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Adress: Univerzitetski trg 2, 18000 Niš, YU, Tel: +381 18 547-095 Fax: +381 18 547-950
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PREVALENCE, CHARACTERISTICS AND THREE YEARS PROGNOSTIC SIGNIFICANCE OF SILENT MYOCARDIAL ISCHEMIA DURING EARLY EXERCISE TESTING IN PATIENTS AFTER THE FIRST MYOCARDIAL INFARCTION

Stevan N. Ilić, Marina Ž. Deljanin Ilić, Branko K. Lović, Aleksandar Nikolić, Vojislava Mitić, Ivan Tasić, Dragan Djordjević, Dragan Mijalković, Ljubiša Nikolić

Institute of Cardiology, Niška Banja, University of Niš, Yugoslavia
e-mail: stevanil@kalca.junis.ni.ac.yu

Summary. *The aim of this study was to evaluate the frequency, some characteristics and prognostic significance of silent myocardial ischemia during early exercise testing in patients after myocardial infarction.*
In the group of 210 patients within three months after myocardial infarction submaximal or symptom-limited exercise test were performed. Out of 210 patients 88 (42%) had ischemic response on exercise electrocardiogram and 2D exercise echocardiogram. Out of 88 patients with ischemic response on exercise electrocardiogram and echocardiogram 54 (61%) had anginal pain or it's equivalents (symptomatic myocardial ischemia) and 34 (39%) had not ischemic symptoms (silent myocardial ischemia). Diabetes mellitus and arterial hypertension was more frequent in patients with silent than in patients with symptomatic myocardial ischemia. Level of exercise test and heart rate at the onset of both types of myocardial ischemia were not differ significantly. Duration of exercise testing was significantly bigger in patients with silent myocardial ischemia. The average magnitude and duration of ST-segment depression in both groups of pts with myocardial ischemia were similar. Before exercise test wall motion score index (WMSI) was similar in both groups of patients. After exercise stress echocardiography WMSI significantly rised in both groups, but more in patients with symptomatic ischemia, and after exercise test WMSI was significantly bigger in patients with symptomatic ischemia. During three years follow-up there were no significant differences in mortality, reinfarction and coronary artery by-pass surgery rate between patients with symptomatic and silent myocardial ischemia.
This study showed that: silent myocardial ischemia, during early exercise testing was frequent finding in patients after myocardial infarction, especialy in those with diabetes mellitus and arterial hypertension; there were not significant differences in characteristics between silent and symptomatic myocardial ischemia on exercise electrocardiogram; and three years prognostic significance of both types of myocardial ischemia was similar.

Key words: *Silent myocardial ischemia, myocardial infarction, exercise testing, stress echocardiographic test*

Introduction

In recent years it has become clear that, whilst patients with ischemic heart disease may complain of angina pectoris, most will have episodes of myocardial ischemia that are not accompanied by chest pain (1-4). These episodes have been termed "silent myocardial ischemia". Many studies have shown that silent ischemic episodes do not differ from ischemia accompanied by angina in terms of the haemodynamic effects on left ventricular function (5-7). Likewise, radionuklide studies using positron tomography and short-lived isotope, rubidium-81m, have shown that episodes of silent ischemia are associated with alterations in myocardial perfusion (8).

Silent myocardial ischemia is an intriguing pathological phenomenon, which has received increasing attention during the last two decades because of its high prevalence and because its potentially worse prognosis (9,10). Silent myocardial ischemia presents itself in one of the four following ways (11): as silent myocardial infarction; as sudden cardiac death being the first manifestation; as ischemic cardiomyopathy and as transient episodes of painless ischemia detected either by exercise stress testing and/or by ambulatory electrocardiographic monitoring during daily activities (12-14). Transient episodes of silent myocardial ischemia may be found in three types of patients: in persons who are totally asymptomatic (type I), in patients who are

asymptomatic following a myocardial infarction, but still demonstrate active myocardial ischemia (type II); and in patients with angina who are asymptomatic with some episodes of myocardial ischemia, but not others (type III) (15).

Episodes of silent myocardial ischemia are best indentified using 24 hours ambulatory monitoring of the electrocardiogram (during daily activities) and exercise electrocardiogram in laboratory conditions. In last years 2D stress echocardiography is wide used in detection of transient myocardial ischemia in patients with coronary artery disease, in order to avoid false positive findings of exercise electrocardiogram (16,17).

