ISSN 1392-9631 ELEKTRONIKA IR ELEKTROTECHNIKA. 2005. Nr. 4(60)

T 115 MEDICINOS TECHNOLOGIJA

Exercise Induced Changes of ST Depression and Its Correlation with QT Dispersion in Myocardial Infarction Patients

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Introduction

The standardized, differentially graded exercise testing is an important method of clinical evaluation of functional capacity in patients and in healthy persons. The biological phenomenon that physical activity is a “conditio sine qua non” for the proper functioning of the human organism is becoming increasingly important for the understanding of cardiovascular diseases and especially for the assessment of appropriate therapies. The exercise test is usually performed (in case of absence of contraindications) to all patients after myocardial infarction (MI) before the discharge [1]. The prognostic value of the exercise test is not sufficiently investigated despite of the high percentage of the persons dying suddenly after MI. The evaluation of depression of ST-segment in the exercise test in predicting the prognosis after MI is not uniform [1, 2, 3]. According to literature and our data, sudden death during 6 months after MI is closely related to the life-threatening arrhythmias, detected in early exercise test after MI. This relation could not be established after MI later [4, 5,]. It is considered the value of the exercise-induced QT dispersion (as a sign of ventricular repolarisation inhomogenity) in predicting ventricular arrhythmias and sudden cardiac death [6]. The data is contradictory in assessing which exercise test parameters are related with survival over 6 months after MI [7]. Some authors regard ST-depression as a borderline parameter and the main attention is paid to the workload, which was obtained during the exercise. This sign is closely related to the survival over 10 as well as 15 years after MI [8]. The aim of our study was to assess the correlation between exercise induced changes of ST-segment depression and QT dispersion in myocardial infarction patients and to evaluate the prognostic capability of these signs.

Patients and Methods

A total of 894 pts with acute MI (aged 50.68 $\pm$ 9.29 yrs; 827/92.5% males and 67/7.5% females) admitted to Kaunas Medical University hospital met the eligibility criteria (cases of absence of contraindications) and were put through early exercise testing.

Cases of noncardiac deaths, patients living outside Kaunas or those subjected to coronary bypass surgery, 426 in total, were excluded from the further analysis and 468 patients were prospectively followed –up. Kaunas Acute Myocardial Infarction Register was used for survival (12 months -10 years) analysis. After 10 years there were 370 survivors and 98 coronary deaths.

The submaximal exercise test (25 W incremental loading every 5 min.) was performed 3 weeks after acute myocardial infarction. A 6 lead ECG was continuously monitored throughout the test and 10 min after it. A blood pressure was measured before the exercise test, every minute during the test and 10 min after the test. The occurrence of significant anginal pain, ventricular tachycardia, major conduction abnormalities, ST-depression > 2 mm, limiting symptoms (such as dyspnoea, dizziness, fatigue, cramp in legs, etc), an excessive increase (above 230 mmHg) or decrease (> 30 mmHg) in systolic blood pressure were regarded as interruption criteria. Both ST depression in one or more leads, excluding aVR and V1, and ST elevation in leads without pathological Q waves were considered. The exercise-induced angina pectoris and/or the presence of horizontal or down sloping ST depression of 1 mm measured 80 ms after J point and of ST elevation of 1 mm measured 40 ms after the J point were regarded as positive criteria. Positive was defined as low-threshold if occurring at workload <75 W (450 kgm/min).Results of the exercise testing 3 weeks after MI were as follows: mean peak workload differed significantly among the survivors: 42.95 $\pm$ 0.87 W and those dying within 10 years after MI: 39.5 $\pm$ 1.8 W ($p<0.05$). ST depression of >1mm was detected in 31 (8.4%) and in 21(21.4%) cases respectively (p<0,01) (Table 1). Indicators for electrical instability (exercise induced serious ventricular arrhythmias) showed no significant differences between the groups: in 19 (5.1%) and in 6 (6.1%) cases respectively ($p > 0.7$). Our patients were in good functional state at entry (no patients had a contraindication to exercise); nonetheless, even in this low risk cohort, exercise capacity provide some prognostic information (Table 2).The results of the present study indicate that exercise induced ST-segment depression and an exercise capacity 3 weeks after MI have a relationship with future cardiac deaths at 6,12,24 months and 10 years post myocardial infarction .The exercise induced significant ventricular arrhythmias have a close relationship with subsequent cardiac death only within 6 months after MI (Table 3). Among 13 patients dying within the first 6 months post infarction, 11 patients died suddenly. Identification of effective risk stratifiers is of critical importance for the prevention of sudden cardiac deaths. Increased dispersion of the QT interval has been proposed as a marker of susceptibility to ventricular arrhythmias, and studies have reached varying conclusions regarding its prognostic value [6, 7]. In this study we compared the ability of exercise induced ST depression and QT dispersion to predict the outcome in myocardial infarction patients. QT dispersion data was obtained from the analysis of the exercise electrocardiogram in 98 patients in whom ST segment depression data had been previously reported (98 cases of cardiac death). Because beta-blockers may affect the dispersion of the QT interval, we included only patients in whom all measurements (QT dispersion, ST depression) were made in the absence of these drugs. 53 patients satisfied these criteria. The characteristics of these patients are shown in Table 4. QT intervals were measured by 2 investigators blinded to the clinical outcome of the patients. QT intervals were manually measured with callipers from the onset of the QRS complex to the end of the T wave defined as the return to the TP baseline. When U –waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. When the end of the T-wave could not be identified, the QT interval was not measured in that lead. A minimum of 6 leads, at 3 or more precordial, was required for QT dispersion to be calculated. The QT value > 440 was considered as a prolonged QT interval. Two indexes of dispersion of the QT interval wave were measured according to standard criteria. For each lead, both the maximum and minimum QT interval duration were measured. The QT dispersion (QTD) was defined as a difference between the maximum and the minimum QT interval across all 6 electrocardiographic leads. Corrected QT dispersion (QTcD) was measured using Bazett formula (QT/square root of the RR interval). QT intervals were assessed from ECG recordings (paper speed 50 mm/s) at rest, at the peak of stress and 3 min after the bicycle stress test at recovery.

