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Risk prediction in acute coronary syndrome depending on the types of myocard revascularization

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Key words: Prognosis, Myocardial Infarction, Risk, Revascularization, NT-proBNP, GRACE.

Risk of complications in patients with acute coronary syndrome determination has received much attention and offered a variety of options for scales in the last years. GRACE scale is the most informative method to assess the risk of death during hospitalization period and during the next 6 months at present. Some studies recommend to complement GRACE scale with detection of the N-terminal prohormone brain natriuretic peptide (NT-proBNP) blood levels.

The purpose of the study was to assess risk factors by GRACE scale and activity in serum levels of NT-proBNP in myocardial infarction depending on the types of coronary arteries revascularization.

Materials and Methods. The study involved 80 patients with acute myocardial infarction with heart failure; the average age of patients was (61.16 ± 5.79) years, 52 (65 %) men. The patients were divided into 4 groups. Group I included patients who were prescribed thrombolytic therapy ($n=10$); group II patients underwent percutaneous coronary intervention (PCI) with stenting of the infarction-depending vessels ($n=35$); group III involved patients ($n=23$) who were administered both methods of treatment. Group IV included 12 individuals who were administered conservative treatment.

Results. The research showed that the lowest levels of NT-proBNP were observed on the 7th day in patients who have been administered percutaneous coronary intervention (PCI) with stenting of the infarction-depending vessels (254.1 ± 11.3 fmol/ml, $p < 0.05$). The risk of adverse events evaluated by the GRACE scale in patients with MI after performed PCI with stenting of the infarction-depending vessels and thrombolytic therapy is lower (12.2 ± 1.35 %) than in patients who were administered thrombolytic therapy (14.23 ± 0.58 %) and those with conservative treatment (15.63 ± 0.89 %).

Conclusion. The risk of death by GRACE scale in patients with myocardial infarction after performed PCI with stenting of the infarction-depending vessels and thrombolytic therapy is lower than in patients without coronary intervention.

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Прогнозування ризику при гострому коронарному синдромі залежно від типів реваскуляризації міокарда

Р. В. Деніна

Протягом останніх років стратифікації ризику несприятливих подій у хворих на гострий коронарний синдром приділялося багато уваги та пропонувалися різноманітні варіанти шкал. Найбільш інформативною на тепер методикою, що дає можливість оцінити ризик смерті як у період госпіталізації, так і протягом найближчих 6 місяців, є шкала GRACE. В окремих дослідженнях рекомендовано доповнити шкалу GRACE визначенням у крові рівня N-кінцевого фрагмента мозкового натрійуретичного пептиду (NT-proBNP).

Мета роботи – оцінити ступінь ризику несприятливих подій за шкалою GRACE та активність сироваткових рівнів NT-proBNP при інфаркті міокарда залежно від способу реваскуляризації коронарних артерій.

Матеріали та методи. Обстежили 80 осіб на гострий інфаркт міокарда з супутньою серцевою недостатністю, середній вік становив $61,16 \pm 5,79$ року. Серед пацієнтів переважали чоловіки 52 (65 %). Хворих поділили на чотири групи: до 1 увійшли хворі, яким застосована тромболітична терапія ($n=10$); 2 група ($n=35$) – це хворі, яким проводили первинне черезшкірне коронарне втручання (ЧКВ) зі стентуванням інфаркт-залежної коронарної артерії (ІЗКА); до 3 групи ($n=23$) увійшли хворі, яким здійснили тромболітичну терапію (ТЛТ) із ЧКВ ІЗКА; до 4 групи – 12 осіб, яких лікували тільки медикаментозно.

Результати. Встановили, що найнижчі рівні NT-proBNP на 7 добу спостерігалися у групі хворих, яким виконали ЧКВ зі стентуванням ІЗКА ($254,1 \pm 11,3$ фмоль/мл, $p < 0,05$). Ризик несприятливих подій, що розраховані за шкалою GRACE, у хворих з ІМ після реваскуляризації ІЗКА та ТЛТ із ЧКВ ІЗКА є нижчим ($12,2 \pm 1,35$ %), ніж у хворих, яким здійснили ТЛТ ($14,23 \pm 0,58$ %) та у тих пацієнтів, які отримували лише медикаментозне лікування ($15,63 \pm 0,89$ %).

