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Frequency Ratio Approach to Estimation of Prognostic Value of Early Exercise Test in Acute Coronary Syndrom Patients

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Background: Exercise electrocardiography still remains the cornerstone of non-invasive evaluation and is almost uniformly performed after myocardial infarction [1], nevertheless the prognostic value of residual ischaemia is still controversial. (1,2) Our task was the design of the prognostic system capable to pick up patients with high risk of coronary death in 2 years time after MI, using the data of early exercise testing.

PATIENTS and METHODS. The submaximal exercise testing was performed within 3 weeks of acute myocardial infarction (MI). Exercise tolerance was assessed employing a bicycle ergom etry test as recommended by ACC\AHA Exercise Testing Protocol . Contraaindications to exercise testing absolute: within 2 days of myocardial infarction; an acute coronary syndrome – without 48 h pain free ; severe aortic stenosis ; severe left ventricular dysfunction; endocarditis, myocarditis, pericarditis . Contraindications to exercise testing relative : hypertension >200/110; hypertrophic cardiomyopathy with outflow tract obstruction; high degree atrioventricular block; electrolyte abnormalities; physical disability such as claudication, arthritis or deformity ; other exertion limiting conditions such as smoking related lung disease.[3, 4, 5]. .Patients performed a symptom-limited, bicycle exercise stress test (25 W incremental loading every 3 min) .A 6-lead ECG was continuously monitored throughout the test. The occurrence of significant anginal pain , ventricular tachycardia ,major conduction abnormalities , ST depression > 2mm,limiting symptoms (such as dyspnoea, dizziness, fatigue, cramp in legs , etc.) an excessive increase (above 230 mm Hg) or decrease (> 30 mm Hg) in systolic blood pressure were regarded as interruption criteria. Both ST depression in one or more leads ,excluding aVR and V one , and ST elevation in leads without pathological Q waves were considered. The presence of horizontal or downsloping ST depression at 1 mm measured 80 ms after the J point and of ST elevation at 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).

The occurrence of complications in the acute stage of myocardial infarction was not considered a contraindication for exercise testing. The major contraindication was poor clinical condition of the patient during the week preceding the testing: frequent or severe anginal pains, rhythm and conduction disorders, the left ventricular failure (LVF). The safety of testing appears to be related to proper patient selection. The main goal of this work was to study correlation between the complications in acute MI and the exercise testing evidence early in the post-MI phase. The first study group comprised 212 pts (aged 26 to 65 yrs): 195 (91.8 percent) were males and 17 (8.2 percent) females. At the acute stage of MI , the LVF was documented in 146 (69 percent) pts; significant arrhythmias - in 34 (16 percent) pts; and conduction disorders- in 12 (6 percent) pts. After three weeks , 73 (33.4 percent) pts complained of chest pain on exertion and 29 (13.7 percent) had pain at rest. There was considerable variation in individual exercise tolerance , 150 to 600 kgm/min (25 to 100 W). The mean threshold workload was 289.32 +-6.48 kgm/min (48.22+-1.08 W). The testing was suspended if critical endpoints were reached. These were a developing anginal pain or ischemic ST segment change ,dyspnea specific changes in blood pressure, attainment of a target submaximal heart rate. The endpoints employed were also related to the safety requirement for the test. According to the workload attained , pts were divided in two groups .Group one consisted of 48 (22.6 percent) pts who had reached the 450 kgm/min (75 W) level (> 5 METS) ,while group two was made up of 164 (74.4 percent) pts who had failed to reach this level.The exercise testing data turned out to be useful for more objective evaluation of the patient's functional state at the discharge.

When the exercice testing data were compared with the complications background,it was found that the occurrence of life – threatening arrhytmias at the acute stage of MI did not correlate with the functional state of the cardiovascular system three weeks later.. However,there was a close relationship between the workload attained and the LVF occuring in the acute stage of disease (Table 1).