Results

Results of the early exercise test are presented in Tables 1, 2, 3, and the baseline clinical characteristics of 53 non survivors are shown in Table 4. Among those dying within the first 6 months post infarction, 11 patients died suddenly (gr. 1); 42 patients died 6 months after the onset of acute MI but within 10 years after infarction (gr. II).

Among patients dying suddenly within the first 6 months after myocardial infarction, exercise induced ST changes (10 cases of depression and 1 case of elevation) and OTc prolongation (> 440 ms) at the early exercise test were found in all of them.

Exercise induced QTc prolongation (>440 ms) was in 97,6 percent (41 of 42) patients dying within 10 years after myocardial infarction.

Table 1. Exercise induced ST-segment depression in patients with myocardial infarction and subsequent development of fatal coronary events

Follow up	ALIVE		DEATHS		p value
Periods	Total	ST depression	Total	ST depression	
6 months	455	42 (9.2%)	13	10 (76.9%)	p<0.01
12 months	436	29 (6.7%)	32	13 (40.6%)	p<0.01
24 months	426	33 (7.8%)	42	19 (45.2%)	p<0.01
10 years	370	31 (8.4%)	98	21 (21.4%)	p<0.01

Table 2. Relationship between exercise capacity in the early exercise test and future fatal coronary events in myocardial infarction patients

Follow up	ALIVE		DEATHS		p value
Periods	Total	Exercise capacity W	Total	Exercise capacity W	
6 months	455	43.7±0.83	13	36.4±4.7	p<0.05
12 months	436	44.1±0.86	32	36.0±4.2	p<0.05
24 months	426	44.5±0.9	42	34.2±3.5	p<0.013
10 years	370	42.95±0.87	98	39.5±1.8	p<0.05

Table 3. Relationship between exercise induced significant ventricular arrhythmias in patients with myocardial infarction and subsequent development of fatal coronary events

Follow up	ALIVE		DEATHS		p value
Periods	Total	Arrhythmia	Total	Arrhythmia	
6 months	455	22 (4.8%)	13	3 (21.5%)	p<0.01
12 months	436	22 (5.1%)	32	3 (9.4%)	p>0.5
24 months	426	21 (4.9%)	42	4 (9.5%)	p>0.3
10 years	370	19 (5.1%)	98	6 (6.1%)	p>0.7

We examined exercise induced differences in QTc interval and QT dispersion dynamics during the early exercise test and recovery. On the basis of our data, we assessed a cutoff of > 60 ms for QTD and QTcD in the early exercise test EKG and calculated the corresponding sensitivity and specificity for this cutoff in predicting the sudden cardiac death within 6 months after acute MI. The exercise induced QTc dispersion >60ms at the early exercise test was found in 8 (out of 11) patients dying suddenly within 6 months after MI and in 27 (out of 42) in patients dying within 10 years after MI (sensitivity-72.7 percent and specificity-64 percent).

