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PREDICTION MODEL OF HOSPITAL MORTALITY AMONG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND CONCOMITANT TYPE 2 DIABETES MELLITUS

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Introduction. Currently, acute myocardial infarction (AMI) is reported as a leading cause of death in type 2 diabetes mellitus (DM2) patients either in Ukraine or worldwide [3,4,7,15]. The usage of new diagnostic markers, introduction of up-to-date approaches to the treatment improved the situation only partially, since the life expectancy for this cohort of patients is significantly worse than for those with no concurrent carbohydrate metabolism disorders [1,9].

A specific role is given to endothelial dysfunction [2,14]. The new markers sCD40-ligand (sCD40L) and sVE-cadherin reflect the presence and degree of endothelial dysfunction manifestation. The former (sCD40L) presents the family of tumor necrosis factors which due to the platelet expression influences the cellular component activation in hemostasis, participates in atherosclerosis formation and progressing [8], mediates coronary artery endothelial inflammatory changes [10,16]. Therefore, the study of sCD40L dynamics may characterize complex processes occurring in coronary artery endotheliocytes under acute occlusion.

Recently, the researchers showed an interest in a new marker of endothelial damage – sVE-cadherin which plays a key role in maintaining the vascular wall integrity [11]. Atherosclerotic plaque destabilization followed with consequent denudation of endothelium leads to disintegration of intercellular tight junctions of endothelial cells and sVE-cadherin release [12]. In spite of the high interest to the search of new criteria for predicting the AMI course, the role of sCD40L, sVE-cadherin has not been studied enough.

During the recent years the scientific community offered some models for stratification of AMI patients into risk groups (TIMI-STEMI, In-TIME II, GUSTO, GRACE, PURSUIT) [5,6,17]. Nevertheless, none of the mentioned above scales cannot be used for evaluating the risk of unfavorable outcome of AMI acute period in the patients with concomitant DM2. Thus, an important medical and social value of high mortality rate in AIM patients with DM2, no scale available for evaluation of the degree of risk of its occurence in the patients became an impulse for the further scientific research.

The purpose of the research was to elaborate the prediction model of hospital mortality in the patients with acute myocardial infarction and type 2 diabetes mellitus.

Material and methods. The study included 60 patients with AMI and type 2 DM (among them 33 (55%) women and 27 (45%) men). The patients were divided into two groups depending on the outcome of acute period of myocardial infarction: group 1-7 patients died during the acute period of myocardial infarction; group 2-53 patients, survives during acute period of myocardial infarction.

Acute myocardial infarction was diagnosed according to the Order of the Ministry of Health of Ukraine № 455 dated 02.07.2014 «Unified clinical protocol of emergent, primary, secondary (specialized) and tertiary (highly specialized) medical aid and medical rehabilitation of the patients with acute coronary syndrome with elevated ST segment» on the basis of clinical, echocardiographic and biochemical criteria.

At days 1 and 10 of AMI the participants were taken 10 mL blood samples under the basal conditions, and sVE-cadherin blood serum level was determined with commercial enzyme linked immunosorbent assay ELISA kit (Bender MedSystems GmbH, Vienna, Austria), insulin level was found with commercial ELISA kit (DRG Instruments GmbH, Germany), and sCD40L level was determined with the usage of commercial ELISA test kit (YH Biosearch Laboratory, Shanghai, China) according to the manufacturer's instruction, and all these were performed with Automated EIA Analyzer «LabLine-90» (Austria). Levels of total cholesterol, low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), high-density lipoproteins (HDL) and triglycerides (TG) were measured biochemically. Quantitative insulin sensitivity check index (QUICKI) index was measured mathematically. The data were processed statistically with Microsoft Office Excel software: the mean arithmetial value (M) and standard error of the mean (m) were calculated, for estimated probability and validity

of the obtained data, Student's t-test (p) was done. For risk stratification modeling, stepwise logistic regression SPSS method was used.

