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POSSIBILITIES OF FORECASTING COMPLICATIONS IN PATIENTS WITH METABOLIC SYNDROME

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In the period from 2013 to 2016, 364 patients aged 20 to 80 years (200 men and 164 women) with newly diagnosed metabolic syndrome were prospectively examined. In patients aged 20–60 years and in the age group 61–80 years, the analysis of the results of the examination of patients with metabolic syndrome allowed us to build a number of regression models that allow predicting variants of metabolic syndrome: diabetic, hypertensive or combined. A study of the incidence of complications of metabolic syndrome showed that in the age group of 20–40 years the incidence of myocardial infarction was 1.9 % and that of ischemic stroke in 0.96 %, in the age group 41–60 years, respectively, 14.5 and 7.6 %; In the group of patients older than 60 years – myocardial infarction was observed in 12.9 % of patients, ischemic stroke in 6.7 % of cases. The analysis of the results of the examination of patients with metabolic syndrome allowed us to build a number of regression models that allow predicting variants of the metabolic syndrome. It has been shown that metabolic syndrome is a factor predisposing to atrial fibrillation and a favourable background for the implementation of risk factors for atrial fibrillation.

Key words: metabolic syndrome, complications, regression analysis, prognostic parameters.

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МОЖЛИВОСТІ ПРОГНОЗУ УСКЛАДНЕННЯ У ХВОРИХ З МЕТАБОЛІЧНИМ СИНДРОМОМ

У період з 2013 по 2016 роки проспективно обстежено 364 пацієнти віком від 20 до 80 років (200 чоловіків та 164 жінки) з вперше діагностованим метаболічним синдромом. У пацієнтів віком 20–60 років та у віковій групі 61–80 років аналіз результатів обстеження хворих на метаболічний синдром дозволив побудувати ряд регресійних моделей, що дозволяють прогнозувати варіанти метаболічного синдрому: діабетичний, гіпертонічний або комбінований. Дослідження частоти ускладнень метаболічного синдрому показало, що у віковій групі 20–40 років частота інфаркту міокарда склала 1,9 %, а ішемічного інсульту – 0,96 %, у віковій групі 41–60 років відповідно 14,5 та 7,6 %; у групі пацієнтів віком від 60 років – інфаркт міокарда спостерігався у 12,9 % пацієнтів, ішемічний інсульт – у 6,7 % випадків. Аналіз результатів обстеження хворих на метаболічний синдром дозволив побудувати ряд регресійних моделей, що дозволяють прогнозувати варіанти метаболічного синдрому. Показано, що метаболічний синдром є фактором, що сприяє фібриляції передсердь і сприятливим фоном для реалізації факторів ризику фібриляції передсердь.

Ключові слова: метаболічний синдром, ускладнення, регресійний аналіз, прогностичні параметри.

The work is a fragment of the doctoral dissertation “Features of the course and prediction of manifestations of metabolic syndrome in individuals of different age groups”

It is widely recognized that the prevalence of metabolic syndrome (MS) in many countries of the world became epidemic [1, 3, 5]. In a number of studies, it was shown that the incidence of myocardial infarction in patients with diabetes mellitus (DM) with arterial hypertension (AH) was 3.5 times, and that of stroke was 16.5 times higher than with DM without AH [2]. Thus, diabetes and hypertension are two interrelating components of a deployed complicated MS that affect a variety of target organs: the heart and trunk vessels, the kidneys, the brain, the microvascular bed of virtually all internal organs. There are data that in persons with MS the total cardiovascular risk of developing myocardial infarction (MI) (estimated

by the PROCAM model, Germany) in the next 8 years will be 30 %, which is 5 times higher in comparison with the isolated AH group and 2 times higher in comparison with a group with a combination of hypertension and hypercholesterolemia [5, 12]. A prospective study of the Kuopio Ischemic Heart Disease Risk Factors Study showed that among patients with MS, ischemic heart disease (IHD) developed 3–4 times more often, the mortality from coronary heart disease was 3 times higher, and the mortality from all causes was 2 times higher than in patients without MS [2, 9].

Recently, more attention has been devoted to studying the possibilities of predicting the development of this pathological condition and its various complications. The use of the integrated approach to the analysis of MS allows, first of all, to improve diagnostics, assess adaptive reserves of the organism, and also identify patients with a high risk of complications, including myocardial infarction and strokes [2, 3, 4].

At the same time, reports on the prognosis of the course of the MS and its complications are not systematized; their results do not yet allow assessing the significance of various signs in the development of complications of this pathological condition in different age groups [2, 5, 9]. All this testifies to the need to carry out attempts of this type of research using methods of mathematical modelling.