Table 4. Baseline clinical characteristics of patients dying suddenly within the first 6 months after acute myocardial infarction and survivors within 6 months after myocardial infarction

	Early sudden deaths	Deaths within10 years after MI
Age years	52.2(42-61)	51.2(29-65)
Sex m/f	11/0	42/0
Hypertension number	0	5
Infarct localization:		
Anterior number	3	17
Inferior number	8	25
Beta-blockers number	0	0
Results of the early		
Exercise test:		
Work load W	36.4±4.7 (25-75)	42.9±2.1 (25-100)
ST depression		
>1mm number (percent)	10(90.9)	13(30.1)
QT prolongation		
>440 ms number (percent)	11(100)	41(97.6)

At the early exercise test QT dispersion >60 ms was found in 7 (out of 11) patients dying suddenly within the 6 months after acute MI and in 17 (out of 42) those dying within 10 years after infarction.

The ST depression during or after the stress test showed a better sensitivity (90.9 percent) and specificity (76.2 percent) to predict the early sudden cardiac death within 6 months after MI as compared to the QTD>60ms during or after the stress test (63.3 percent vs. 59.5 percent).

Crosstabulation of exercise induced QTD > 60 ms and exercise induced ST depression showed such variables in the equation: Exp (B) – 2.689;[95,0 percent CI for Exp (B): lower-1.140; upper-6,343.] (p-0,024). According to our data, exercise induced ST depression >2.5 (2.689) times increases probability of QT dispersion at the early exercise test in myocardial infarction patients.

Sensitivity and specificity of QTD measurements at rest (QTDr) ,at the peak of exercise (QTDex) and 3 min after exercise, at recovery (QTDp) carried out to predict of transient myocardial ischemia (exercise induced ST depression) were estimated using ROC curves. The results of the present study demonstrate that contrary to QTDr and QTDex, QTD assessed after 3 min post exercise into recovery was significantly associated with exercise induced ST depression. (Fig. 1, 2, 3).

Kaplan – Meier survival curves according to the absence or presence of ST depression at the early exercise test are presented in Fig. 4.

Discussion

The patients of gr II had better exercise capacity and ST depression was registered only in 30.1 percent of patients as compared with 90.9 percent of patients of gr. I.

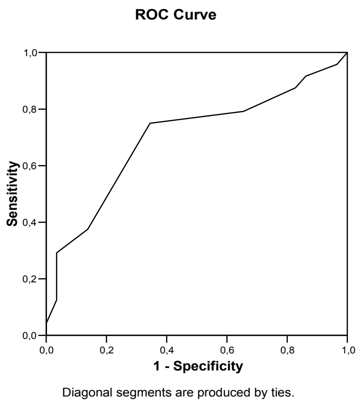

Fig. 1. QTDp R O C Plot of all QTDp measurements carried out to predict exercise induced ST depression .Area under the ROC curve – 0.698; standard error – 0.075; Asymptotic 95 percent confidence interval: [lower bound – 550 and upper bound - 846]; p-0.014

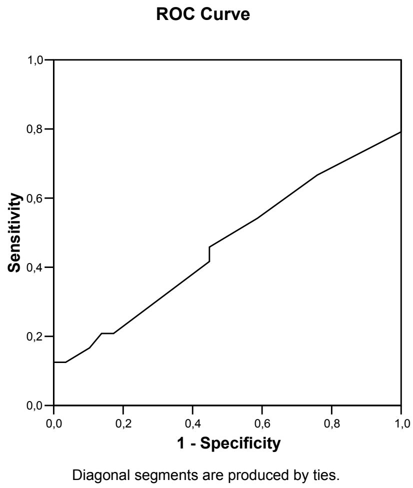

Fig. 2. ROC plot of all QTDex measurements carried out to predict exercise induced ST depression. Area under the ROC curve – 0.463; standard error 0.083. Asymptotic 95 percent confidence interval: [lover bound – 300; upper bound – 627]; p – 0.649

