PREDICTIVE VALUE OF A POSITIVE EXERCISE STRESS TESTING AND CORRELATIONS WITH CARDIOVASCULAR RISK FACTORS

O. Mitu¹, M. Roca², Maria Magdalena Leon², F. Mitu²
University of Medicine and Pharmacy “Grigore T. Popa” – Iași
Faculty of Medicine
1. Ph.D. Student
2. Department of Internal Medicine I

PREDICTIVE VALUE OF A POSITIVE EXERCISE STRESS TESTING AND CORRELATIONS WITH CARDIOVASCULAR RISK FACTORS (Abstract): Electrocardiogram exercise stress test (EST) is a widespread technique in assessment of coronary artery disease, stratifying cardiovascular risk and prognosis. **Aim:** Evaluation of the impact of cardiovascular risk factors upon the results of EST. **Methods:** The 2-year retrospective study included 294 patients referred to an EST. All patients were assessed according to: presence of typical angina chest pain at admission, medical history of angina or myocardial infarction, resting electrocardiogram, global ejection fraction at echocardiographic exam and traditional cardiovascular risk factors. We compared the results between two groups: positive and negative EST. **Results:** The patients were age- and sex-matched. 160 patients (54.42%) had a positive EST. Positive EST was associated with typical angina chest pain at admission (88.12% vs. 76.11%, p=0.008), coronary artery disease history (61.87% vs. 41.04%, p=0.0003), resting ECG abnormalities (49.37% vs. 36.56%, p=0.026), arterial hypertension (85.62% vs. 74.62%, p=0.019). Ejection fraction was higher in the negative EST group (63.34±8.57% vs. 61.18±11.34%, p=0.035). Type 2 diabetes mellitus, smoking, obesity, dyslipidemia and inflammatory syndrome did not significantly influence the results of the EST. **Conclusions:** Typical angina, medical history of coronary artery disease, arterial hypertension, and reduced ejection fraction are strong predictors for a positive exercise stress test. **Keywords:** CARDIOVASCULAR RISK FACTORS, EXERCISE STRESS TESTING, PREDICTIVE VALUE.

Electrocardiogram exercise stress testing (EST) is an appropriate tool in diagnosis of coronary artery disease (CAD) (1). Even if the new European Society of Cardiology (ESC) guidelines recommend the use of stress imaging tests when available, EST still remains a useful option taking into account its widespread availability and easily interpretation (2). EST provides diagnostic and prognostic information like exercise capacity, chronotropic response to exercise, heart rate (HR) recovery, blood pressure (BP) response to exercise and for guiding cardiac rehabilitation (3). It offers quantitative and qualitative results, regarding chest pain (Kattus scale), perceived patient exertion (Borg scale), work-load (W and METs), maximum HR achieved and BP response, and electrocardiographic alterations. EST has an excellent safety profile, the risk being further reduced by a personalized careful medical history and clinical examination in order to define possible risks and contraindications (4). However, there are still de-
bates concerning categories of subjects that may benefit more from an EST and more studies emphasize on the limited clinical value of EST in asymptomatic adults (5).

CAD is related to the presence of risk factors. This led to developing total risk assessment charts, like the Framingham risk chart of total cardiovascular disease (CVD) and the SCORE risk chart of CVD death (6). Male sex and increasing age are unchangeable cardiovascular risk factors, very important determinants in clinical practice to stratify risk. Smoking affects 20% of the people worldwide and is responsible for one third of serious disease outcomes, mostly CVD, even in young adults and after an exposure of only a few years (7). Multiple studies showed that arterial hypertension causes endothelial injury which finally leads to cardiovascular events (8). Hypercholesterolemia is one of the most studied CV risk factors, predicting mortality, independently of age, both in subjects with and without preexistent CVD (9). Type 2 diabetes mellitus (DM) and metabolic syndrome are other conditions that favor the developing of coronary atherosclerosis (10). CAD is directly associated with obesity (body mass index > 30 kg/m²) but particularly with central obesity (waist circumference or waist-hip ratio) (11). Even if the cardio protective effects and health benefits of physical activity are irrefutable, increasing sedentary habits affect the quality of life and are correlated with a greater amount of chronic diseases, especially CVD (12). High resting heart rate has a worse prognostic in patients with or without CAD (13). Other cardiovascular risk factors, such as a positive family history, significant depression or reduced left ventricular ejection fraction influence the prognosis of CVD by accelerating the atherosclerotic processes, with worse outcomes in these patients (2).

However, very few studies appreciated comprehensively the influence of different traditional risk upon the EST. The aim of the study was to assess the impact of cardiovascular risk factors upon the positive EST results in patients referred for exercise testing.