Висновки. Ризик смерті за шкалою GRACE у хворих на інфаркт міокарда після реваскуляризації шляхом стентування ІЗКА є нижчим, ніж у хворих, які отримували лише медикаментозне лікування.

Ключові слова: ризик, інфаркт міокарда, реваскуляризація, NT-proBNP, GRACE.

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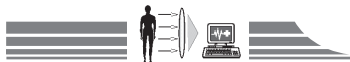
Прогнозирование риска при остром коронарном синдроме в зависимости от типов реваскуляризации миокарда

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В течение последних лет стратификации риска больных с острым коронарным синдромом уделялось много внимания и предлагались различные варианты шкал. Наиболее информативной на сегодняшний день методикой, позволяющей оценить риск смерти как в период госпитализации, так и в течение ближайших 6 месяцев, является шкала GRACE. В отдельных исследованиях рекомендуется дополнить шкалу GRACE определением в крови уровня N-конечного фрагмента мозгового натрийуретического пептида (NT-proBNP).

Цель работы – оценить степень риска неблагоприятных событий по шкале GRACE и активность сывороточных уровней NT-proBNP при инфаркте миокарда в зависимости от способа реваскуляризации коронарных артерий.

Материалы и методы. Обследовано 80 больных острым инфарктом миокарда с сопутствующей сердечной недостаточностью, средний возраст которых составил $(61,16 \pm 5,79)$ года. Среди обследуемых преобладали мужчины 52 (65 %). Больных разделили на четыре группы: 1 группа – больные, которым проведена тромболитическая терапия ($n=10$); 2 группа ($n=35$) – первичное чрескожное



коронарное вмешательство (ЧКВ) со стентированием инфаркт-зависимой коронарной артерии (ИЗКА), 3 группа (n=23) – больные, которым проводили тромболитическую терапию (ТЛТ) с последующим ЧКВ ИЗКА; 4 группу составили 12 человек, которых лечили только консервативно без ЧКВ.

Результаты. В ходе работы установлено, что самые низкие уровни NT-proBNP на 7 сутки наблюдались в группе больных, которым проводили ЧКВ со стентированием ИЗКА ($254,1 \pm 11,3$ фмоль/мл, $p < 0,05$). Риск неблагоприятных событий, рассчитанных по шкале GRACE, у больных с инфарктом миокарда после проведённой реваскуляризации ИЗКА и ТЛТ с ЧКВ ИЗКА ниже ($12,2 \pm 1,35\%$), чем у больных, которым проводили ТЛТ ($14,23 \pm 0,58\%$), и тех, которые получали только медикаментозное лечение ($15,63 \pm 0,89\%$).

Выводы. Риск смерти по шкале GRACE у больных с инфарктом миокарда после проведённой реваскуляризации путём стентирования ИЗКА ниже, чем у больных без коронарного вмешательства.

Ключевые слова: риск, инфаркт миокарда, реваскуляризация, NT-proBNP, GRACE.

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The choice of treatment strategy in patients with acute coronary syndrome (noninvasive, invasive or both) is based on the assessment of hospital morbidity prediction and remain the most important task in cardiology.

There are a few quantitative scales (TIMI, GRACE, RAMI, CADILLAC), that allow to optimize risk stratification of ischemic cases in early stages and long term disease [1–3,9]. Doctors estimate the risk of unfavorable result not only for the prediction specification of illness, but also in order to determine the treatment tactic and duration of hospitalization. Most often we use the TIMI or GRACE scale to estimate the risk of adverse cases [3,4]. GRACE scale is the most informative for today. It allows assessing the risk of morbidity during hospitalization and 6 months later. We use 3 indices for GRACE calculations: 1 – history of disease (patient's age, Killip classification, myocardial infarction (MI) in anamnesis); 2 – indices of haemodynamic and coronary flow on admission (heart rate, blood pressure level, deviation of ST segment); 3 – indices during hospitalization (creatinine level, cardiac levels (troponin T, I, enzymes) and coronary interventions) [4,5].

