SIMPLE HEART RATE ADJUSTMENT OF ST SEGMENT DEPRESSION DURING EXERCISE TESTING

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In sum: 
*Poor sensitivity* of the standard exercise ECG for ischemia is the major diagnostic weakness and the critical limitation of the test.

*Why is this?*
The standard exercise test is defined by a *threshold ST segment depression partition*:

- $\frac{1}{2} \text{ mm STD} = \text{negative test}$
- $1 \text{ mm STD} = \text{positive test}$
- $2 \text{ mm STD} = \text{very positive test}$

So..., what’s the problem?
 WHAT’S WRONG WITH THE EXERCISE ECG?

ST segment depression is the problem:

ST depression at peak exercise does not work very well for the identification of coronary artery disease or for the assessment of its anatomic severity, and it is not a strong marker for the presence of vulnerable plaque that leads to acute coronary syndromes.

We need to go beyond the ST segment
ST segment depression is directly related to both:

- A spatial factor: the solid angle subtended by the induced ischemic boundary (anatomic area of ischemia)
- A non-spatial factor: the voltage drop across the ischemic boundary (metabolic severity of ischemia)
SPATIAL AND NONSPATIAL DETERMINANTS OF VOLTAGE

ST segment depression is directly related to both:

The *anatomic extent* of ischemia

The *functional severity* of ischemia
Relation of ST depression to *number* of SPECT ischemic segments during exercise

ST segment depression, mm

<table>
<thead>
<tr>
<th>NIS &lt;7</th>
<th>NIS =&gt;7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+17%</td>
</tr>
</tbody>
</table>

p = .07

(n=102)

*Am J Card* 2005; 96:1356
STD IN RELATION TO THE PRESENCE AND EXTENT OF CAD

ST depression (uV)

Extent of CAD (number of obstructed arteries)

p=ns
NON-SPATIAL FACTORS AND STD

Relation of ST depression to average stress severity score in SPECT ischemic segments

ST segment depression, mm

SSA≤2

SSA>2

p<0.005

+29%

(n=102)

Am J Card 2005; 96:1356
Because STD is driven by *variable exercise load*,

- *1 mm of STD* is an empiric partition, not a physiologically stable marker for identification of coronary artery disease

and....
Peak exercise STD is the wrong variable for evaluating the presence and extent of CAD, because it is workload dependent.

To derive more useful information about ischemia, STD must be adjusted for dynamic factors that cause it to change during the course of exercise.
ST DEPRESSION AND EXTENT OF MYOCARDIAL ISCHEMIA

From exercise physiology and the solid angle relationship:

ST segment depression during exercise-induced ischemia is directly related to both the extent of coronary disease and the severity of ischemia induced by a changing myocardial workload:

Apparent ischemia = Extent of disease x Severity of ischemia
(ST depression) (CAD) (Cardiac work)

\[ \Omega \Delta V \]
Voltage across the ischemic boundary in isolated perfused myocardium is linearly related to driving (heart) rate

\[ \Delta V = c \cdot \Delta HR \]

● *Time* (exercise duration) is the *wrong* variable for dynamic evaluation of ST segment depression

● *Heart rate* is a more relevant physiologic parameter for the analysis of ischemia (heart rate is linearly related to $\text{MVO}_2$)
HEART RATE ADJUSTMENT OF ST SEGMENT DEPRESSION

ST depression can be *adjusted* for the varying severity of ischemia (as HR) during higher levels of exercise *to clarify the extent of disease*:

Apparent ischemia = Extent of disease x Severity of ischemia (ST depression) (CAD) (HR)

So:

\[
\text{Extent of disease} = \frac{\Delta \text{ST depression}}{\Delta \text{Heart rate}}
\]
THE ST/HR SLOPE AND THE ST/HR INDEX

ST segment depression

- Mean exercise ST/HR index (simple division)
- Peak exercise ST/HR slope (linear regression)

Heart rate
By percentile estimation, 95% of normal subjects found to have ST/HR Index < 1.6 uV/bpm (where 100 uV = 1.0 mm). And therefore:

ST/HR Index > 1.6 uV/bpm can serve as criterion for CAD:

**Applied as test criterion:**
At high specificity, the ST/HR index improves the sensitivity of the exercise ECG for detection of CAD:

(n=549)
IDENTIFICATION OF CAD BY ST/HR INDEX CRITERIA IN MEN AND WOMEN

Sensitivity of ST/HR index and standard criteria at matched specificity (96%):

Circulation 1995;92:1209

Circulation 1995;92:1209

n=246  n=91
Revised Sensitivity of the ST/HR INDEX vs Standard Test

- Identification of more patients with 1 and 2 vessel CAD
- High prevalence of correct classification of CAD patients with “equivocal” tests
- Identification of some CAD patients with truly negative standard tests

Reasons for test improvement: reduction in “false negative” test outcomes
“EQUIVOCAL” ETTs: RELATION OF ST DEPRESSION TO HEART RATE IN CAD

ST/HR Index = 1.6

(n=73)
EQUIVOCAL EXERCISE ECG IN PATIENT WITH ISCHEMIA

ST/HR index = 130 μV/ 62 bpm = 2.1 μV/bpm
EQUIVOCAL EXERCISE ECG IN PATIENT WITHOUT CAD

