Heart Rate Recovery in association with exercise stress testing

Daniel E. Forman, M.D.
Director, Exercise Laboratory
Brigham and Women’s Hospital
April 21, 2006
Stress Testing

• Historical Rationale for Exercise Testing
  – Test sensitive and specific to diagnose CAD
    • Symptoms and ECG changes

• Has this rationale for testing changed?
  – Diagnosis is often not the question
  – Shifting emphasis on prognosis
  – What constitutes meaningful endpoints?
    • What is the best test??
Limitations of Stress Test for CAD:

- Normal vessel
- Minimal CAD
- Moderate CAD
- Severe CAD

Compensatory expansion maintains constant lumen
Expansion overcome: lumen narrows

lumen may be patent

Limitation of Stress Test for CAD:
Cardiac Cath is a flawed Gold Standard

We’ve based our diagnostic standards on 2D imaging

Courtesy of Steven Nissen
Limitations of Stress Test for CAD:

No assessment of plaque stability
Bottom Line

• It is often hard to detect ischemia

• And even when ischemia is detected, it is difficult to discern the implications

• Prognosis is more important than diagnosis
Prognostic Endpoints

- Functional capacity
- Prognostic Scores
- HR indices: heart rate recovery
Exercise Heart Rate Responses

- Vagal withdrawal
- Sympathetic increase
- Vagal Reactivation

Heart Rate

Rest | Peak | 1 minute

Exercise | Recovery
Heart Rate Recovery

- Biological rationale
- Seminal research
- Confounding, interactions
- External validation
- Clinical applications
Heart Rate Recovery

- Biological rationale
- Seminal studies
- Confounding, interaction
- External validation
- Clinical applications
HR Recovery: After Atropine

Recovery Time (minutes) vs. Log Heart Rate

- Athlete
- Normal
- Heart Failure

Imai JACC 24;1529;1994
Autonomic Function and Mortality

- Increased Risk of Death
  - Sympathetic Tone
  - Vagal Tone
  - Chronotropic Incompetence
  - HR Recovery
Heart Rate Recovery

- Biological rationale
- Seminal studies
- Confounding, interaction
- External validation
- Clinical applications
Heart Rate Recovery and Mortality

Abnormal (120/639)

Abnormal ≤ 12 bpm
Log-rank $\chi^2=115$, $P<0.0001$

Hazard Ratio 4.0 (95% CI 3.0-5.2)

HRR and Duke Exercise Score

Survival

Years of Follow-up

Log-rank $\chi^2 = 383, P < 0.0001$

Nishime, Lauer, JAMA 2000;284:1392-1398
Heart Rate Recovery

- Biological rationale
- Seminal studies
- Confounding, interaction
- External validation
- Clinical applications
Demographic Subsets

Test Subsets

Medication Subsets

Stress Echocardiography

Survival

Years After Test

Normal heart rate recovery (N=4633, 115 deaths)

Abnormal heart rate recovery, (N=805, 75 deaths)

Log-rank $\chi^2 = 99$, $P < 0.0001$  
Cut-off = 18 bpm

Watanabe, Lauer. Circulation 2001;104:1911-1917
HR Recovery and LVEF

Survival

Years After Test

Log-rank $\chi^2_3 = 170, \ P<0.0001$

Watanabe, Lauer. Circulation 2001;104:1911-1917
Years After Stress Test
Survival

Both Normal
Severe CAD
Abnormal HR Recovery
Both Abnormal

Vivikenathan D and Lauer MS, J Am Coll Cardiol 2003;42:831-8
Heart Rate Recovery

- Biological rationale
- Seminal studies
- Confounding, interaction
- External validation
- Clinical applications
External Validation: Stanford

Technical differences

- 1 minute vs. 2 minute recovery
- Cool down vs. supine recovery protocol
Neither
Exercise
Recovery
Both

1862 deaths
Log-rank $\chi^2 = 133, P < 0.0001$

Heart Rate Recovery

- Biological rationale
- Seminal studies
- Confounding, interaction
- External validation
- Clinical applications
Combining Prognostic Indices: Function and HR recovery

Shetler et al. JACC. 2001; 38: 1980-7
Risk for CV death according to FRS categories and HRR/METs groups

A 10-YEAR FOLLOW-UP

FRS-adjusted Hazard Ratio for CVD Death

P\text{\textsubscript{trend}} = 0.10
P\text{\textsubscript{trend}} = 0.001

<table>
<thead>
<tr>
<th>Total #: CVD Death #:</th>
<th>&lt; 6</th>
<th>6-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,439</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>1,883</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>1,36</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

B 20-YEAR FOLLOW-UP

FRS-adjusted Hazard Ratio for CVD Death

P\text{\textsubscript{trend}} < 0.001

<table>
<thead>
<tr>
<th>Total #: CVD Death #:</th>
<th>&lt; 6</th>
<th>6-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,439</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>1,883</td>
<td>37</td>
<td>52</td>
</tr>
<tr>
<td>1,36</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Implications

• Does this supplant the emphasis on diagnostic testing with imaging?
Treatment Implications of HRR