New Concepts in the Evaluation for Coronary Artery Disease in Women: The Role of Cardiopulmonary Exercise Testing (CPET)

S. Jay Mathews, MD, MS, FACC

Interventional Cardiologist/Endovascular Specialist
Bradenton Cardiology Center
Clinical Associate Professor, LECOM
Bradenton, FL
Disclosures

**Speaker’s Bureau:**
- Astra Zeneca
- Maquet
- Spectranetics

**Grant/Research Support**
- Astra Zeneca
- Terumo
- Cordis
- Medtronic
- Bard
- Veryan Medical
- Spectranetics

**Medical/Scientific Boards:**
- Abbott Vascular
Background

- CAD is the leading cause of death for both men and women in the United States
  - More women than men die of CAD
  - More women have died from CAD than of cancer (including breast cancer), chronic lower respiratory disease, Alzheimer disease, and accidents combined
  - Overall rates of CAD declined 30.6% (1998-2008), but the rates are increasing in young women (<55 years)
  - The effect of obesity on the development of CAD appears to be greater in women than in men (From Framingham Heart Study RR of CAD 64% in women vs. 46% in men)

- The average age at first myocardial infarction (MI) is 64.5 years for men and 70.3 years for women.
  - Among women with premature MI (age < 50) there is a 2x increased mortality over men
  - Among older women (over the age of 65), women are more likely to die within the first year after MI
  - 45 to 64 years of age, women are more likely than men to have CHF within 5 years of MI

Background

• **Cardiopulmonary Exercise Testing** - Possible Effective Initial Tool in the Detection of CAD in Women

• **Components**
  - **Exercise Treadmill** (Or Ergometry/Bicycle)
  - Pulmonary Testing
    - VO2/VCO2 (Pulmonary Gas Exchange) – Useful in Identifying HF Populations As VO2 Max Related to the Cardiac Output
    - VE (Expiratory Ventilation)
  - **Electrocardiogram**
  - Blood Pressure
  - Heart Rate

Background

• **MET**- Estimated of Maximal O2 Uptake for a Given Workload
  • Measure of Ventilatory Oxygen Consumption Expressed as Multiples of Basal Resting Requirements
  • 1 MET = 1 Unit Basal O2 Consumption = 3.5 mL O2 Consumption/kg/min
  • Can be Estimated by Grade and Speed of the Treadmill via Bruce Protocol

• **Duke’s Treadmill Score**
  • DTS = Exercise Time - (5 x Max ST) - (4 x Angina Index)
  • Lower Score Correlates with Increased CV Mortality

• **Framingham Risk Score**
  • Point System - TC, HDL, Age, SBP, DBP, DM Status, Smoking Status
  • -17 to 25 (Increased Score = Increased Risk Factors)

---
Background

- **Heart Rate**
  - Measure of Chronotropic Competence
  - Inability to Reach 85% of the MPHR = Chronotropic Incompetence

- **Heart Rate Recovery**
  - HRR = PHR – HR at 2 min Recovery
  - Useful for Patients Even on Beta Blockers

Duke’s Treadmill Score

- Low Risk ≥ +5
- Mod Risk +4 to -10
- High Risk ≤ -11

<table>
<thead>
<tr>
<th>DTS Risk Category</th>
<th>1-Yr Mortality</th>
<th>No Stenosis &gt;=75%</th>
<th>1 VD &gt;=75%</th>
<th>2 VD &gt;=75% or 3VD &gt;=75%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.9%</td>
<td>52.6%</td>
<td>22.4%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Mod</td>
<td>2.9%</td>
<td>17.8%</td>
<td>15.6%</td>
<td>27.9%</td>
</tr>
<tr>
<td>High</td>
<td>8.3%</td>
<td>1.8%</td>
<td>9.1%</td>
<td>17.5%</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.5%</td>
<td>80.9%</td>
<td>9.4%</td>
<td>6.2%</td>
</tr>
<tr>
<td>Mod</td>
<td>1.1%</td>
<td>65.1%</td>
<td>14.2%</td>
<td>8.3%</td>
</tr>
<tr>
<td>High</td>
<td>1.8%</td>
<td>10.8%</td>
<td>18.9%</td>
<td>24.3%</td>
</tr>
</tbody>
</table>