Nowadays biomarkers of myocardial necrosis are widely used; they help a lot in diagnostics of disease. Moreover, they allow determining the choice of treatment and prognosticating the risk. One of them is brain natriuretic peptide (BNP) and N-terminal prohormone brain natriuretic peptide (NT-proBNP) [5–7,10].

High level of BNP/NT-proBNP depends on the size of infarction zone [2]. The level of BNP/NT-proBNP in these patients increases proportionally to the degree of left ventricle dysfunction with heart insufficiency class, level of pulmonary hypertension and generally show the size of personal cardiovascular risk [2,8,10].

High level of BNP/NT-proBNP helps to predict adverse events of myocardial infarction [2,5,8]. In seniors it is more informative due to cardiovascular morbidity than GRACE scale. When we assess the hospital morbidity risk the measurement of BNP/NT-proBNP increases the prompt diagnosis [3,7].

The purpose of the study was to assess risk factors by GRACE scale and activity in serum levels of NT-proBNP in myocardial infarction depending on the types of coronary arteries revascularization.

Materials and methods

The study involved 80 patients with concomitant heart failure. The patients' age ranged from 40 to 75 years, the average age was (61.16 ± 5.79) years. We examined 52 (65%) men and 28 (35%) women.

Q–MI in acute phase was found in 63.5%, QS–MI in – 36.5% of men. Among women the Q–MI was diagnosed in 67.9% and

QS–MI in 32.1% of patients. While assessing acute noncompensated heart failure on admission according to Killip classification we found 70% with Killip–I and 30% with Killip–II cases.

The risk factors were evaluated in each case. The most common MI risk factors were bad habits (smoking) – 47.5%, lower physical activity – 70.0% of patients. Lack of exercise preceded the development of MI in 16.0% of patients. Overweight ($BMI > 27 \text{ kg/m}^2$) was diagnosed in 22.5% of patients, family history of cardiovascular diseases was present in 54.0% of cases.

The estimation of concomitant diseases is also important. The diabetes mellitus and impaired glucose tolerance occurred in 40% of cases (11% of men and 13% of women), stage II hypertension – in 42.5% of patients, stage III hypertension (EH) was diagnosed in 10% of examined patients. Hypercholesterolemia (general cholesterol level $\geq 5 \text{ mmol/l}$) was noticed in 60% of patients. In their menopause period were 78.6% of women.

All patients had diastolic dysfunction of the left ventricle with ejection fraction of $50.03 \pm 0.46\%$ (echocardiography was performed by 2–3 days).

There were no statistically significant differences in the presence of risk factors described in groups.

Distribution of patients was held on admission to the department of minimally invasive therapy.

All patients were divided into 4 groups. Group I involved 10 patients who were administered thrombolytic therapy. Group II included 35 patients who were applied percutaneous coronary intervention (PCI) with stenting of the infarction–depending vessels. Group III included 23 patients who underwent pharmacoinvasive therapy (percutaneous coronary intervention (PCI) with stenting of the infarction–depending vessels).

In this group of patients PCI with stenting of the infarction–depending vessels was performed 12 hours after ineffective thrombolysis in the prehospital phase, which was confirmed by coronary angiography (6.48 ± 2.23 hours). Group IV included 12 patients who underwent conservative treatment (without TLT).

Drug treatment included: antiplatelet agents (aspirin – 75 mg/day), clopidogrel – 75 mg/day or tykahrelor – 90 mg/day; anticoagulants (enoxaparin for the first 4 days, 1 mg/kg * 2 times a day of transition to rivaroxaban at a dose of 2.5 mg 2 times a day); beta-adrenoblocker – bisoprolol – 2.5 mg/day; ACE inhibitor – enalapril – 5–10 mg/1–2 times a day; nitrate – isosorbide dinitrate: nitrosorbid – 10 mg/2–3 times a day; lipid-reducing therapy – atorvastatin – 20 mg per day.