**MATERIAL AND METHODS**

The current retrospective study included 294 patients, hospitalized over a two-year period (01.01.2011–31.12.2012) in the Cardiovascular Rehabilitation Clinic of the Rehabilitation Hospital at Iași, Romania, in whom an electrocardiogram EST was performed. We included patients with and without known CAD who were able to exercise and had no contraindications to performing the EST.

The patients were assessed according to: gender, age, rural or urban environment, obesity – body mass index (BMI) over 30 kg/m², smoking status, typical angina chest pain at admission, medical history of either angina or myocardial infarction, previous documented diagnostic or newly diagnosed arterial hypertension or type 2 DM. Dyslipidemia was defined, according to the ESC guidelines, as either total cholesterol over 190 mg/dl (4.9 mmol/L) or LDL-cholesterol over 115 mg/dl (3 mmol/L) or use of statin treatment for at least 6 months (6). According to the local laboratory, the inflammatory syndrome was present if the erythrocyte sedimentation rate was above 20 mm/1h or fibrinogen above 350 mg/dl or C-reactive protein (CRP) above 1 mg/dl. All patients performed a resting ecg and a transthoracic echocardiogram (Esaote MyLab50 ecocardiograph device) before the EST.

The EST was performed at the cycloergometer according to a standard protocol, starting with a power output of 25 W/min,
Predictive value of a positive exercise stress testing and correlations with cardiovascular risk factors

followed by an increment of 25 W every three minutes until endpoints were reached. We analyzed the maximal HR (according to the formula: \(220 - \text{patient's age}\)) and BP, the Borg scale, work-load in Watts and METs, and the reasons for ending the EST. We considered a cut-off value for the submaximal exercise of 85% of age-predicted maximum HR. The EST was considered positive in the following situations: moderate to severe angina (≥ 3/4 on Kattus scale), severe exertional dyspnea, ST depression 80 ms after the J point more than 1 mm in three consecutive beats and in leads without diagnostic Q waves, pseudonormalization of T waves. The EST was terminated if systolic BP reached 240 mmHg or dropped more than 10 mmHg.

Statistical analysis was performed with SPSS 11.0 software. The mean values, standard deviations, frequencies were calculated. The significant differences were assessed by using the “t” Student test for two mean values and the “chi” square test for two frequencies, considering a “p” value < 0.05 statistically significant.

RESULTS

Mean age of patients was 55.75 ± 7.28 years (median 56 years); 51.7% were men. 294 ESTs were performed and 160 (54.42%) were positive, having at least one of the previous mentioned criteria for a positive EST.

In the positive EST (EST+) group, a submaximal HR was achieved in 59 patients (36.87%) while in the negative EST (EST-) group only 34 patients (25.37%) performed more than 85% of the maximal calculated HR (p=0.5). The two groups were matched for mean age, sex, and rural/urban origin (tab. I).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EST+ Group</th>
<th>EST- Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>55.87 ± 6.50</td>
<td>55.61 ± 8.14</td>
</tr>
<tr>
<td>Male gender (no, %)</td>
<td>76 (47.5%)</td>
<td>76 (56.71%)</td>
</tr>
<tr>
<td>Urban origin (no, %)</td>
<td>76 (47.5%)</td>
<td>55 (41.04%)</td>
</tr>
</tbody>
</table>

As to the cardiovascular risk factors evaluated upon admission, we found statistically significant differences between the two groups. Typical angina chest pain was found in 88.12% of EST+ group compared with 76.11% in the EST- group (p=0.008). Personal medical history of angina or myocardial infarction was present in only 41.04% in the EST- group as to 61.87% in the EST+ group (p=0.0003). Arterial hypertension had a higher prevalence in the EST+ group (85.62% vs. 74.62%, p=0.01), as well as a lower ejection fraction in the EST+ group (61.18 ± 11.34 % vs. 63.34 ± 8.57 %, p=0.03). Resting ECG abnormalities (e.g. negative T waves, low ST segment depression, premature supraventricular or ventricular beats) were associated with a higher probability for a positive EST (49.37%) in the EST+ than in the EST- group (36.56%), p=0.02.