<table>
<thead>
<tr>
<th>Lead</th>
<th>ST/Medians (µV)</th>
<th>0:01</th>
<th>2:00</th>
<th>4:00</th>
<th>6:00</th>
<th>8:00</th>
<th>10:00</th>
<th>12:00</th>
<th>14:00</th>
<th>16:01</th>
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<tbody>
<tr>
<td>I</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-10</td>
<td>-10</td>
<td>-5</td>
<td>-15</td>
<td>-25</td>
<td>-35</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-50</td>
<td>-75</td>
<td>-95</td>
<td>-105</td>
<td>-145</td>
<td>-140</td>
<td>-85</td>
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<tr>
<td>III</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-85</td>
<td>-65</td>
<td>-80</td>
<td>-100</td>
<td>-135</td>
<td>-125</td>
<td>-50</td>
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<tr>
<td>CM5</td>
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<td>0</td>
<td>-5</td>
<td>-55</td>
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<td>-90</td>
<td>-85</td>
<td>-150</td>
<td>-110</td>
<td>-60</td>
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<tr>
<td>(aVL)</td>
<td>0</td>
<td>0</td>
<td>-5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>aVF</td>
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<td>0</td>
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<td>0</td>
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<td>V1</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>V2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>V3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>V4</td>
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<td>-25</td>
<td>-30</td>
<td>-45</td>
<td>-50</td>
<td>-80</td>
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<tr>
<td>V5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-50</td>
<td>-50</td>
<td>-60</td>
<td>-40</td>
<td>-95</td>
<td>-65</td>
<td>-40</td>
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<tr>
<td>V6</td>
<td>0</td>
<td>0</td>
<td>-20</td>
<td>-50</td>
<td>-40</td>
<td>-50</td>
<td>-25</td>
<td>-75</td>
<td>-45</td>
<td>-35</td>
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<tr>
<td>HR (bpm)</td>
<td>80</td>
<td>104</td>
<td>111</td>
<td>100</td>
<td>105</td>
<td>121</td>
<td>133</td>
<td>144</td>
<td>155</td>
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</tr>
</tbody>
</table>

ST/HR index = 85 µV/ 75 bpm = 1.1 µV/bpm
LINEARITY OF EXERCISE INDUCED ISCHEMIC ST DEPRESSION

Ischemic

Non-ischemic
NEGATIVE ETTs: RELATION OF ST DEPRESSION TO HEART RATE IN CAD

(n=54)

ST/HR Index = 1.6

(n=54)
STANDING REST: 83 BPM, 116/68

No symptoms
2 MIN 1.7 MPH, 10%: 100 BPM

Just prior to onset of angina
1 MIN 2.5 MPH, 12%: 111 BPM, 140/60

Exercise-limiting angina 7/10, 0.5 mm STD
3 MIN RECOVERY: 85 BPM

Resolving angina 2/10
## PT WHJ: EXERCISE PERFORMANCE

<table>
<thead>
<tr>
<th>PHASE</th>
<th>WORK LOAD</th>
<th>HR</th>
<th>BP</th>
<th>ST DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upright control</td>
<td>0 mph</td>
<td>83</td>
<td>116/68</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0 %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak exercise</td>
<td>2.5 mph</td>
<td>111</td>
<td>140/60</td>
<td>0.5 mm = 50 μV</td>
</tr>
<tr>
<td></td>
<td>12 %</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

\[ \Delta HR = 28 \text{ bpm} \]
\[ \Delta ST = 50 \mu V \]

ST/HR Index = 50/28 = 1.8 μV/bpm [>1.6]
STD AND ST/HR INDEX IN RELATION TO PRESENCE AND EXTENT OF CAD

ST depression (uV)

ST/HR Index (uV/bpm)

Extent of CAD (number of obstructed arteries)

p=ns

p<0.05
Absolute risk of cardiac events during 4-year follow-up predicted by standard ETT and by ST/HR index:

(Relative risk = 3.1)
Relative risk of future cardiac events associated with ST/HR index > 1.6 during 4 year follow-up, by sex:

<table>
<thead>
<tr>
<th>Group</th>
<th>Relative Risk (RR)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3.1</td>
<td>3168</td>
</tr>
<tr>
<td>Men</td>
<td>2.6</td>
<td>1521</td>
</tr>
<tr>
<td>Women</td>
<td>5.4</td>
<td>1647</td>
</tr>
</tbody>
</table>
Absolute risk of mortality during 7-year followup predicted by standard ETT and by ST/HR index:

(Relative risk = 4.0)
SUMMARY: HEART RATE AND THE ST SEGMENT DURING EXERCISE

- Simple heart rate adjustment of ST depression during exercise controls for the increasing metabolic severity of ischemia to clarify the underlying extent of disease.

- Improvement of exercise test sensitivity with the ST/HR index results from reclassification of otherwise “equivocal” and even “negative” test responses, including increased identification of one and two-vessel disease in men and in women.

- The ST/HR index can increase the prognostic value of the exercise ECG by prediction of cardiac risk and mortality.
**FURTHER READING**

- Okin PM, Kligfield P. Heart rate adjustment of ST depression and performance of the exercise electrocardiogram: a critical evaluation. *Journal of the American College of Cardiology* 25:1726-1735, 1995