DECLARATION OF CONFLICT OF INTEREST
FACTORS AFFECTING SENSITIVITY, SPECIFICITY AND POSITIVE PREDICTIVE VALUE OF EXERCISE TESTING IN DIFFERENT GROUPS OF CAD PATIENTS

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Exercise testing remains a remarkably durable and versatile tool that provides valuable diagnostic and prognostic information regarding patients with cardiovascular and pulmonary disease.

BUT...

We noticed there is a great number of

1. Significant stenosis found on coronaryography that had no significant changes on ergometry
2. Positive ergometries with no significant stenosis found on coronaryography
CASE No. 1.

- Patient M.V., 57 years old male, local functionery
- Arterial hypertension, hyperlipidaemia, obesity, smoker (60 cig/day)
- One year ago had typical chest pain during physical activity and at cold, in progression in last two weeks
- Ergometry: 175 Watts, 7,0 METs, 101% of theoretical maximum for age/gender, max. BP 220/120 mmHg
- No angina
- No significant changes of the ST segment in EKG
Coronarography:

Result: CABGx4 (D1 cum RIMA, R1 jump OM1 cum LIMA, PD cum VSM)
CASE No 2: IS CORONAROGRAPHY ALWAYS GOLDEN STANDARD?

- Patient P.V., 45 year old male, businesman
- Arterial hypertension, hyperlipidaemia, obesity, smoker (40 cig/day), positive family history
- August 2010 - chest pain consistent with angina pectoris occurred, positive ergometry test at 125W, 6.0 METs
- Coronarography 27.08.2010.: no significant patomorphological changes on coronary arteries
- 08.09.2010. Significant ST depression on 24-hours ECG monitoring correlating with presence of chest pain
- Highly significant stenosis of proximal LAD
- 21.09.2010. CABG (LAD cum LIMA)
- 11/2010., 05/2011 ET 9.1 and 8.1 MET, negative (V3 to V6 shown)
AIM:

To determine factors that affect sensitivity, specificity and positive predictive value of exercise testing in patients with suspected coronary artery disease (CAD).
We compared data from symptoms limited cycle-ergometry testing and coronarography in 901 consecutive pts. with presumed CAD. All patients underwent both procedures. Horizontal or down-sloping depression of ST segment equal or greater than 1 mm (1 mV) was considered as positive ergometry test result and 75% or greater coronary artery diameter stenosis on coronarography was considered significant.
PATIENT CHARACTERISTICS

- Average age was 59±10 years, 77% were male.
- 347 (38%) had previous myocardial infarction, 474 (53%) had previous PCI, 38 (4%) had CABG and 27 (3%) had both, PCI and CABG
- 596 (66%) had arterial hypertension, 150 (16%) had diabetes mellitus, 471 (52%) had dyslipidaemia, average BMI was 28.6 kg/m²
- They achieved average of 7.2 METs and 92% of theoretical maximal oxygen consumption were achieved.
- 59% had single vessel disease on coronaryography

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>≤ 24.9</th>
<th>25-29.9</th>
<th>30-34.9</th>
<th>≥35</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>132 (15)</td>
<td>466 (52)</td>
<td>264 (29)</td>
<td>39 (4)</td>
</tr>
</tbody>
</table>
Results: sensitivity, specificity and positive predictive value of exercise testing (I)

<table>
<thead>
<tr>
<th>GROUP</th>
<th>N</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>overall</td>
<td>901</td>
<td>43</td>
<td>86</td>
<td>71</td>
</tr>
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</table>

Depending on the gender:

<table>
<thead>
<tr>
<th>GROUP</th>
<th>N</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>694</td>
<td>44</td>
<td>85</td>
<td>72</td>
</tr>
<tr>
<td>female</td>
<td>207</td>
<td>39</td>
<td>89</td>
<td>67</td>
</tr>
</tbody>
</table>
Results: sensitivity, specificity and positive predictive value of exercise testing (II)

Depending on the prior MI or intervention:

<table>
<thead>
<tr>
<th>GROUP</th>
<th>N</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>no prior MI</td>
<td>554</td>
<td>48</td>
<td>85</td>
<td>67</td>
</tr>
<tr>
<td>with prior MI</td>
<td>347</td>
<td>38</td>
<td>88</td>
<td>79</td>
</tr>
<tr>
<td>no intervention</td>
<td>362</td>
<td>45</td>
<td>86</td>
<td>65</td>
</tr>
<tr>
<td>after PCI / CABG</td>
<td>539</td>
<td>41</td>
<td>87</td>
<td>80</td>
</tr>
</tbody>
</table>

Depending on the symptoms during test:

<table>
<thead>
<tr>
<th>GROUP</th>
<th>N</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>angina during exercise</td>
<td>189</td>
<td>65</td>
<td>71</td>
<td>78</td>
</tr>
<tr>
<td>no angina pectoris</td>
<td>712</td>
<td>34</td>
<td>88</td>
<td>66</td>
</tr>
</tbody>
</table>
Depending on the risk factors present:

<table>
<thead>
<tr>
<th>GROUP</th>
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<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>arterial hypertension</td>
<td>596</td>
<td>46</td>
<td>85</td>
<td>74</td>
</tr>
<tr>
<td>no hypertension</td>
<td>305</td>
<td>35</td>
<td>89</td>
<td>63</td>
</tr>
<tr>
<td>dyslipidaemia</td>
<td>471</td>
<td>45</td>
<td>86</td>
<td>77</td>
</tr>
<tr>
<td>no dyslipidaemia</td>
<td>430</td>
<td>41</td>
<td>87</td>
<td>63</td>
</tr>
<tr>
<td>BMI &lt; 30 kg/m²</td>
<td>596</td>
<td>49</td>
<td>84</td>
<td>71</td>
</tr>
<tr>
<td>BMI ≥ 30 kg/m²</td>
<td>305</td>
<td>30</td>
<td>91</td>
<td>72</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>150</td>
<td>46</td>
<td>82</td>
<td>78</td>
</tr>
<tr>
<td>no diabetes mellitus</td>
<td>751</td>
<td>42</td>
<td>87</td>
<td>80</td>
</tr>
</tbody>
</table>
451 pts. (50%) had at least one vessel with significant stenosis on coronarography – 262 had one, 133 had 2 and 56 pts. had 3 or more stenotic vessels.