Table 1. Relationship between complications in the acute stage of myocardial infarction and exercise three weeks after MI (n-212)

	Dysrhythmia			LVF		
Group	Yes		No	Yes		No
n/proc	n	proc	n proc	n	proc	n proc
Group one	10	20.8	38 79.2	25	52.1	23 47.9
Group two	24	14.6	140 – 85.4	121	73.8	43 26.2
- p		p<0.3			p<0.01	-

Patients with low exercice tolerance (< 5 METS) were more likely to have the LVF during the acute phase.Thus,there was a positive relationship between the occurrence of LVF during the acute stage of MI and the impairement of the functional state of patient as evaluated at the discharge from hospital.

A total of 894 pts (aged 50.68+-0.29 yrs; 827/92.5 percent males and 67/ 7.5 percent females) admitted to Coronary Care Unit have met the eligibility criteria and were put through submaximal exercise testing within 3 weeks of the onset of acute MI.

Cardiovascular responses to exercise testing three weeks after MI were as follows: peak workload – 44.0 +- 0.7 W (264+-4.2 kgm/min) ; peak HR – 110.0 +-0.5 bpm; peak systolic BP–157.4 +-0.9 mm Hg ; peak double product – 176.4 +- 2.8 bpm x mm Hg : 100 . In 375 (41.9 percent) cases exercise testing elicited angina and / or ST depression of > 1 mm (ischemic response) ; in 51 case (5.7 percent) serious ventricular arrhythmias were detected; in one case ventricular fibrillation had developed, but the patient was successfully resuscitated .Cases of noncardiac deaths, patients living outside Kaunas or those subjected to coronary bypass surgery, 391 in total, were excluded from the further analysis. The mean peak workload in the remaining group (n-503) was 42.9 +- 0. 9 W (257.4+-5.4 kgm/min). On testing 150 pts experienced angina and 64 had ST depression of >1 mm. A total of 190 pts displayed an ischemic response (either > 1 mm ST depression or/and angina during exercise testing).

Kaunas Acute Myocardial Infarction Register was used for survival analysis. After 11 yrs there were 405 survivors, with the long-term survival in the 313 pts without an ischemic response being markedly better than that of the 190 ischemic ones, even though the difference was not statistically significant (except for the cases of ST depression). The workload levels attained provided additional information. Exercise-induced ST segment depression occurring early after MI appears to have prognostic significance for the subsequent development of fatal coronary events at 6, 12, 24 months and 11 yrs post MI. Our patients were in good functional state at entry (no patients had a contraindication to exercise); nonetheless , there were 8.5 percent of cardiac deaths within the first two yrs among the acute MI survivors. Among those dying within the first two yrs, only 45.2 percent had the exercise-induced ST segment depression. This shows that the prognotic value of ST depression is not sufficient and demands research of more consistent signs.

The cardiovascular response to exercise was interpreted as a transition process in the self-regulation of cardiovascular system (system's reaction to the stress). The survival was predicted by the shape of heart rate (HR) and systolic blood pressure (BP) curves (their dynamic characteristics) during exercise testing and after it. The signs specific to cardiovascular response to exertion were selected as follows: (1.) the extent of systolic BP changes at the beginning of the exercise testing; (2.) the extent of HR changes at the beginning of the exercise testing; (3.) the character of HR changes one minute after the exercise discontinuation; (4.) the character of systolic BP changes one minute after the exercise discontinuation; (5.) the correlation strength between HR and systolic BP curves within the exercise test; (6.) the character of HR curves at rest after the exercise; (7.) the character of systolic BP curves at rest after the exercise; (8.) the character of HR changes at the last minute of exercise; (9.) the character of systolic BP changes at the last minute of exercise. The prognostic value of these signs was determined. The dynamic characteristics of HR and BP are presented in Figures 1 and 2.

At the end of 2 yrs after MI there were 426 survivors (gr I) and 42 cases of cardiac death (gr II).

