Frequency and characteristics of myocardial ischemia recorded during stress echocardiography in patients with high coronary risk

Učestalost i karakteristike miokardne ischemije tokom ehokardiografskog stres testa kod asimptomatskih osoba sa visokim koronarnim rizikom

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Abstract

Background/Aim. Ischemic heart disease is the major cause of morbidity and mortality in the world as well as in our country. Ischemic heart disease has the multifactorial origin and the presence of several risk factors increases the risk of myocardial ischemia. The aim of the study was to evaluate the frequency and characteristics of myocardial ischemia in asymptomatic subjects with two or more risk factors for coronary artery disease during stress echocardiography. Methods. In 240 high risk asymptomatic subjects (an absolute risk of fatal cardiovascular disease of more than 5%, according to the Systemic Coronary Risk Evaluation Chart), the exercise stress echocardiography test was performed. The criterion for myocardial ischemia was the appearance of transient segmental wall motion abnormality (WMA). The wall motion score index was calculated before and after the exercise stress echocardiography. Results. During exercise stress echocardiography, in 36 (15%) subjects WMA occurred. Out of 36 subjects with myocardial ischemia, in 10 (27.8%) subjects WMA and ST segment depression were accompanied with the first occurrence of chest pain (the subgroup with symptomatic myocardial ischemia), in 20 (55.6%) subjects WMA and ST segment depression were detected and in 6 (16.6%) subjects only WMA occurred (the subgroup with silent myocardial ischemia). There were no significant differences between the subgroups with symptomatic and silent myocardial ischemia with regard to exercise tolerance, heart rate at the onset of WMA, and time to the onset of WMA, but the wall motion score index was significantly higher in the subjects with symptomatic myocardial ischemia (p < 0.01). In all the individuals with symptomatic myocardial ischemia, significant stenosis of the coronary arteries was found by coronary angiography. Out of 26 subjects with asymptomatic myocardial ischemia, coronary angiography was performed in 18 and significant stenosis of the coronary arteries was diagnosed in all of them. The number and grade of coronary stenosis in subjects with symptomatic and silent myocardial ischemia were similar. Conclusion. The obtained results presented the incidence of myocardial ischemia in 15% of asymptomatic subjects with high coronary risk during stress echocardiography. Silent myocardial ischemia was markedly more frequent than symptomatic one, but in the subjects with symptomatic ischemia, the wall motion score index was significantly higher.

Key words: myocardial ischemia; echocardiography, stress; risk factors.

Apstrakt

Uvod/Cilj. Ishemijska bolest srca uzrokovana koronarnom aterosklerozom vodeći je uzrok smrti u svetu i kod nas. Mno- gobrojni epidemiološki studijevi potvrdile su da je koronarna aterosklerozna multifaktorijskog nastanka. Udruženost faktora rizika povećava verovatnoću pojava ishemijske bolesti srca. Otkrivanje miokardne ischemije pre njene kliničke manifesta-cije od velikog je značaja za prevenciju kardiovaskularnih do- gadaja. Cilj rada bio je određivanje učestalosti i procena kara- kteristika miokardne ischemije kod asimptomatskih osoba sa dva ili više faktora rizika od ishemijske bolesti srca tokom ehokardiografskog stres testa. Metode. Kod 240 asimpto- matskih osoba sa visokim rizikom (veći od 5% apsolutnog ri- zika od fatalnog kardiovaskularnog oboljenja, prema kriteri- jumima za određivanje ukupnog koronarnog rizika), urađen je ehokardiografski stres test. Kriterijum za miokardnu ischemiju bila je pojava poremećaja segmentne pokretljivosti (wall motion abnormality – WMA) zida leve komore. Indeks WMA izraču- nat je pre i posle ehokardiografskog stres testa. Rezultati. U stres ehokardiografskom testu kod 36 (15%) osoba registro- vani su WMA zida leve komore. Iz grupe od 36 ispitanika sa miokardnom ischemijom, kod 10 (27.8%) osoba WMA bili su praćeni anginoznim bolom (koji se u testu po prvi put javio) i depresijom ST segmenta na elektrokardiogramu ishemijskog tipa (podgrupa sa simptomatskom miokardnom ischemijom), kod 20 (55,6%) osoba registrovani su WMA i depresija ST segmenta, ali bez pojava anginoznog bola, a kod šest (16,6%) osoba registrovani su samo WMA (podgrupa sa asimptomatskom miokardnom ischemijom). Tolerancija fizič-
Introduction

Ischemic heart disease caused by coronary atherosclerosis is the leading cause of death throughout the world and in our country. Numerous epidemiologic studies have confirmed that coronary atherosclerosis is a multifactorial disease in origin, and identification of all factors associated with increased risk for the coronary artery disease is of utmost importance. A large number of risk factors has been described, some of which are related to lifestyles, others to biochemical or physiologic characteristics (modified risk factors), and some of them are personal characteristics of individuals (non-modified risk factors).