The purpose of this study was to evaluate the frequency, some characteristics and prognostic significance of silent myocardial ischemia recorded on exercise electrocardiogram and echocardiogram in patients after the first myocardial infarction.

Methods

Patients selection: We studied 210 patients within three months after myocardial infarction (Table 1). Patients with following criteria were excluded from the study: unstable angina pectoris; abnormal ST-segment on resting electrocardiogram; congestive heart failure and conduction disturbances.

Table 1. Some clinical characteristics of examined patients population

Number of patients	210	(100%)
Mean age (years)	52.6 ± 8.3	
Male sex	158	(75%)
Anterior myocardial infarction	94	(45%)
Inferior myocardial infarction	116	(55%)
Arterial hypertension	95	(45%)
Diabetes mellitus	52	(25%)

Exercise electrocardiogram: All patients underwent exercise testing in the postabsortive state, after all antianginal drugs had been discontinued for at least 12 hours. Exercise, on bicycle ergometer in the upright position, was begun with work load of 25 watts that was than increased by 25 watts every 4 minutes. Before, during and up to 10 minutes after exercise electrocardiogram was continuously monitored and blood pressure at each stress step were recorded. Criterion for myocardial ischemia was depression of ST-segment more than 0.1 mV relative to resting electrocardiogram.

Echocardiography: In patients with ST segment depression more than 0,1 mV exercise stress echocardiography was additionally performed in order to confirm myocardial ischemia during stress testing. Exercise protocol was equal to the protocol described for exercise electrocardiogram. Echocardiography was performed using a 3.5 MHz transducer in the parasternal long- and short axis and apical four- and two chamber views. For wall motion analysis the left ventricle was divided into 11 segments (16) and wall motion was assessed qualitatively and graded as normal, hypokinetic, akinetic and dyskinetic. A score from 1 (normal) to 4 (dyskinetic) was assigned to each segment under basal condition and at the end of test. Wall motion score index (WMSI) was calculated before and after exercise stress echocardiography by summation of the individual segments scores divided by the number of segments. Criterion for myocardial ischemia was detection of new WMA with or without > 1 mm ST-segment depression relative to resting electrocardiogram.

End points for both tests were: achievement of 85% of age predicted maximal heart rate, symptoms, significant ST-segment shift (more than 2 mm), severe hypertension (blood pressure > 220/120 mm Hg) or significant arrhythmias and detection of a new wall motion abnormality (WMA).

All patients were follow-up three years, during which period subsequent cardiac events (cardiac death, recurrent myocardial infarction and coronary by-pass surgery) were noted.

Results

Prevalence of silent myocardial ischemia: One hundred and eighteen patients (56%) had a normal exercise test (without chest pain and ischemic ST-segment depression). Fifty-four patients (26%) had ST-segment depression and anginal pain or its equivalents during exercise test. All of them had also echocardiographic sign of ischemia (patients with symptomatic myocardial ischemia) and 38 patients had ST-segment depression without ischemic symptoms. Out of 38 patients with asymptomatic ST segment depression 34 patients (patients with silent myocardial ischemia) had and four patients had no ehocardiographic marker of myocardial ischemia - patients with false positive exercise electrocardiogram (Fig. 1).

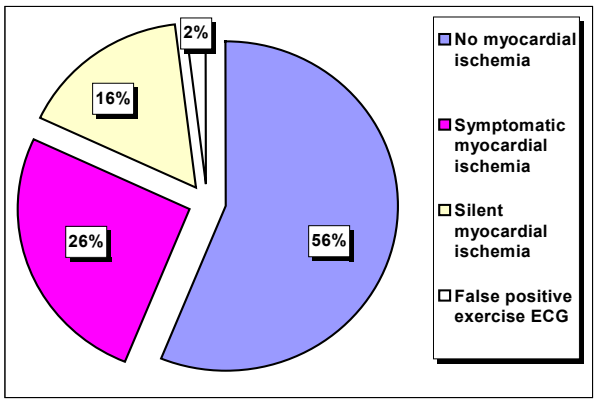

Fig. 1. Frequency of silent myocardial ischemia on exercise tests in population of 210 patients after the first myocardial infarction

Thus, more than one third of patients after myocardial infarction have silent myocardial ischemia on exer-

cise stress test (exercise electrocardiogram and exercise echocardiogram), Fig. 2.