The average term of percutaneous coronary intervention performance was 9.5 ± 3.4 hours from the beginning of ACS (from 6 to 12 hours).



Clinical and instrumental researches included: complaints, anamnesis, objective data, results of instrumental (ECG, coronary angiography) and laboratory analyses.

Measurement of NT-proBNP level was performed by ELISA test ("Peninsula Laboratories", USA). NT-proBNP 45.14 mmol/ml was considered standard, "a gray zone" – 250–350 mmol/ml. Determination of serum in patients with NT-proBNP performed within the first 12–24 hours of hospitalization and observation for 7 days.

The assessment of hospital and 6-months survival rate (GRACE scale) was calculated by special calculating program for personal computers "Macromedia Flash Player 7". The points were calculated and determined the total risk of death during hospitalization (D), 6 months after (D6), risk of death or MI relapse during hospitalization (DM) and 6 months after (DM6).

Statistical analysis was performed using the biostatistics methods of Statistica 8.0 (StatSoft Inc., USA) program. The arithmetic middlings (M), average errors (m), Student t-test for paired variables have been taken for consideration. The data have been presented in the form of (M±m).

The evaluation of patients' condition, determination of risk (GRACE scale) were performed during hospitalization and on the 7th day of examination.

Results

The level of NT-proBNP was (474.34±04.12) fmol/ml in patients who received thrombolytic therapy (metalize) at the time of hospitalization. On the 7th day this index increased to (497.85±16.21) fmol/ml (p>0.01). During the observation period we detected rhythm disturbances by paroxysmal atrial fibrillation type (33.3%), ventricular premature beats and class II at Lown (50.0%), ventricular fibrillation in 16.7% of patients, there was an asystolic patient with successful resuscitation.

At the same time, patients who underwent PCI with stenting of the infarction-depending vessels (n=35) had decreased NT-proBNP level on the 7th day from (407.44±21.2) fmol/ml to (254.1±11.3) fmol/ml (p<0.05). In 28.6% of patients we detected the right coronary artery lesions, in 48.6% – anterior interventricular branch of the left coronary artery lesions and 22.8% of patients had multivessel disease (performed PCI with stenting of the infarction-depending vessels), due to which they were redirected to coronary bypass surgery. Angiographic success was achieved in 98 (98%) of patients and was accompanied by positive clinical effects and resolution of ST segment. These patients had paroxysms of atrial fibrillation/atrial flutter (11.4%), ventricular beats and classes for Lown (22.8%), atrial beats (31.4%).

Primary PCI with stenting of the infarction-depending vessels after ineffective TLT underwent 23 (28.75%) patients. It has been established that after 7 days of treatment the NT-proBNP level, as compared with values before treatment, decreased from (403.11±15.02) fmol/ml to (376.27±23.13) fmol/ml (p>0.05).

The group of patients who received only medical therapy (n=12) included older patients with contraindications to thrombolytic therapy and PCI with stenting of the infarction-depending vessels.

NT-proBNP level before treatment was (512.06±06.4) fmol/ml, and on the 7th day it decreased to (501.14±13.37) fmol/ml (p>0.05). Ventricular extrasystoles class I–III by Lown (66.7%) often occurred in this group of patients. Other arrhythmias or conduction disturbances in this group of patients was not detected.

A risk assessment of mortality, reinfarction and repeated myocardial infarction for GRACE risk scale is presented in Table 1.