VD = Vessel Disease; LM = Left Main

Duke’s Treadmill Score

• Not As Useful as Other Measures
  • 26,500 consecutive women (5,939 age greater than or equal to 65 years, with a control sample of 20,561 age less than 65 years) who underwent clinical exercise testing at a tertiary care hospital with a median follow-up of 7.1 years. Cox hazard model was used to identify the best set of predictors of all-cause mortality, from potential clinical and exercise-derived variables.
  • In both age groups, **peak exercise METs had the strongest association with death.**
  • DTS not a predictor of mortality over other clinical exercise variables
  • In elderly women, abnormal HRR and peak METS best predictor

The Importance of Exercise Capacity

- St. James Women Take Heart Project
- 5721 Asymptomatic Women (Age 52 ± 11 years) followed for 8 Years
  - Bruce Protocol Exercise
  - FRS Calculated

The Importance of Exercise Capacity

- FRS and Exercise Capacity vs. Survival

The Importance of Exercise Capacity

- Exercise Capacity Adjusted for FRS
  - Each 1 MET Increase = 17% Reduction in Mortality
  - Exercise Capacity is the Best Predictor of Mortality (HR 3.1 vs. 1.0 for <5 METS vs > 8 METS)

The Importance of Exercise Capacity

- Lipid Research Clinics Prevalence Study

- 2994 Asymptomatic Women over 20 Years (Age 30-80) Followed for CV and All Cause Mortality

- Lower Exercise Capacity Associated with Mortality

The Importance of HRR with Mortality

- Lipid Research Clinics Prevalence Study
- 2994 Asymptomatic Women over 20 Years (Age 30-80) Followed for CV and All Cause Mortality
- Lower Heart Rate Recovery Associated with Mortality

The Importance of HRR with Ex Capacity

- The Combination of Low METS with Low HRR has the Highest Mortality
- ST Segment Depression is Not Predictive of Mortality

<table>
<thead>
<tr>
<th></th>
<th>Cardiovascular Death</th>
<th></th>
<th>All-Cause Death</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>No. of Deaths</td>
<td>Adjusted Hazard Ratio (95% CI)</td>
<td>No. of Deaths</td>
</tr>
<tr>
<td>High METs, high HRR</td>
<td>822</td>
<td>7</td>
<td>1.00</td>
<td>39</td>
</tr>
<tr>
<td>Low METs, high HRR</td>
<td>644</td>
<td>19</td>
<td>1.66 (0.69-4.00)</td>
<td>78</td>
</tr>
<tr>
<td>High METs, low HRR</td>
<td>579</td>
<td>17</td>
<td>1.92 (0.78-4.72)</td>
<td>74</td>
</tr>
<tr>
<td>Low METs, low HRR</td>
<td>940</td>
<td>103</td>
<td>3.52 (1.57-7.86)</td>
<td>257</td>
</tr>
</tbody>
</table>

What About Perfusion Imaging?

- What Is the Optimal Method for Ischemia Evaluation in Women (WOMEN) Trial
  - Symptomatic Women with Suspected CAD (n = 844)
  - Randomized to Exercise or Exercise MPI
  - Low Risk Population- ETT is a More Cost Effective Option

Summary

• Exercise Treadmill Testing (ETT) is a Good First Tool In Both Low Risk Symptomatic and Asymptomatic Women for Predicting CV Mortality

• DTS is Not Predictive as Exercise Capacity

• ST Segment Depression is Not Predictive of Mortality

• The Combination of Exercise Capacity and Heart Rate Recovery Can be Useful

• MPI is Probably Not Cost Effective in Low Risk Female Populations Over ETT
New Concepts in the Evaluation for Coronary Artery Disease in Women: The Role of Cardiopulmonary Exercise Testing (CPET)

S. Jay Mathews, MD, MS, FACC

Interventional Cardiologist/Endovascular Specialist
Bradenton Cardiology Center
Clinical Associate Professor, LECOM
Bradenton, FL