Results of the research and their discussion. According to the obtained results demonstrated in **table** it was established that the mean age of AMI and DM2 patients who died within AMI acute period was 74.4 ± 2.9 year, while of those who survived – 66.6 ± 1.4 year (p<0.05), mortality within AMI acute period was also associated with higher LDL levels compared to the survived patients (1.34 ± 0.15 mmol/L and 2.86 ± 0.18 mmol/L correspondingly; p<0.05). Besides, increased blood insulin level and decreased QUICKI in the died patients compared to the survived AMI and DM2 patients (44.0 ± 2.5 mcLU/mL and 37.0 ± 0.9 mcLU/mL, correspondingly; p<0.05) and (0.307 ± 0.018 and 0.272 ± 0.045. correspondingly; p<0.05) were revealed.

Evaluation of levels of endothelial cell injury markers, namely sCD40-ligand, is of great interest: insufficient decrease of sCD40-ligand level during 10 days under the effect of treatment is associated with the higher death risk (-12.0 ± 3.0% and -21.0 ± 1.0% correspondingly; p<0.05). Evaluation of sVE-cadherin established that its insufficient decrease was also associated with hospital mortality in AMI and DM2 patients (-11.0 ± 3.0% and -18.0 ± 1.0% correspondingly; p<0.05). There were revealed no statistically significant differences at comparison of the patients who died and those survived by triglycerides level (1.80 ± 0.16 mmol/L and 2.07 ± 0.12 mmol/L correspondingly; p>0.05), VLDL (0.64 ± 0.05 mmol/L and 0.91 ± 0.07 mmol/L, correspondingly; p<0.05), blood glucose (11.74 ± 1.7 mmol/L and 9.49 ± 0.58 mmol/L, correspondingly; p<0.05).

Determination of sVE-cadherin at day 1 (1.73 ± 0.08 ng/mL and 1.80 ± 0.03 ng/mL, correspondingly; p<0.05) and at day 10 (1.54 ± 0.08 ng/mL and 1.47 ± 0.03 ng/mL, correspondingly; p<0.05); sCD40-ligand at day 1 (3.73 ± 0.06 ng/mL and 3.85 ± 0.04 ng/mL, correspondingly; p<0.05) and at day 10 (3.28 ± 0.08 ng/mL and 3.04 ± 0.05 ng/mL, correspondingly; p<0.05) demonstrated no significant differences.

To evaluate the risk of hospital mortality within acute period of myocardial infarction in the patients with type 2 DM a prediction model was built by stepwise logistic regression SPSS method. This model allows to divide all patients into the groups of high and low risk of fatal outcome by means of L calculation (logit, i. e., combination of values of predictive indices with coefficients which have the most predictive effect.

Y= 1/ (1+EXP(-L)).

If the value of Y<0.5, the patient is referred to the high risk group of hospital mortality; if the value of Y<0.5, the patient is referred to a low risk group of hospital mortality.

In our case the linear equation is as follows:

L= -286.5+16.9*A+887.1*B+1.25*C, i.e.

Table.

Mean values in patients with AMI and type 2 DM depending on the outcome of acute period of myocardial infarction

Parameter	Lethal outcome (n=7)	Favorable outcome (n=53)	p
Age, years	74.4 ± 2.9	66.6 ± 1.4	<0.05
TG, mmol/L	1.80 ± 0.16	2.07 ± 0.12	<0.05
LDL, mmol/L	2.86 ± 0.18	1.34 ± 0.15	<0.05
VLDL, mmol/L	0.64 ± 0.05	0.91 ± 0.07	<0.05
Blood glucose, mmol/L	11.74 ± 1.7	9.49 ± 0.58	<0.05
Insulin day 1, mcLU/mL	44.0 ± 2.5	37.0 ± 0.9	<0.05
QUICKI index	0.272 ± 0.045	0.307 ± 0.018	<0.05
sCD40L day 1, ng/mL	3.73 ± 0.06	3.85 ± 0.04	<0.05
sCD40L day 10, ng/mL	3.28 ± 0.08	3.04 ± 0.05	<0.05
Δ sCD40L, %	-12.0 ± 3.0	-21.0 ± 1.0	<0.05
sVE-cadherin day 1, ng/mL	1.73 ± 0.08	1.80 ± 0.03	<0.05
sVE-cadherin day 10, ng/mL	1.54 ± 0.08	1.47 ± 0.03	<0.05
Δ sVE-cadherin, %	-11.0 ± 3.0	-18.0 ± 1.0	<0.05

Note: p – difference validity (p<0.05).