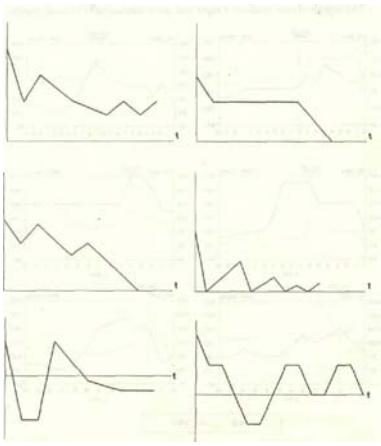

Fig.1. The typical forms of the dynamic characteristics

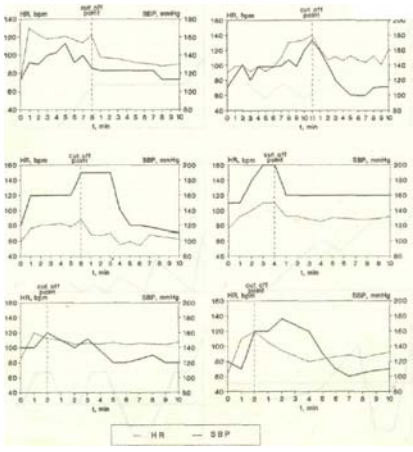

Fig. 2. Samples of heart rate and systolic blood pressure dynamic characteristics from different patients

Results

The cardiovascular responses to exercise testing 3 weeks after MI were as follows: mean peak workload showed significant difference between groups: 44.5+- 0.9 W (267+-5.4 kgm/min) in gr. I and 34.2+- 3.5 W (205.2+-21 kgm/min) in gr.II ($p < 0.01$). The exercise testing elicited angina and/or ST depression of >1 mm (ischemic response) in 132 (31 percent) patients of gr. I, and in 24 (57.1 percent) patients of gr. II. ($p < 0.01$). ST depression of > 1 mm was detected in 33 (7.8 percent) and in 19 (45.2 percent) respectively ($p < 0.01$). Exercise test positive ST-segment only was detected in 17 (4 percent) patients of gr. I and in 9 (21.4 percent) patients of gr.II ($p<0.01$). Indicators for electrical instability (exercise induced serious ventricular arrhythmias) showed no significant differences between groups: in 21 (4.9 percent) patients of gr II. and in 4 (9. 5 percent) patients of gr.II ($p >0.3$)

The patients of gr. I had better exercise capacity and ST depression was registered only in 7.8 percent of patients as compared with 45.2 percent of patients of gr.II. Our results comfirm the data of other investigators that spontaneous events are poorly predicted by provocative tests in low-risk patients after myocardial infarction, however exercise ECG can predict a favourable outcome with a very high negative predictive value (1, 4). A combined use of both, the usual data (indicators for residual myocardial ischaemia) and the new signs - dynamic characteristics of HR and BP curves considerably increased the predictive power of the test. Each sign included several manifestations. For example, the character of systolic BP and HR changes at the beginning of the exercise testing may be manifested by the different degrees of change intensity, BP and HR may increase and decrease, with or without delay. All these specific features are described as characterisic of sign. All the data obtained in exercise testing in the early period of MI was divided in two parts. One, named group C, was used as a learning assembly. In this C group we chose all cases of death in 0.5 year after MI and named this group A; all cases of death in the period between 0.5 and 2 years after MI and named this gruop B. So the remaining group D included the cases with no death in the period of 2 years after MI.
D=C – (A + B).

Then the prognostic value in prediction of the high risk of coronary death of characteristics of signs was determined. For this purpose we computed the frequency rate of each characteristic of all the signs in group A, A + B, C and D, and denoted frequency rate of x-characteristic of i-sign in the group A as ${}^{i}\varphi_{A}(x)$ in the group A + B ${}^{i}\varphi_{A+B}(x)$, in the group C ${}^{i}\varphi_{c}(x)$ and in the group D ${}^{i}\varphi_{D}(x)$. If the frequency rate of x–characteristic is the same or nearly the same in group A as in group C or D, this characteristic has no prognostic value. In contrast, if the value of frequency rate (rfr) in group A is considerably greater in comparison with C or D, this characteristic has higher prognostic value, higher informativity. We denote informativity as a relation:

$${}^{i}\sigma_{A}(x) = \frac{{}^{i}\varphi_{A}(x)}{{}^{i}\varphi_{D}(x)}\,;\ {}^{i}\sigma_{A+B}(x) = \frac{{}^{i}\varphi_{A+B}(x)}{{}^{i}\varphi_{D}(x)}\,.$$

We reject $\sigma(x)$ if $\sigma(x) < 1{,}5$.