Table 1

The relative risk of death, reinfarction and repeated myocardial infarction by GRACE scale (M±m)

	D, %	D6, %	DM, %	DM6, %
Group 1. TLT (n=10)	8.84±0.55	14.23±0.58	22.55±1.04	28.34±1.23
Group 2. PCI with stenting of the infarction-depending vessels (n=35)	3.43±0.12	6.46±0.34	6.97±0.45	24.95±1.18
Group 3. TLT with PCI with stenting of the infarction-depending vessels (n=23)	4.68±1.7	12.2±1.35	21.1±1.03	34.25±1.70
Group 4. Medical treatment (n=12)	9.76±0.55	15.63±0.89	26.85±1.54	26.65±1.83
p ₁	>0.05	<0.03	>0.05	>0.05
p ₂	<0.05	<0.01	>0.05	>0.05
p ₃	>0.05	>0.01	>0.05	>0.05
p ₄	>0.05	>0.05	>0.01	<0.01
p ₅	<0.05	<0.05	<0.05	>0.05
p ₆	>0.05	<0.01	<0.05	>0.01

Notes:

1. D – probability of death during hospitalization; D6 – probability of death after 6 months; DM – probability of death or MI relapse during hospitalization; DM6 – probability of death or MI relapse during hospitalization after 6 months.

2. p₁ – the probability of difference compared with Group 1 & Group 2; p₂ – the probability of difference compared with Group 1 & Group 3; p₃ – the probability of difference compared with Group 1 & Group 4; p₄ – the probability of difference compared with Group 2 & Group 3; p₅ – the probability of difference compared with Group 2 & Group 4; p₆ – the probability of difference compared with Group 3 & Group 4.



While assessing the risk of mortality, reinfarction and repeated myocardial infarction with the help of GRACE scale, we found out that the risk of total mortality, reinfarction, or repeat myocardial infarction during hospitalization (D) in patients with myocardial infarction after conducted PCI with stenting of the infarction-depending vessels was (3.43±0.12)%, after 6 months (D6) – (6.46±0.34)% (p>0.01); the risk of death with the possibility of occurrence of reinfarction during the hospitalization (Dm) was (16.97±0.45)%, and risk of death or reinfarction after 6 months (DM6) was (24.95±1.18)% (p<0.05). In patients who underwent TLT with next PCI with stenting of the infarction-depending vessels the total mortality risk, reinfarction, or repeated myocardial infarction during the hospitalization (D) was (4.68±1.7)%, after 6 months (D6) – (12.2±1.35)% (p>0.01); the risk of death with the possibility of occurrence of reinfarction during the hospitalization (DM) was (21.1±1.03)%, and risk of death or reinfarction after 6 months (DM6) – (34.25±1.70)% (p<0.05).

In patients after TLT endpoints were as follows: D – (8.84±0.55)%, D6 – (14.23±0.58)% (p<0.05), Dm – (22.55±1.04)%, and DM6 – (28.34±0.31)% (p>0.05).

In patients with myocardial infarction who received only medical treatment endpoints were: D – (9.76±0.55)%, D6 – (15.63±0.89)% (p<0.05), Dm – (26.85±1.54)% and DM6 – (26.65±1.83)% (p>0.001). Also, we have established correlational connections between level of NT-proBNP and

GRACE scale (r=0.85; p<0.05).

Consequently, the risk of death in patients with myocardial infarction after performed revascularization of the infarction-depending vessels and thrombolytic therapy with PCI with stenting of the infarction-depending vessels is lower than in patients who underwent thrombolytic therapy and those who received only medical treatment.

Conclusions

1. Use of GRACE scale in combination with assessment of the NT-proBNP/BNP – biomarker level allows to identify the most “dangerous” risks for patients during the first day at the hospital, both in hospital and in remote period, it is important to prevent the unfavorable effects of optimal drug and interventional treatment.

2. Determination of NT-proBNP/BNP may serve not only as diagnostic tool for heart failure identification in patients with ACS, but as the prevalence index of ischemia, due to the nearest and long-term prognosis of AMI in relation to fatal cardiac vascular events, of recurrent coronary events and heart failure. It is established that the risk of death by GRACE scale in patients with heart failure with MI after performed PCI with stenting of the infarction-depending vessels is lower than in patients without undertaken reperfusion.

Conflicts of Interest: author have no conflict of interest to declare.

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