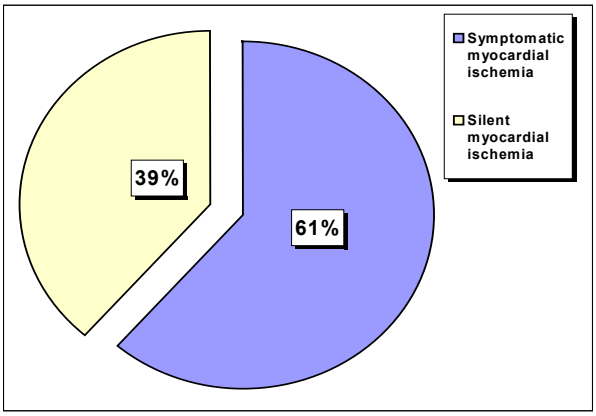

Fig. 2. Frequency of silent myocardial ischemia among 88 patients with ischemic response on exercise tests

Some characteristics of silent myocardial ischemia: There were no differences in age, sex and site of myocardial infarction between groups of patients with silent and symptomatic myocardial ischemia, but there was an excess of arterial hypertension and diabetes mellitus in group of patients with silent myocardial ischemia (Table 2).

Table 2. Pre-test variables grouped according to the type of myocardial ischemia (m.i.) on exercise test

Variable	Silent m.i.	Symptomatic m.i.
Age (years)	51.8 ± 8.1	52.1± 9.2
Male / Female	26 / 8	42 / 12
Arterial hypertension	20 (59%)	22 (41%)
Diabetes mellitus	16 (47%)	7 (13%)
Anterior myocardial infarction	15 (44%)	22 (41%)
Inferior myocardial infarction	19 (56%)	29 (54%)
Time from acute myocardial infarction (months)	1.8 ± 0.7	1.7 ± 0.7

Level of exercise test, heart rate at 0.1 mV ST-segment depression and time to 0.1 mV ST-segment depression, as well as final double product were no significantly different in patients with silent and symptomatic myocardial ischemia. Duration of exercise test was significantly longer in patients with silent myocardial ischemia (Table 3).

Table 3. Exercise test data in patients with silent and symptomatic myocardial ischemia (m.i.)

Exercise data	Silent m.i.	Symptomatic m.i.	P
Level of exercise test (watts)	80.1 ± 24.6	78.8 ± 18.9	NS
Duration of exercise test (min)	13.8 ± 2.4	12.6 ± 2.3	0.05
Heart rate at 0.1 mV ST depression	119.3 ± 12.1	118.2 ± 13.4	NS
Time to 0.1 mV ST depression (min)	9.5 ± 3.5	8.9 ± 3.8	NS
Final double product (HR×SBP/100)	209.8 ±45.6	211.8 ± 42.3	NS

During exercise echocardiography, transient new wall motion abnormalities were detected in all patients with symptomatic ST-segment depression and in 34 out of 38 patients with asymptomatic ST segment depression on exercise electrocardiogram. In patients with symptomatic myocardial ischemia value of WMSI on stress echocardiography was significantly higher compared to the baseline values ($P < 0.005$). In patients with silent myocardial ischemia value of WMSI after stress echocardiography was also significantly higher ($P < 0.05$) compared to the value before test (Fig. 3). Values of WMSI in patients with symptomatic and in patients with asymptomatic myocardial ischemia did not differ significantly before, but after test WMSI was significantly bigger in patients with symptomatic myocardial ischemia (Fig. 3).

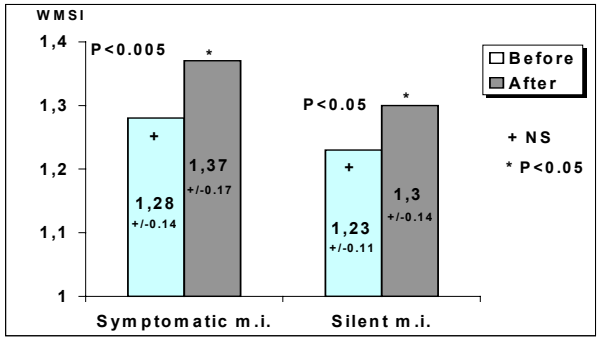

Fig. 3. Value of wall motion score index (WMSI) before and after exercise echocardiography test in patients with symptomatic and in patients with silent myocardial ischemia