We denote the prognostic power of characteristic of sign by following expressions:

$${}^{i}\xi_{A}(x) = 10^{i}\cdot\sigma_{A}(x)\cdot\varphi_{A}(x)\,;$$

$${}^{i}\xi_{A+B}(x) = 10^{i}\cdot\sigma_{A+B}(x)\cdot\varphi_{A+B}(x)\,.$$

After evaluation of separate characteristics of sign, the prognostic power of sign is determined as a set of selected prognostic powers of characteristics of this sign

$$P_i = {}^{i}\xi(x_j) \vee {}^{i}\xi(x_l) \vee \ldots \vee {}^{i}\xi(x_n)$$

$x_j, x_l, \ldots x_n$ are deminations of characteristics of sign.

An example (for sign SAFP – the extent of systolic BP changes at the beginning of exercise test):

If SAFP (x = D1), then ${}^{1}\xi_{A}(D1) = 4{,}4$

SAFP (x = D2), then ${}^{1}\xi_{A}(D2) = 3{,}5$

SAFP (x = D5), then ${}^{1}\xi_{A}(D5) = 1{,}9$

SAFP (x = m), then ${}^{1}\xi_{A}(Dm) = 2{,}6$.

The same method is used for evaluation of other signs: P_2, $P_{3,\ldots}P_n$

The full prognostic power

$$\prod_{Z} = \sum_{i=1}^{n} P_i^{A}\,;$$

n - the number of used signs, z - identificator of individe.

In accordance with this method , a programme for the computer was developed, and withthis programme the values of

$\prod_{Z}^{A}$ and $\prod_{Z}^{A+B}$

for each member of group "C " were estimated.

It was found that with increase of numeral quantity of prognostic power the risk of coronary death after MI increases.

After computation of prognostic power of each member in groups A, A+B, C and D, the arithmetical mean of group V_A^d, V_{A+B}^d, V_C^d and V_D^d was estimated (obtained):

$V_A = 28.66$; $V_{A+B} = 31.05$; $V_C = 23.45$; $V_D = 21.0$.

These quantities may by used as criteria to pick up the patients with high risk of coronary death . The same method was applied for evaluation of prognostic values of widely accepted data of early exercise testing. The combined use of both the widely accepted data of early exercise testing and the dynamic characteristics of HR and systol BP considerably increased the predictive power of the test. Computation of arithmetical mean gave following quantites

$V_A^b = 40.69$; $V_{A+B}^b = 39.83$; $V_C^b = 27.55$; $V_D^b = 26.82$.

After these investigations with the learning assembly and determination of prognostic power of signs, an examination on the other part of data of early exercise testing was performed It demonstrate that early cardiac deaths were correctly predicted in 80 % of cases.

Conclusion

The combined use of both ,the widely accepted data of early exercise testing and the dynamic characteristic of heart rate and systolic blood pressure , considerably increased the predictive power of the test; the early cardiac deaths being correctly predicted in 80 percent of cases.

References

1. **Bigi R., Galati A., Curti G**., et al. Prognostic value of residual ischaemia assessed by exercise electrocardiography and dobutamine stress echocardiograph // European Heart Journal. – 1997. – 18. – P. 1873 – 1888.
2. **Bloznelienė K.L., Blužas J., Bloznelis M.J**. Prognostic value of early exercise testing in patiens with myocardial infarction // 2-nd Alpe Adria cardiology meeting: Abstracts book. – Brijuni, Croatia, 1994, June 22 – 25. – P. 21.
3. **Ashleyy E.A., Froelicher V.** The post myocardial infarction exercise test: still Worthy after all of these years. // European Heart Journal , 2001. – 22. – P. 273 – 276.
4. **Gibbons R.J., Balady G.J., Bricker J.T**. **et al**. ACC / AHA 2002 Guideline update for exercise testing // Circulation. – 2002. – 106. – P. 1883 – 189.
5. **Marchioli R., Avanzini F., Barzi F**. **et al.** Assessment of absolute risk of death after myocardial infarction by use of multiple-risk-factor assessment equations // European Heart Journal. – 2001. – 22. – P. 2085 – 22103.