A positive EST was not significantly correlated with the presence of type 2 DM (p=0.12), with smoker status or with obesity (p=0.37). Patients with cardiovascular risk factors such as dyslipidemia or increased inflammatory markers were not prone for having a positive EST (tab. II).
TABLE II
Cardiovascular risk factors in the EST study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EST+ Group</th>
<th>EST- Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina chest pain at admission (%)</td>
<td>88.12</td>
<td>76.11</td>
<td>0.008</td>
</tr>
<tr>
<td>Medical history of angina or myocardial infarction (%)</td>
<td>61.87</td>
<td>41.04</td>
<td>0.0003</td>
</tr>
<tr>
<td>Rest ECG abnormalities (%)</td>
<td>49.37</td>
<td>36.56</td>
<td>0.026</td>
</tr>
<tr>
<td>Arterial hypertension (%)</td>
<td>85.62</td>
<td>74.62</td>
<td>0.019</td>
</tr>
<tr>
<td>Type 2 DM (%)</td>
<td>29.37</td>
<td>21.64</td>
<td>NS</td>
</tr>
<tr>
<td>BMI &gt; 30 kg/m² (%)</td>
<td>50</td>
<td>44.77</td>
<td>NS</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>47.5</td>
<td>47.01</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>66.25</td>
<td>61.94</td>
<td>NS</td>
</tr>
<tr>
<td>Inflammatory syndrome (%)</td>
<td>16.87</td>
<td>17.16</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>61.18 ± 11.34</td>
<td>63.34 ± 8.57</td>
<td>0.035</td>
</tr>
</tbody>
</table>

The ECG stress test parameters were quite similar in the two groups. Maximum achieved HR was a bit lower in the EST- group (127.68 ± 19.51 / min) than in the EST+ group (129.85 ± 19.23 / min) but without statistical significance. Workload measured in METS showed no marked differences (5.65 ± 1.43 in EST+, 5.76 ± 1.60 in EST-) the same being true for the patient perceived exertion measured on Borg scale (14.27 ± 2.87 in EST+, 14.20 ± 2.67 in EST-).

Fig. 1. Reasons for EST termination in the two groups

With regard to the reasons for terminating the EST, most patients in the EST- discontinued the test due to muscle fatigue (69.4%), severe arterial hypertensive re-
Predictive value of a positive exercise stress testing and correlations with cardiovascular risk factors

sponse (29.85%) or dyspnea (10.44%). In the EST+ group, most subjects presented moderate-severe angina (68.75%), ST segment depression more than 1 mm (66.87%), and less patients stopped because of muscle fatigue (27.5%) or high BP values (23.12%) (fig.1). Exercise-induced premature ventricular beats were present in about 30% of the patients in both groups.

DISCUSSION

According to the latest guidelines on the management of stable coronary artery disease, EST has a sensitivity of 45-50% and a specificity of 85-90% in detecting CAD, being especially indicated in patients with intermediate pre-test probability and left ventricular ejection fraction higher than 50% (2). However, if stress imaging testing is not available, ECG EST remains the first option in detecting CAD.

According to our study, 82.65% of the patients referred for an EST presented typical angina chest pain at admission, of which only 58% had a positive EST. This is in agreement with literature findings, EST being in about 50% non-conclusive with high false positive test results (14). The logical association between a positive EST and the presence of a medical history of angina or myocardial infarction is probably overrated in our study (64.28%), in comparison with 30-35% in other studies that made the same correlations (15). This probably due to an overestimation of angina in patients presented with symptoms of chest pain.

Resting ECG abnormalities were seen in half of patients with positive EST, being a good marker for predicting a positive EST. In patients with known CAD, ST-segment abnormalities at rest are associated with a positive EST in more than 2/3 of cases (16).

Arterial hypertension is a strong predictor for CAD as well as for positive EST and is one of the major targets for treatment in both primary and secondary prevention (17).

As for type 2 DM and dyslipidemia, most patients having these risk factors associated a positive EST but without significant differences between groups. This may be due to the insufficient number of patients included in the study or to the high prevalence of these risk factors in patients with suspicious CAD (18).

Smoking and obesity also correlate with higher probabilities of CAD. In our study, they did not have a high predictive value for positive EST but it is well known that they are very important cardiovascular risk factors and could be integrated in risk scores in order to reach at least 80% negative predictive value for EST (19).

In our research, a high ejection fraction was associated with lower probability of positive EST. Our results are similar with other studies which state that patients with normal ejection fraction, without diabetes and good exercise capacity are unlikely to have a positive test result (20).

CONCLUSIONS

According to our research, typical angina chest pain, medical history of angina or myocardial infarction, resting ECG abnormalities, arterial hypertension and a lower ejection fraction are strong predictors for a positive EST.

Other important cardiovascular risk factors, such as type 2 DM, smoking, BMI over 30 kg/m², dyslipidemia or increased inflammatory markers, were not correlated with a positive EST and have a less predictive value.
REFERENCES