Y= 1/(1+EXP(286.5+16.9*A+887.1*B+1.25*C)), *where*

Y – the group of hospital death risk in AMI patients with DM2;

A – LDL level, mmol/L;

B – QUICKI;

C – correlation between sCD40L-ligand level at day 1 of AMI and sCD40L-ligand level, determined at day 10 of AMI, %.

Diagnostic efficiency of the above mentioned model (percentage of right predictions) was 96.7%. Constructing the model demonstrated its connection with probability of cardiovascular death development in acute period of myocardial infarction as a ROC-curve **(figure).**

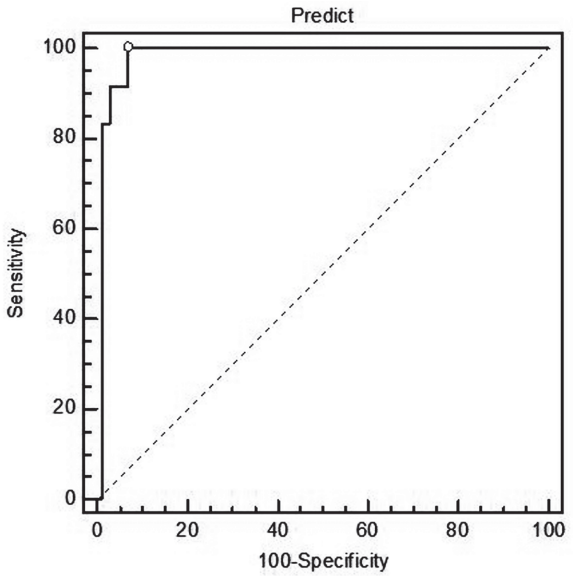

Figure. Predictive power ROC-curve for the model of AMI hospital mortality prediction.

The ROC-curve analysis revealed a 96.7% specificity of the model in prediction of mortality within the acute period of myocardial infarction in patients with type 2 DM (AUC=0.984; p<0.0001).

Conclusions

1. It has been established that for those patients with concurrent type 2 diabetes mellitus died in acute period of myocardial infarction it was typical to demonstrate higher levels of LDLP, blood insulin; less level of insulin resistance index QUICKI level, as well as less dynamics of decrease of the marker of endothelium injury – sVE-cadherin and sCD40L-ligand on the background of the treatment that proves negative influence of insulin resistance, dyslipidemia and endothelial dysfunction on the outcome of the disease.

2. With the aim to predict cardiovascular death within the acute period of myocardial infarction, the model of risk group stratification of the patients with concurrent type 2 diabetes mellitus was developed that will allow to increase survival and widen the possibilities of the treatment tactics for the patient management in this category.

Prospects for further studies. Thus, the carried research determined a model of prediction of hospital mortality in the patients with type two diabetes mellitus has been developed, that widens considerably the resources of their therapeutic correction and favors the survival increase for further studies.

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МОДЕЛЬ ПРОГНОЗУВАННЯ ГОСПІТАЛЬНОЇ ЛЕТАЛЬНОСТІ У ХВОРИХ НА ГОСТРИЙ ІНФАРКТ МІОКАРДА З СУПУТНІМ ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ

Заїкіна Т. С.

Резюме. Обстежено 60 хворих на гострий інфаркт міокарда з супутнім цукровим діабетом 2 типу, яких було розподілено на групи в залежності від настання або ненастання несприятливої кінцевої точки (серцево-судинної смерті) протягом гострого періоду інфаркту міокарда. Задля оцінки впливу ендотеліальної дисфункції, інсулінорезистентності та дисліпідемії на короткостроковий прогноз хворих інфарктом міокарда, на 1-й та на 10-й день інфаркту міокарду визначалися рівні маркерів пошкодження ендотелію – sCD40-ліганду,