In the assessment of the impact of risk factors on occurrence of ischemic heart disease, multiple risk factors phenomenon play the important role. The risk of ischemic heart disease is increased in the presence of multiple risk factors. Moreover, also important are the intensity of risk factors (blood pressure value, glycemia level, number of cigarettes smoked) and duration of exposure to risk factors. The principal aim of both the doctors and their patients is to prevent atherosclerosis or to delay the disease until later in life by modification of variable risk factors.

Myocardial infarction and sudden cardiac death are commonly the first clinical manifestations of ischemic heart disease, and in order to reduce mortality, it should be detected and treated early in its course. Exercise electrocardiography is considered to be the first method in detecting myocardial ischemia in individuals with a suspected ischemic heart disease. However, electrocardiography during exercise stress testing has relatively low sensitivity and specificity, so that nowadays radionuclide or echocardiography methods have been increasingly used in detecting myocardial ischemia.

The aim of the paper was to establish the frequency and assess the characteristics of myocardial ischemia in asymptomatic subjects with two or more risk factors for ischemic heart disease during stress echocardiography test (SET).

Methods

The study enrolled 240 subjects (160 men and 80 women, mean age 53.5 ± 6.8 years). The inclusion criteria were as follows: age from 40 to 65 years, absence of anginal pain or its equivalent, absence of contraindications for exercise test, without diagnosis of ischemic heart disease, presence of two or more risk factors for coronary atherosclerosis lasting at least five years (arterial hypertension: blood pressure ≥ 140/90 mmHg, active smoking, type 2 diabetes mellitus, and hypercholesterolemia: total cholesterol ≥ 5 mmol/L). All of the examined subjects had high values of risk (more than 5% of absolute risk for a fatal cardiovascular event in a period of ten years, according to the Systemic Coronary Risk Evaluation Criteria – SCORE). The study did not enroll the patients with symptomatic or asymptomatic left ventricular dysfunction, complex and frequent ventricular arrhythmias, atrial fibrillation, conduction abnormalities, ST segment changes, T wave changes suspect of myocardial ischemia, and subjects with technically poor two-dimensional echocardiographic image.

In all the examinees SET was performed on bicycle ergometer in a sitting position, with the initial workload of 25 W and progressive increases of 25 W every four minutes. Maximal exercise test was performed, and test was stopped earlier in cases of ischemic chest pain of increasing intensity, left ventricular wall motion abnormality (WMA), complex ventricular arrhythmias, high blood pressure values (≥ 220/120 mmHg). Before and during the exercise and in the period of rest, 12-lead electrocardiography and 2D echocardiography (Acuson – Sequoia C256, Mountain View, CA USA, Harmonic mode) were continually recorded. Heart rate and blood pressure values were measured before SET, at the end of each workload level, and in the period of rest. For the purpose of echocardiographic analysis of segmental motion, the left ventricle was divided into 11 segments, according to the model by Edwards et al., modified so that apex represented one segment. Segmental wall motion was analyzed and numerically scored as follows: 1 = normo/hyperkinesia; 2 = hypokinesia; 3 = akinesia; 4 = dyskinesia. Segmental wall motion score index (WMSI) was obtained by dividing the sum of scores with the number of segments of the left ventricle. WMSI was calculated before and at the end of SET. The criterion for myocardial ischemia was the onset of left ventricle segmental WMA.

The results were presented as means with standard deviations. The student’s t-test with a statistically significant cutoff of $p < 0.05$ was used to assess the statistical significance of parameters observed.
Results

Most common risk factors for coronary disease were smoking and arterial hypertension (Table 1).

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Patients</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Male</td>
<td>160</td>
</tr>
<tr>
<td>Smoking</td>
<td>186</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>172</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>98</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>74</td>
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<tr>
<td>Two risk factors</td>
<td>43</td>
</tr>
<tr>
<td>Three risk factors</td>
<td>145</td>
</tr>
<tr>
<td>Four risk factors</td>
<td>52</td>
</tr>
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</table>

Left ventricular wall motion analysis before SET demonstrated normal segmental motion in all our subjects. During the test, WMA were detected in 36 (15%) examinees, while in 204 subjects there were no new WMA during SET. In the group without WMA, there was no anginal pain or its equivalent, but in 15 (6%) subjects ST segment depression was recorded on electrocardiogram during exercise.

In the group of 36 patients with myocardial ischemia on SET, WMA were associated with anginal pain (occurring for the first time during the exercise stress test) and ischemic type of ST segment depression on ECG in 10 (27.8%) patients (the subgroup of those with symptomatic myocardial ischemia). WMA and ST segment depression, without anginal pain, were detected in 20 (55.6%), and only WMA was detected in 6 (16.6%) patients (these 26 individuals comprised the group with asymptomatic myocardial ischemia), (Table 2).