Subsequent cardiac events: During three years follow-up period 40 (19%) of 210 patients died. Exercise-induced ST-segment depression had high predictive value for cardiac mortality during the follow-up period: thirty-two out of 88 patients (36%) with ST-segment depression died, compared with only eight (7%) out of 118 patients without ST- segment depression ($P < 0.05$). During three years period 12 (35%) out of 34 patients with silent myocardial ischemia died and 20 (37%) of 54 patients with symptomatic myocardial ischemia died (NS).

Reinfarction was seen in 14% of patients without myocardial ischemia on exercise test, in 38% of patients with silent and in 33% of patients with symptomatic myocardial ischemia. Difference between patients with silent and symptomatic myocardial ischemia was not significant.

Patients with silent myocardial ischemia on exercise test developed angina more frequently (50%) in three years period than those without myocardial ischemia (17%), but not as frequently as patients with symptomatic myocardial ischemia (83%). Coronary artery bypass grafting (CABG) was undertaken more frequently in patients with than in those without myocardial ischemia ($P < 0.05$). Coronary artery bypass grafting was performed more frequently in those with symptomatic myocardial ischemia, but when corrected for the number

of patients in the silent and symptomatic groups who subsequently developed angina the CABG rates were similar (Table 4).

Table 4. Subsequent cardiac events in patients without and with silent and symptomatic myocardial ischemia (m.i.)

Three years events	No m.i.	Silent m.i.	Symptomatic m.i.
Cardiac mortality	8 (7%)	12(35%)	20 (37%)
Reinfarction	16 (14%)	13(38%)	18 (33%)
Developed angina	20 (17%)	17(50%)	45 (83%)
CABG as % of those with angina	70%	65%	67%

Discussion

Silent myocardial ischemia is frequent phenomenon in patients with coronary artery disease during daily life and exersise stress testing (18). Exercise-induced silent myocardial ischemia apears frequently in patients with known coronary artery disease. In our study in patients with previous myocardial infarction, we observed silent myocardial ischemia in more than one third of patients (39%), during both exercise electrocardiogram and exercise stress echocardiogram. Echocardiography is more accurate method for detection of myocardial ischemia during exercise test than exercise electrocardiogram (19,20), especially to avoid false positive exercise electrocardiogram. In our study population there were four patients (2%) with false positive findings for myocardial ischemia on exercise electrocardiogram.

Previous study have reached conflicting conclusions as to whether painless ischemia identified during noninvasive cardiac testing is related to a lesser extent of myocardial ischemia or a different prognosis than ischemia accompanied by angina. Some studies have shown that silent myocardial ischemia is accompanied by haemodynamic changes equal in severity to those observed in patients who experience angina (21,22), but others shown that the degree of hypoperfusion is greater in the presence of symptoms during exercise stress testing in a consecutive cohort of patients with ischemic heart disease (23-25). In our study, patients with silent ischemia and those with exercise angina had comparable level of exercise test and magnitude of ST-segment depression but longer duration of exercise test was recorded in patients with silent myocardial ischemia. After exercise stress echocardiography value of WMSI was greater in patients with symptomatic than in patients with silent myocardial ischemia. Those findings (longer duration of exercise test and smaller wall motion abnormality) indicated that silent ischemia may be less severe than symptomatic myocardial ischemia. In population of diabetic and hypertensive patients silent myocardial ischemia is more frequently (26-29). Likewise, in our diabetic as well as hyperensive patients silent ishemia on exercise test was more frequent than in non-diabetic patients and in patients with normal arterial pressure.

The clinical significance of both symptomatic and silent ischemia lies in the association with future coronary events. The clinical significance of exercise-induced chest pain remains controversial, as reflected by sharply discordant clinical results within the medical literature. Some studies shown that both types of myocardial ischemia (silent and symptomatic) are associated with similar future adverse outcomes (30-33), the other shown that symptomatic ischemia is more severe ischemia with more pronounced haemodynamic abnormalities and with more serious future clinical events (25,34). In our study there was not significant difference in three years mean coronary events (that is, cardiac mortality and myocardial infarction), but subsequent angina pectoris was more frequent in patients with symptomatic myocardial ischemia on exercise test. Coronary artery bypass grafting during three years period was performed more frequently in those with symptomatic than in patients with silent myocardial ischemia, but when corrected for the number of patients in the silent and symptomatic groups who subsequently developed angina the CABG rates were similar.

