- CAC is defined as a lesion above a threshold of 130 Hounsfield units, with an area of > 3 adjacent pixels
- The Agatson score is determined by the product of the calcified plaque area and maximal calcium lesion density
Coronary Artery Calcium Scoring: Agatson Score

- 0 – absence of a calcified plaque
- 1-10 – minimal plaque
- 11-100 mild plaque
- 101-400 moderate plaque
- > 400 severe plaque
Calciu̇m Percentile

- By comparing a subject's calcium score with that of others of the same age, sex, and ethnicity through the use of large databases of asymptomatic patients, a calcium % is generated.

- Higher than 75th percentile is considered high risk, regardless of the score and indicates premature atherosclerosis.
Coronary Artery Calcium Scoring

- In population-based studies CAC scoring by CT accurately stratified CV risk in asymptomatic individuals.

- Presence, extent, and progression of CAC has been shown to be associated with MACE and death.

Am Coll Cardiol Img. 2015;8(8):900-909
Does a CAC score of 0 confer long-term protection against poor survival?

- ~9700 asymptomatic patients without known CAD
- ~4800 had a CAC score of 0
- At a mean f/u of 14.6 years CAC score > 0 was the strongest predictor of death in the overall population beyond individual CV risk factors. The risk of death increased proportionally with the severity in CAC score

Am Coll Cardiol Img. 2015;8(8):900-909
CAC score of 0

- Individuals with a CAC score of 0 had the lowest mortality independent of FRS or NCEP ATP III.

- Mortality rates in individuals with a CAC of 0 were < 1% over almost 15 years in low and intermediate risk patients younger than 60 with no disparity between sexes.

- Individuals considered at high clinical risk but with a CAC score of 0 had a longer “warranty” period than those at low or intermediate clinical risk with any CAC score.

Am Coll Cardiol Img. 2015;8(8):900-909
Coronary CT Angiogram

- Provides a method to assess plaque burden but also stenosis

- More accurate method to determine who has obstructive or functionally significant stenosis compared to functional testing
Prognostic Value of Coronary CTA for Prediction of All-Cause Mortality

- Single-center retrospective cohort of ~1100 pts > 45 with chest symptoms
- Stenosis graded as minimal (< 30%) to severe (> 70%)
- 12-18 month follow up of all cause death using Cox proportional hazards model adjusted for pretest CAD likelihood and risk factors

J Am Coll Cardiol. 2007; 50(12):1161-1170
Prognostic Value of Coronary CTA for Prediction of All-Cause Mortality

Figure 3 Cumulative Survival in Patients With Moderate (>50%) Plaque by CCTA

Risk-adjusted p < 0.001 (controlling for age, family history, and dyslipidemia). CCTA = coronary computed tomographic angiography

J Am Coll Cardiol. 2007; 50(12):1161-1170
Prognostic Value of Coronary CTA for Prediction of All-Cause Mortality

- Risk of death increased proportionally with increasing number of epicardial vessels involved

- Higher risk associated with left main or proximal LAD disease

- The absence of any plaque was associated with a high negative predictive value
Prognostic Value of CTA versus exercise ECG in patients with suspected CAD

- Retrospective cohort study of ~3000 pts from 2003-2009 who underwent both coronary CTA and exercise ECG

- In patients with suspected CAD coronary CTA discriminates future risk of MACE independent of exercise ECG

- Exercise ECG has additive value in patients only with moderate to severe stenosis on CTA

J Am Coll Cardiol. 2012; 60(21):2205-2215
PROMISE Trial

- 10,000 symptomatic patients with suspected CAD to functional testing (ECG only, stress echo, SPECT) versus CTA

- Primary endpoint was a composite of all-cause mortality, MI, hospitalization for UA and complications from CV procedure

- Median follow-up 25 months

N Engl J Med. 2015 Apr 2;372(14):1291-300
PROMISE Trial Conclusions

- No difference in primary outcome between functional testing versus anatomic testing.

- Was the studied powered to show a difference (low event rates)?

- Choice of outcome appropriate?

- Should a higher risk population have been studied?

N Engl J Med. 2015 Apr 2;372(14):1291-300
Choosing the right test for your patient
Questions to consider before ordering a stress test in patients without a prior history of CAD

- How typical are the patient’s symptoms? The history is CRITICAL.

- What is the pre-test probability of significant coronary disease?

- Are there any functional limitations?
Estimating your patient’s risk of obstructive CAD

Table 10. Comparing Pretest Likelihood of CAD in Low-Risk Symptomatic Patients With High-Risk Symptomatic Patients (Duke Database)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Nonanginal Chest Pain</th>
<th>Atypical Angina</th>
<th>Typical Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>45</td>
<td>9–47</td>
<td>2–22</td>
<td>21–70</td>
</tr>
<tr>
<td>55</td>
<td>23–59</td>
<td>4–21</td>
<td>45–79</td>
</tr>
<tr>
<td>65</td>
<td>49–69</td>
<td>9–29</td>
<td>71–86</td>
</tr>
</tbody>
</table>
More recent tools for risk stratification

- Using the 2013 atherosclerotic cardiovascular (ASCVD) calculator

- Consideration of risk factors not captured by currently available prediction tools

2013 ASCVD Calculator

- Derived from a pooled cohort of ~25,000 patients including ~5000 AA men and women
- Input race, gender, age, smoking status, diabetes, hypertension, total cholesterol, HDL
- Generates a 10 yr estimate of risk of coronary death, non fatal MI, fatal or non fatal stroke in age 40-79 yo
## 2013 ASCVD Calculator

http://tools.acc.org/ASCVD-Risk-Estimator/

<table>
<thead>
<tr>
<th>Estimator</th>
<th>Clinicians</th>
<th>Patients</th>
<th>About</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASCVD Risk Estimator</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### All fields are required to compute ASCVD risk.

- **Gender**
  - Male
  - Female

- **Age**
  - 20-79

- **Race**
  - White
  - African American
  - Other

- **HDL - Cholesterol (mg/dL)**
  - 20-100

- **Total Cholesterol (mg/dL)**
  - 150-320

- **Diabetes**
  - Yes
  - No

- **Treatment for Hypertension**
  - Yes
  - No

- **Systolic Blood Pressure**
  - 90-200

- **Smoker**
  - Yes
  - No

---

*Intended for use if there is not ASCVD and the LDL-cholesterol is <190 mg/dL.

**Optimal risk factors include: Total cholesterol of 170 mg/dL, HDL-cholesterol of 60 mg/dL, Systolic BP of 110 mm Hg. Not taking medications for hypertension, not a diabetic, not a smoker.*
2013 ASCVD Calculator

- A moderate or high intensity statin is recommended for a 10yr risk > 7.5%

- Can the data be extrapolated to inform us when stress testing may be beneficial?
Non traditional Risk Factors – especially important for women

- History of pre-eclampsia, gestational diabetes, gestational hypertension
- Underlying rheumatologic disorder
What do the guidelines recommend?
Thank you