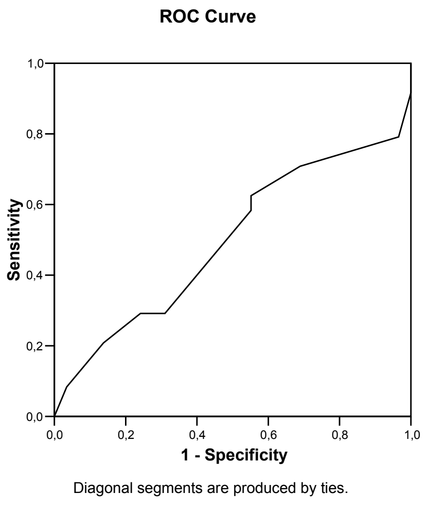

Fig. 3. ROC Plot of all QTDr measurements carried out to predict exercise induced ST depression. Area under the ROC curve - 0.496; standard error –0.083; asymptotic 95 percent confidence interval: [lower bound 335; upper bound – 65]; p – 0.964

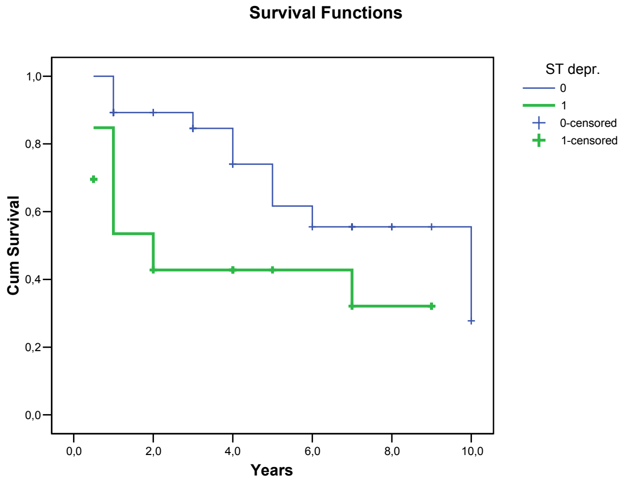

Fig. 4. Kaplan - Meier curves of the survival rates on the basis of the presence or absence of exercise induced ST depression. Long rank – 6.03; p – 0.014

In this study we compare exercise induced ST depression, QT prolongation, QT dispersion and QTc dispersion as predictors of susceptibility to sudden cardiac death within 6 months after MI.

Among those dying suddenly within the first 6 months after MI QTc prolongation (>440 ms) and ST , changes (10 cases of depression and 1 case of elevation) were found in all of them (11 patients-100 percent).

It is known that the double product (BPxHR/100) attained during the exercise test represents the survival prognosis and the decrease of BP during the exercise correlates with unfavourable outcomes [5]. According to our data, exercise induced hypotension was registered more frequently in the group of survivors [9]. The hypotension was established in 8.6% of the survivors and in 7.16% among those dying within the first 6 months after MI. In the group of 1-year survivors after MI, exercise hypotension was established in 9% of patients and in non-survivors – in 3.1% of cases. 2 years after MI the results were 9.2% and 2.4% respectively. Hypotension in the early exercise test was detected in 10% of patients in the group of 10 years survivors and in 5.1% of patients dying during this period after MI. Our patients undergoing early exercise test after MI were in a relative good physical condition, without any contraindications for the test. In this case we can explain the relative rare hypotension cases in our early exercise tests after MI and no established correlation to the unfavourable outcomes. According to our data, dynamics of BP and HR during the exercise and after it were related to survival after MI.

It is important to pay attention to such an easily detectable marker of sudden cardiac death as the absence of T-wave pseudonormalisation during the early exercise test after MI. This sign is not sufficiently investigated. There is an opinion [10] that this could be related to the absence of the metabolic myocardial activity. Necrotic myocardium has no metabolic and electrical activity, so in these cases negative T-waves can not undergo the changes (absence of pseudonormalisation). Our data revealed that in the group of 11 patients dying suddenly during the first 6 months after MI, all of them had negative T-waves in the zone of infarction. 10 (90.9%) of them had no T-pseudonormalisation pattern during the exercise test. Negative T-waves in the third week after MI were detected in 58 (66%) of 87 patients dying during 10 years after MI. The early exercise test did not induce T-pseudonormalisation in 21 (36.2%) of these patients (significantly lower (p<0.01) as compared to the death cases during the first 6 months after MI) [11]. Thus, our data shows, that the absence of T-wave pseudo-normalisation during the early exercise test after MI may predict early sudden death after MI.