Thus, silent myocardial ischemia during early exercise testing was frequent finding in patients after the first myocardial infarction, especialy in those with diabetes mellitus and arterial hypertension. There were not significant differences in characteristics between silent and symptomatic myocardial ischemia on exercise electrocardiogram. Wall motion abnormality during exercise test was significantly bigger in patients with symptomatic than in those with silent myocardial ischemia. Three years prognostic significance on mean coronary events (cardiac mortality and reinfarction) of both types of myocardial ischemia was similar.

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UČESTALOST, KARAKTERISTIKE I TROGODIŠNJI PROGNOSTIČKI ZNAČAJ ASIMPTOMATSKE MIOKARDNE ISHEMIJE REGISTROVANE U TESTU FIZIČKIM OPTEREĆENJEM U BOLESNIKA S PREŽIVELIM INFARKTOM MIOKARDA

Stevan N. Ilić, Marina Ž. Deljanin Ilić, Branko K. Lović, Aleksandar Nikolić, Vojislava Mitić, Ivan Tasić, Dragan Djordjević, Dragan Mijalković, Ljubiša Nikolić

Institut za prevenciju, lečenje i rehabilitaciju reumatičkih i kardiovaskularnih bolesti, Niška Banja

Kratak sadržaj: *Cilj ove studije je odredjivanje učestalosti, nekih karakteristika i prognostičkog značaja asimptomatske miokardne ishemije koja je registrovana tokom ranog testa fizičkim opterećenjem u bolesnika s preživelim infarktom miokarda.*

Grupi od 210 bolesnika, unutar tri meseca od akutnog infrakta miokarda uradjen je submaksimalni ili simptomom limitirani test fizičkim opterećenjem. Od 210 bolesnika u 88 (42%) registrovane su ishemijske promene na

elektrokardiogramu i 2D ehokardiogramu u opterećenju. Simptomatska miokardna ishemija (anginozni bol ili ekvivalenti anginoznog bola) nadjena je u 54 od 88 bolensika (61%), dok u 34 (39%) bolesnika miokardna ishemija nije bila praćena ishemijskim simpotomima (asimptomatska miokardna ishemija). Dijabetes i artarijska hipertenzija bili su čeći u bolesnika sa asimptomatskom miokardnom ishemijom. Nivo opterećenja, srčana frekvencija pri pojavi miokardne ishemije, kao i veličina ST segment depresije bili su slični u obe grupe bolesnika sa miokardnom ishemijom. Trajanje opterećenja bilo je značajno duže u bolesnika sa asimptomatskom miokardnom ishemijom. Abnormalnosti pokreta zidova leve komore tokom opterećenja (WMSI) bili su izraženiji u bolesnika sa simptomatskom miokardnom ishemijom. Tokom trogodišnjeg praćenja nije postojala značajna razlika u pojavi velikih srčanih dogadjaja (kardijalnog mortaliteta i ponovnog infrakta miokarda) u bolesnika sa simptomatskom i asimptomatskom miokardnom ishemijom. U bolesnika sa simptomatskom miokardnom ishemijom bila je češća pojava angine pektoris a potreba za hirurškom revaskularizacijom bila je slična, kada se analiziraju podgrupe bolesnika kod kojih se tokom praćenja javila angina pektoris.

Naša studija je pokazala da asimptomatska miokardna ishemija postoji u više od trećine bolesnika sa preživelim infarktom miokarda i miokardnom ishemijom u testu fizičkim opterećenjem, da je češća u bolesnika sa arterijskom hipertenzijom i dijabetesom, da bolesnici sa asimptomatskom miokardnom ishemijom imaju duže trajanje opterećenja i manje abnormalnosti pokreta zidova leve komore u opterećenju i da je trogodišnje prognoza bolesnika sa simptomatskom i asimptomatskom miokardnom ishemijom slična.

Ključne reči: *Asimptomatska miokardna ishemija, angina pektoris, infarkt miokarda, test fizičkim opterećenjem, ehokardiografski stres test*

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