With one stenotic vessel 61% ergometry tests were false negative, with 2 vessels 53% and with 3 or more 44%.
340 pts. had PCI (304) or CABG (25) or both (11) and no significant stenosis on recoronarography.

Only 1 (4%) patient after CABG had positive ergometry and negative coronaryography finding.

2 (18%) patients that had both, PCI and CABG, had positive ergometry and no significant stenosis on coronaryography.

After PCI 45 (15%) patients had positive ergometry and no significant stenosis on coronaryography.

50 (15%) of these 340 patients had angina during or after exercise testing, 14 (28%) of them had positive ergometry.
Sensitivity of ergometric testing is relatively low when using only criteria of ST denivelation although its specificity is around 90% and PPV around 70%.

Other variables should be included in interpretation of the results.

Angina during testing significantly raised sensitivity but lowered specificity.

More than half of the pts. with one or two stenotic vessels have negative ergometry test.

Female sex, obesity, prior MI and lack of symptoms during testing are associated with lower sensitivity.

Ergometry testing primary detects signs of cardiac ischemia, coronarography shows coronary artery disease.
I) 24,045 patients who underwent coronaryography and ETT, mean sensitivity of 68% (range 23-100%) and mean specificity of 77% (range 17-100%)

II) patients with a previous MI excluded, 11,691 patients involved, mean sensitivity of 67% and mean specificity of 72%

III) three studies with patients that undergo both procedures, sensitivity and specificity of 1 mm of horizontal or downsloping ST depression for diagnosis of CAD were 50% and 90%, respectively.

Only significant ST depression was considered

I) overall sensitivity and specificity of exercise stress testing is 70% and 80% respectively.

II) in women the sensitivity and specificity are 72% and 75% respectively;

III) in asymptomatic subjects the sensitivity and specificity are 50% and 85% respectively.

IV) after anterior infarction, the sensitivity and specificity are 58 and 85% respectively

V) after inferior infarction, 85 and 84% respectively.

Review of the literature:

- **FALSE POSITIVE STRESS TEST... OR FALSE NEGATIVE REST ANGIOGRAMS?** Gaibazzi N, J AM Coll Cardiol 2009 27;54(18)e9

- **ANGINA PECTORIS WITHOUT CORONARY STENOSIS**
  
  Endothelial dysfunction, abnormalities of the smooth muscle cells in the media as well as genetic predisposition or specific immunological abnormalities are discussed as underlying reasons. Intracoronary provocative testing (such as the acetylcholine-test) may help to diagnose.
  

- **ROLE OF CORONARY SPASM FOR A POSITIVE NONINVASIVE STRESS TEST RESULT IN ANGINA PECTORIS PATIENTS WITHOUT HEMODINAMICALLY SIGNIFICANT CORONARY ARTERY DISEASE.**

  Intracoronary ergonovine testing induced coronary spasm in over 50% of patients who had suspected ischemic chest pain, a positive noninvasive stress test, and no hemodynamically significant CAD.


- **PSEUDOISCHEMIC ST-segment DUE TO ATRIAL REPOLARIZATION DURING EXERCISE TEST**

  Atrial repolarization wave ... is opposite in direction to P wave, may have a magnitude of 100 to 200 microV and may extent into the ST segment A role of atrial repolarization in ST-segment depression was found in 5.5% of 144 consecutive and non-selected individuals evaluated with exercise testing.

  Slavich G, G Ital Cardiol, 2006;7(10):670-4
Improving accuracy of exercise testing

- **ST–Heart Rate Adjustment**: maximal slope of the ST segment relative to heart rate is derived either manually or by computer.
- **ST/HR index**: it divides the difference between ST depression at peak exercise by the exercise-induced increase in heart rate.
- **QRS score** improves diagnostic ability of treadmill exercise testing in woman, Michaelides AP, Coron Artery Dis 2007;18(4):313-8
- Is it possible to increase the diagnostic value of exercise electrocardiography by **post-exercise B-type natriuretic peptide levels**?, Yildnir A, Acta Cardiol, 2007;62(1):39-45
Prognostic value

- One of the strongest and most consistent prognostic markers identified in exercise testing is **maximum exercise capacity**. (can be expressed as maximal exercise duration, maximal metabolic equivalent (MET) level achieved, maximum workload achieved, or maximum heart rate and heart rate–blood pressure product)

- A second group of prognostic markers relates to **exercise-induced ischemia** (includes exercise-induced ST deviation - elevation or depression and exercise-induced angina)

- **HEART-RATE RECOVERY IMMEDIATELY AFTER EXERCISE AS A PREDICTOR OF MORTALITY** delayed decrease in the heart rate during the first minute after graded exercise, which may be a reflection of decreased vagal activity, is a powerful predictor of overall mortality, independent of workload, the presence or absence of myocardial perfusion defects, and changes in heart rate during exercise.
  

- **Duke treadmill score** incorporates both groups of prognostic markers
THANK YOU FOR YOUR ATTENTION