Patients after MI can be divided into relative high and low-risk groups for subsequent cardiac events if all information available on the exercise test is used. The use of the dynamic characteristic of the heart rate and systolic blood pressure considerably increase the predictive power of the test; the cardiac deaths within 2 years after MI being correctly predicted in 80% of cases [2].

The identification of effective risk stratifiers is of critical importance for the prevention of sudden death.

Conclusion

Among patients dying suddenly within the first 6 months after myocardial infarction, exercise induced QTc prolongation (>440ms) and ST changes (10 cases of depression and 1 case of elevation) at the early exercise test was found in all of them.. According to our data, exsercise induced ST depression.> 2.5 times increases probability of QTD at the early exercise test in myocardial infarction patients (p – 0.024). QT dispersion 3 min after exercise (at recovery) was significantly associated with exercise induced ST depression., (p- 0.014).

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K. L. Bloznelienė, J. Brazdžionytė, L. Talijūnienė, L. Linonienė, R. Navickas, R. Grybauskienė. Krūvio sukeltas ST depresijos kitimas ir jo koreliacija su QT dispersija sergančiųjų miokardo infarktu ankstyvojo krūvio mėginio elektrokardiogramoje // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2005. – Nr. 4(60). –P. 58-62.

Nagrinėjamos 53 ligonių, mirusių per 10 metų po miokardo infarkto (MI) ankstyvojo fizinio krūvio mėginio (FKM), prospektyviai mūsų atlikto trečiąją savaitės po infarkto, elektrokardiogramos. Visų (vienuolikos) per pirmus 6 mėnesius po MI staiga mirusių ankstyvojo FKM elektrokardiogramose nustatyta pailgėjusi QTc trukmė (>440 ms) ir išeminiai ST pokyčiai (10 atvejų ST depresijos ir 1 – elevacijos). Krūvio sukelta ST depresija 2,5 karto didinao QT dispersijos tikimybę krūvio elektrokardiogramoje (p-0,024). Ryškiausiai su krūvio sukelta ST segmento depresija QT dispersija siejosi trečiąją poilsio minutę (p-0,014). Il. 4, bibl. 11 (anglų kalba; santraukos lietuvių, anglų ir rusų k.).

K. L. Bloznelienė, J. Brazdžionytė, L. Talijūnienė, L. Linonienė, R. Navickas, R. Grybauskienė. Exercise Induced Changes of ST Depression and Its Correlation with QT Dispersion in Myocardial Infarction Patients // Electronics and Electrical Engineering. – Kaunas: Technologija, 2005. – No. 4(60). –P. 58-62.

The aim of this study was to assess the correlation between exercise induced changes of ST segment depression and QT dispersion in myocardial infarction patients and to evaluate the prognostic capability of these signs . We prospectively assessed exercise induced ST depression and QT dispersion from the early exercise test electrocardiograms at rest, peak of exercise and 3 min after exercise (at recovery) in 53 myocardial infarction patients dying within 10 years after infarction. Among patients dying suddenly within the first 6 months after myocardial infarction, exercise induced QTc prolongation (>440 ms) and ST changes (10 cases of depression and 1 case of elevation) at the early exercise test were found in all of them. The exercise induced ST depression >2.5 times increased probability of QT dispersion p-0.024). The QT dispersion into recovery was significantly associated with exercise induced ST depression (p-0.014). Ill. 4, bibl. 11 (in English; summaries in Lithuanian, English and Russian).

К.Л. Блознялене, Ю. Бразджените, Л. Талиюнене, Л. Линонене, Р. Навицкас, Р. Грибаускене. Корреляция между депрессией сегмента ST и дисперсией интервала QT во время ранней нагрузочной пробы у больных инфарктом миокарда // Электроника и электротехника. – Каунас. Технология, 2005. – № 4(60). –Р. 58-62.

Описываются результаты пробы 53 больных, умерших в периоде 10 лет после инфаркта. Депрессия сегмента ST 2,5 раза увеличивает вероятность дисперсии QT (p=0,02). Наибольшая связь между дисперсией QT и депрессией сегмента ST установлена на 3 минуте после нагрузки (p=0,014). Ил. 4, библ. 11 (на английском языке; рефераты на литовском, английском и русском яз.).