The purpose of the work was to develop approaches to predicting the development of complications of metabolic syndrome and to receive models for statistical data.

Materials and methods. The study was carried out on the basis of the Educational–therapeutic building of the Azerbaijan Medical University. In the period from 2013 to 2016 years, 364 patients aged from 20 to 80 years (200 men and 164 women) with a newly diagnosed MS were prospectively examined. Among them 134 were patients aged 20 to 40 years, there were 131 patients at the age of 41–60 years, 129 patients – 61 years of age and older. To study the features of MS in these patients, a clinical examination was conducted with the study of complaints and anamnesis of patients, the use of clinical, instrumental and laboratory methods of examination.

The study included individuals who had different manifestations of MS: abdominal obesity (AO), AH, impaired glucose tolerance (IGT) and/or type 2 diabetes mellitus (DM2), dyslipidemia (DLP), overweight and/or obesity of different degrees.

The criteria for the excluding patients from the survey were: symptomatic hypertension; signs of cerebral circulation disorders or myocardial infarction in history, chronic nonspecific lung diseases, kidney and liver diseases, unstable angina, atrial fibrillation, signs of heart failure. The study also did not include patients receiving permanent medical therapy for hypertension, stress angina or type 2 diabetes, as well as those taking glucocorticoids, oral contraceptive drugs, nonsteroidal anti-inflammatory drugs and more than 50 grams of alcohol daily.

To diagnose metabolic syndrome, the definition of the expert commission of the International Federation of Diabetes (2015) was used.

The analysis of complications of MS was carried out according to the incidence of myocardial infarction (MI) and acute cerebrovascular disturbances of the ischemic stroke (IS) in MS patients in different age groups.

In order to predict the nature of the course of the MS and its complications, regression analysis of the obtained data set was carried out. It is known that the purpose of regression analysis is to measure the relationship between the dependent variable and one (paired regression analysis) or several (multiple) independent variables. Independent variables are also called factorial, explanatory, determinative, repressors and predictors. A dependent variable is sometimes called a definable, explainable, response. As independent variables in the present study, we used individual characteristics characterizing the states of patients with MS, whereas the dependent outcome was the outcome of the disease or the nature of the course of MS (AH, CD2 and combination of AH and CD2) or its complications (myocardial infarction, stroke, disorders of cardiac rhythm of high gradations).

To include in the regression analysis of the necessary characteristics characterizing the patients included in the study, the informative character of the independent signs of MS was previously determined.

Statistical processing of the results was carried out in the statistical analysis system STATISTICA 10 (software package STATISTICA USA, version 10 for Windows 8). In all samples, the nature of the distribution for normality was determined according to the Kolmogorov–Smirnov, Shapiro–Willkie and Leuven tests. The parametric Student's test was used for comparative analysis.

The influence of individual signs of patients and their weight coefficients on the nature of the course of MS and its complications was investigated using factor analysis in the Statistics 10 program.

Results of the study and their discussion. The studies have shown the heterogeneity of the manifestations of MS and its complications in different age groups, which are characterized by different prognostic parameters. Taking these parameters into account will make it possible to predict both variants of the MS flow and its complications.

Assessment of the frequency of complications of MS during the observed period (five years) – myocardial infarction and ischemic stroke (IS) in different age groups showed that in the general group of patients MI developed in 12.9 % of patients, IS in 6.7 % of cases. (table 1).

Table 1

The frequency of MI and IS during 5-year period in patients with MS in different age groups

Complications	20–40 years n=104		41–60 years n=131		61–80 years n=129		Total n=364	
	abs.	%	abs.	%	abs.	%	abs.	%
MI	2	1.9	19	14.5	26	20.1*	47	12.9
IS	1	0.96	10	7.6*	14	10.8*	25	6.7

Note: The differences are significant (at $p < 0.05$) with respect to the age group of 20–40 years.

A significant increase in the frequency of MI and IS from the age of the patients was revealed. So, in the age group of 20–40 years during the observed period, the IM rate was 1.9 %, IS was observed in 0.96 % of the patients. In the group of patients aged 41 to 60 years, the incidence of MI was 14.5 %, the incidence of IS was 7.6 %. The values of these indicators were significantly higher than the corresponding indices in the first age group ($p < 0.05$). There was an increase in the incidence of MI and IS in patients older than 60 years, which were noted respectively in 20.1 % and 10 % of patients, the values of these parameters were higher than of young patients ($p < 0.05$), but did not differ significantly from those in patients of the second group.