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K. L. Bloznelienė, R. Grybauskienė, L. V. Linonienė, L. Talijūnienė, A. Zakarienė. Dinaminių charakteristikų panaudojimas sergančiųjų ūminiu išeminės ligos sindromu ankstyvojo fizinio krūvio mėginio prognozinei vertei nustatyti // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2004. – Nr. 3(52). –P. 59-62.

Ankstyvasis fizinio krūvio mėginys iki šiol turi didelę reikšmę skirstant sergančius ūminiais išeminės ligos sindromais į rizikos grupes , įvertinant išgyvenimo prognozę. Fizino krūvio mėginys trečiąją savaitę po miokardo infarkto atliktas 894 ligoniams. Mirusiųjų per pirmuosius dvejus metus grupėje ankstyvasis fizinio krūvio mėginys sukėlė ST segmento depresiją tik 45,2 procento ligonių. Tai rodo, kad krūvio sukeltos ST depresijos prognozinė vertė yra nepakankama ir būtina ieškoti naujų prognozinių požymių. Kardiovaskulinės sistemos atsakas į krūvį buvo interpretuojamas kaip šios sistemos savireguliacijos procesas . Nauji prognoziniai požymiai buvo rasti ištyrus širdies susitraukimų dažnio ir sistolinio arterinio kraujospūdžio kitimo kreives krūvio metu ir po krūvio, įvertinus jų dinamines charakteristikas. Naudojant įprastus krūvio mėginio duomenis bei šiuos naujus prognozinius požymius ankstyvosios, kardialinės mirtys buvo prognozuojamos 80 procentų atvejų. Il.2, bibl. 5 (anglų kalba; santraukos lietuvių, anglų ir rusų k.).

K. L. Bloznelienė, R. Grybauskienė, L. V. Linonenė, L. Talijūnienė, A. Zakarienė. Frequency Ratio Approach to Estimation of Prognostic Value of Early Exercise Test in Acute Ccoronary Syndrom Patients // Electronics and Electrical Engineering. – Kaunas : Technologija, 2004. – No. 3(52). – P. 59-62.

During 11 years period submaximal exercise testing within 3 weeks of acute myocardial infarction was performed with 894 patients. Exercise induced ST segment depression appears to have prognostic significance of subsequent development of fatal coronary events at 6, 12, 24 months and 11 years post infarction. At fillow-up at 2 years post infarction in the non survivors group there were only 45.2 percent exercise induced ST segment depression. This shows, that prognostic importance of ST depression is insufficient and demands of research of more consistent signs. The cardiovascular response to exercise was interpretate as transisting process of the selfregulation of cardiovascular system , and the new predictive signs were found on the basis of heart rate and systolic blood pressure curves during the exercise and after it . The prognostic value of these sigcns were established .The combined use both the new predictive signs and the usual data of early exercisetest shows the high predictive possibility of test – the early cardiac death was predicted in 80 percent cases. Ill. 2, bibl. 5 (in English; summaries in Lithuanian, English and Russian).

К. Л. Блознялене, Р. Грибаускене, Л. В. Линонене, Л. Талиюнене, А. Закарене. Методика использования динамических характеристик для определения прогностической ценности ранней нагрузочной пробы у больных острым коронарным синдромом // Электроника и электротехника. – Каунас.Технология, 2004. – № 3(52). – С. 59-62.

Дифференцированная и стандартизированная проба с физической нагрузкой является сегодня важным клиническим методом исследования для установления физической способности организма (толерантности к физической нагрузке) здоровых и больных, причем на переднем плане для клинической эргометрии стоит ступенчатая аэробная нагрузка на велоэргометре или тредмиле. На основе проведения ранней нагрузочной пробы у 894 больных инфарктом миокарда разработана методика оценки реакции сердечно-сосудистой системы на пробу толерантности к дозированной физической нагрузке по динамическим характеристикам систолического артериального давления (АД) и частоты сердечных сокращений (ЧСС) с учетом периода восстановления после нагрузки. Использование показателей динамических характеристик позволяет правильно прогнозировать 80 процентов летальных случаев за первые два года после инфаркта миокарда. Ил. 2, библ. 5 (на английском; рефераты на литовском, английском и русском яз.).