Asymptomatic myocardial ischemia was significantly more frequent in the diabetic patients (Figure 1).

The level of physical workload and SET duration, time to WMA, and value of heart rate at the onset of WMA were not significantly different between those with symptomatic and those with asymptomatic myocardial ischemia (Table 3).

The value of ST segment depression in our stress test (mean value of ST segment depression in all ECG leads) did not differ significantly between the patients with symptomatic and those with asymptomatic myocardial ischemia (Table 3).

![Figure 1](image1.png)

**Fig. 1 – Frequency of symptomatic and asymptomatic myocardial ischemia (MI) in the patients with diabetes mellitus type 2**

![Figure 2](image2.png)

**Fig. 2 – Wall motion score index (WMSI) in the patients with symptomatic and asymptomatic myocardial ischemia (MI)**

### Table 1

<table>
<thead>
<tr>
<th>Frequency of risk factors in the examined subjects</th>
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<tbody>
<tr>
<td>Risk factors</td>
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<tr>
<td>--------------</td>
</tr>
<tr>
<td>Male</td>
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<tr>
<td>Smoking</td>
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<td>Arterial hypertension</td>
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<td>Hypercholesterolemia</td>
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<tr>
<td>Diabetes mellitus type 2</td>
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<tr>
<td>Two risk factors</td>
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<tr>
<td>Three risk factors</td>
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<tr>
<td>Four risk factors</td>
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</table>

### Table 2

<table>
<thead>
<tr>
<th>Markers of myocardial ischemia during stress echocardiography test</th>
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<tr>
<td>Markers of myocardial ischemia</td>
</tr>
<tr>
<td>WMA+ ST↓ + chest pain</td>
</tr>
<tr>
<td>WMA+ ST↓</td>
</tr>
<tr>
<td>WMA</td>
</tr>
</tbody>
</table>

WMA – wall motion abnormality; ST↓ – ST segment depression

### Table 3

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Symptomatic MI</th>
<th>Asymptomatic MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of physical workload (W)</td>
<td>82 ± 12.6</td>
<td>78 ± 10.8</td>
</tr>
<tr>
<td>Duration of stress (min)</td>
<td>13.9 ± 2.9</td>
<td>12.7 ± 2.7</td>
</tr>
<tr>
<td>HR at onset WMA (beats/min)</td>
<td>124.3 ± 12.8</td>
<td>121.2 ± 13.7</td>
</tr>
<tr>
<td>Time to onset WMA (min)</td>
<td>11.0 ± 3.5</td>
<td>10.4 ± 3.8</td>
</tr>
<tr>
<td>ST segment depression (min)</td>
<td>2.4 ± 0.3</td>
<td>2.5 ± 0.4</td>
</tr>
</tbody>
</table>

HR – heart rate; WMA – wall motion abnormality

In all patients with symptomatic myocardial ischemia, significant coronary artery stenoses were found by coronary angiography. Out of 26 patients with asymptomatic myocardial ischemia, coronary angiography was done in 18 (8 patients did not accept the suggested diagnostic procedure) and in all of them significant stenosis of the coronary arteries was diagnosed. Angiographic finding of stenosis of the coronary arteries matched the registered WMA in SET. The number of involved arteries and degree of coronary artery stenosis was not significantly different between the patients with symptomatic and those with asymptomatic myocardial ischemia.

Discussion

Anginal pain is the most important symptom in the clinical presentation of ischemic heart disease, but it is commonly absent, and its first clinical manifestation can be acute myocardial infarction or a sudden cardiac death. Numerous studies performed in recent decades have shown that asymptomatic myocardial ischemia is very common in coronary patients, with prognostic significance similar to symptomatic ischemia. Early detection of myocardial ischemia is of utmost importance for prevention of adverse cardiac events in patients with ischemic heart disease.

In individuals with high risk of coronary atherosclerosis and without symptoms and/or signs of ischemic heart disease, the procedures should be undertaken to detect coronary disease before it becomes clinically evident. Exercise test is the first method to detect ischemic heart disease in asymptomatic individuals. If the symptoms of coronary disease do not occur during the test and ischemic changes cannot be identified in ECG, the existence of coronary disease can be excluded with a high degree of probability. In such individuals periodic retesting is required, together with modification of risk factors. However, ECG changes identical to those in myocardial ischemia can be sometimes observed in persons without the disease (false positive ECG finding in exercise test). In order to overcome the limitations of ECG in exercise test, and in view of the well-known sequence of events in an ischemic cascade, echocardiographic observation of the left ventricular wall motion has been increasingly used in recent years to detect myocardial ischemia. At the Institute for Treatment and Rehabilitation in Niška Banja stress echocardiography has been done since 1990 in order to detect myocardial ischemia, to monitor the course of ischemic heart disease, or to observe the effects of medication and/or surgical treatment.