sVE-кадгерину, а також інсуліну крові, рівні загального холестерину та його фракцій. Потім за методом покрокової логістичної регресії побудовано модель прогнозування госпітальної летальності. Встановлено, що померлі в гострий період інфаркту міокарда хворі з супутнім цукровим діабетом 2 типу, характеризувалися більш високими рівнями ЛПНЩ, інсуліну крові, меншим рівнем індексу інсулінорезистентності QUICKI, а також меншою динамікою зниження маркеру пошкодження ендотелію sVE-кадгерину та sCD40-ліганду на тлі лікування, що свідчить про негативний вплив інсулінорезистентності, дисліпідемії та ендотеліальної дисфункції на результат захворювання.

Ключові слова: гострий інфаркт міокарда, цукровий діабет 2 типу, госпітальна летальність, короткостроковий прогноз, ендотеліальна дисфункція.

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МОДЕЛЬ ПРОГНОЗИРОВАНИЯ ГОСПИТАЛЬНОЙ ЛЕТАЛЬНОСТИ У БОЛЬНЫХ С ОСТРЫМ ИНФАРКТОМ МИОКАРДА И СОПУТСТВУЮЩИМ САХАРНЫМ ДИАБЕТОМ 2 ТИПА

Заикина Т. С.

Резюме. Обследовано 60 больных с острым инфарктом миокарда и сахарным диабетом 2 типа, которые были разделены на группы в зависимости от развития неблагоприятной конечной точки (сердечно-сосудистая смерть) в течение острого периода инфаркта миокарда. Для оценки влияния эндотелиальной дисфункции, инсулинорезистентности и дислипидемии на краткосрочный прогноз больных с инфарктом миокарда, на 1-й и 10-й день определялись уровни маркеров повреждения эндотелия – sCD40-лиганда, sVE-кадгерина, а также инсулина крови, уровни общего холестерина и его фракций. Затем методом пошаговой логистической регрессии была построена модель прогнозирования госпитальной летальности. Установлено, что умершие в острый инфаркт миокарда больные с сахарным диабетом 2 типа, характеризовались более высоким уровнем ЛПНП, инсулина крови, сниженным уровнем индекса инсулинорезистентности QUICKI, а также замедленным снижением уровней маркеров повреждения эндотелия – sVE-кадгерина и sCD40-лиганда на фоне лечения, что подтверждает негативное влияние инсулинорезистентности, дислипидемии и эндотелиальной дисфункции на краткосрочный прогноз заболевания.

Ключевые слова: острый инфаркт миокарда, сахарный диабет 2 типа, госпитальная летальность, краткосрочный прогноз, эндотелиальная дисфункция.

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sVE-cadherin blood serum level and sCD40L level were determined with commercial enzyme linked immunosorbent assay ELISA kit, and all these were performed with Automated EIA Analyzer «LabLine-90» (Austria). Levels of total cholesterol, LDL, VLDL, HDL and TG were measured biochemically. QUICKI index was measured mathematically. The data were processed statistically with Microsoft Office Excel software: the mean arithmetial value (M) and standard error of the mean (m) were calculated, for estimated probability and validity of the obtained data, Student's t-test (p) was done. For risk stratification modeling, stepwise logistic regression SPSS method was used.

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L= -286.5+16.9*A+887.1*B+1.25*C, i.e.

Y= 1/(1+EXP(286.5+16.9*A+887.1*B+1.25*C)), where

Y – the group of hospital death risk in AMI patients with DM2; A – LDL level, mmol/L; B – QUICKI; C – correlation between sCD40L-ligand level at day 1 of AMI and sCD40L-ligand level, determined at day 10 of AMI, %.

Diagnostic efficiency of the above mentioned model (percentage of right predictions) was 96.7%.

Conclusions. With the aim to predict cardiovascular death within the acute period of myocardial infarction, the model of risk group stratification of the patients with concurrent type 2 diabetes mellitus was developed that will allow to increase survival and widen the possibilities of the treatment tactics for the patient management in this category.

Keywords: acute myocardial infarction, diabetes mellitus, hospital mortality, short-term prognosis, endothelial dysfunction.

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