In this study, by assessment of segmental wall motion of the left ventricle in completely asymptomatic subjects during SET, WMA was detected in 36 (15%) patients. Coronary angiography, done in 28 out of 36 patients with WMA during SET, revealed significant stenoses of coronary arteries. In 15 (6%) individuals ST segment depression was detected in the absence of left ventricular WMA (false positive ECG finding), and in six persons there were abnormalities of segmental motion in the absence of ECG signs of ischemia (false negative ECG finding). This finding clearly confirmed the advantage of SET over electrocardiography during exercise testing to detect myocardial ischemia.

Symptomatic myocardial ischemia, detected for the first time in the subgroup of our patients with myocardial ischemia is significantly rarer compared to asymptomatic disease, which can be explained by the selection of tested subjects. The absence of coronary disease symptoms during everyday activities in these persons can be explained by a lower level of workload than in exercise tests.

Asymptomatic myocardial ischemia is a common type of ischemia in coronary patients. It can be observed in completely asymptomatic individuals (type I), those with survived myocardial infarction (type II), and patients with episodes of symptomatic or asymptomatic myocardial ischemia (type III). Asymptomatic myocardial ischemia has a prognostic significance in coronary patients similar to symptomatic ischemia. The frequency of asymptomatic myocardial ischemia in asymptomatic population is not known, but its detection is of an utmost importance regarding the prevention of cardiovascular events. Stress echocardiography has been proven to be more sensitive, more specific, and diagnostically more accurate compared to exercise testing detecting myocardial ischemia. However, stress echocardiography screening of the general population is expensive, so that stress echocardiography should be reserved for individuals with higher probability of coronary disease – these are asymptomatic individuals with a high coronary risk. On that account, in order to establish the frequency of myocardial ischemia, we selected the individuals with an absolute risk of over 5% for fatal cardiovascular disease.

The reason why myocardial ischemia is not accompanied by pain in some patients is the question that still awaits a full explanation. Some studies have shown that the episodes of asymptomatic myocardial ischemia are of lower intensity and never reach the “anginal threshold”. There is some evidence of no difference between symptomatic and asymptomatic episodes of myocardial ischemia in the parameters of severity of the disease, including the number of involved coronary arteries and the degree of stenosis of coronary arteries, the magnitude of ST depression in exercise tests, or the degree of reversible thallium defects during exercise.

In our study, the parameters obtained during SET (level and duration of stress, time to WMA, and heart rate at the onset of WMA) did not differ significantly between the persons with symptomatic and those with asymptomatic myocardial ischemia. However, the index of WMA is significantly higher in patients with symptomatic myocardial ischemia, indicating a higher degree of myocardial ischemia.

The diseases accompanied by autonomous neuropathy, such as diabetes, are traditionally regarded as responsible for the manifestation of asymptomatic myocardial ischemia. There are contradictory data on asymptomatic ischemia in diabetic patients. Some studies have confirmed a higher prevalence of asymptomatic ischemia in stress tests or during Holter monitoring in diabetics. Study of Caraccio et al. has shown similar frequencies of symptomatic and asymptomatic ischemia in diabetic and non-diabetic patients.

asymptomatic myocardial ischemia in diabetics. In our pa-
tients, asymptomatic myocardial ischemia was significantly
more common in the individuals with diabetes.

Our study demonstrated that asymptomatic myocardial
ischemia is common in subjects with a high coronary risk.
Although the etiopathogenesis of asymptomatic ischemia has
not been fully elucidated, it can be said with certainty that it
is not a benign ischemia and that it has prognostic effects
similar to symptomatic ischemia. It is therefore necessary to
look for myocardial ischemia in any individual with a higher
number of risk factors for coronary disease.

Conclusion

The results obtained in this study demonstrated a
frequency of myocardial ischemia of 15% in asympto-
matic subjects with two or more risk factors for coronary
atherosclerosis during stress echocardiography. Asympto-
matic myocardial ischemia is more frequent than sym-
tomatic one. Asymptomatic myocardial ischemia is more common in patients with type 2 diabetes.

Exercise tolerance, time to the onset of WMA, and
magnitude of ST segment depression in stress echocardi-
ography did not differ significantly between the patients
with symptomatic and asymptomatic myocardial ischemia,
while the wall motion score index of the left ventric-
ule was significantly higher in patients with symptomatic
myocardial ischemia. The number of involved arteries and
degree of stenosis of coronary arteries were similar in pa-
tients with symptomatic and asymptomatic myocardial is-
chemia.

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