Taking into account a relatively low incidence of complications, such as MI and IS in the age group of patients 20–40 years, a prognosis of the development of these complications in the age groups of 20–60 years and 60–80 years was made.

Based on the obtained data, a regression model for MI as a dependent factor (MI) was constructed. This model was significant ($p < 0.05$), it correctly explains the relationship between the studied variables, that is, the dependence of MI in the groups of 20–60 and 61–80 years on independent variables, the determination coefficient of the models was $R=0.59$ and $R=0.65$.

Assessment of the probability of occurrence of MI in the age group of 20–60 years showed high predictive value of such indicators as AO duration, duration of ischemic heart disease (IHD), duration of IGT (impaired glucose tolerance), IGT, Triglycerides (TG), low-density lipoproteins (LDL), prothrombin index (PTI), high-frequency waves (HF), ST-segment depression and ejection fraction (EF). Based on these indicators, regression equations are constructed for predicting MI in persons of this group:

$IM(20-60) = 0.74 + 0.01 \text{ AO long} + 0.02 \text{ IHD long} + 0.028 \text{ IGT long} + 0.01 \text{ IGT} + 0.029 \text{ TG} + 0.12 \text{ LDL} + 0.04 \text{ PTI} - 0.6 \text{ HF} + 0.008 \text{ ST dep} - 0.027 \text{ EF}$

Note:

AO long – Duration of abdominal obesity

IHD long – Duration of IHD

IGT long – Duration of IGT

Model specifications:

The results for the dependent variable are: MI (Spreadsheet 3);

$R=0.776778794$; $RI=0.589486$; $F(22.212)=2.6994$; $p < 0.0001$

In the age group of 61–80 years, the prognostically informative index was the duration of the AO, the duration of IHD, the duration of IGT, IGT, TG, high-density lipoproteins (HDL), PTI, HF, ST segment depression and APSr (systolic arterial pressure), which allowed to construct the regression equation of the following type:

$IM(61-80) = 0.74 + 0.013 \text{ AO long} + 0.02 \text{ IHD long} + 0.045 \text{ IGT long} + 0.18 \text{ IGT} + 0.17 \text{ TG} - 2.04 \text{ HDL} + 0.006 \text{ PTI} - 0.009 \text{ HF} + 0.35 \text{ ST dep} + 0.126 \text{ APSr}$

Model specifications:

The results for the dependent variable: DM2 (Spreadsheet 3)

$R=0.80538497$; $RI=0.64864494$; $F(22.106)=1.2606$; $P < 0.0216$

In both equations, the duration of previous MI states – AO duration, IHD duration, IGT duration, as well as IGT, ST-segment depression and low-frequency wave spectrum in spectral analysis of cardiac rhythm (HF), are of considerable informative value.

Similarly, using the multiple regression method, prognostic models of the probability of IS development in age groups of 20 to 60 years and 61 to 80 years have been constructed. The obtained prognostic models are statistically significant for both age groups ($p < 0.05$).

It has been established that the following parameters are predictive for IS: the duration of the AO, the duration of IHD, the duration of IGT, IGT, LDL, PTI, APSr, the blood flow velocity in the internal cerebral artery in systole, ($V_{ps} \text{ Iy}$) and the blood flow velocity in the internal cerebral artery in diastole

(Ved Iy) (for the age group of 20–60 years), as well as BMI, AOlong, IGT long, Glucose level, IGT, LDL, PTI, Vps Iy and Ved Iy – for the age group of 61–80 years.

The regression equations constructed on the basis of these parameters for the group of patients aged 20–60 years are as follows:

IS (20–60)=– 0.84+0.12 AO long+0.10 IHD long+0.07 IGT long+0.06 IGT+0.12 LDL+0.15 PTI+0.24 APSr+0.17Vps Iy+0. 10Ved Iy

Model specifications:

Regression results for the dependent variable: MI (Spreadsheet 3) R=0.79993674; RI=0.639898788; F (26.208)=1.1163; P<0.0325

Model for the age group of 61–80 years:

IS (61–80)=4.73+0.15 BMI+0.04 AO long+0.14 IGT long + 0.05 Glucose + 0.30 IGT + 0.12 LDL + 0.20 PTI + 0.26Vps Iy + 0.22Ved Iy

Model specifications:

Regression results for the dependent variable: DM2 (Spreadsheet 3);

R=0.83988036; RI=0.705398; F (26.102)=0.94121; P<0.0452

As it can be seen, the members of the regression equations are the main prognostic signs of cerebral stroke in the study groups. Both of patients aged 20–60 years and in the age group of 61–80 years, the following are the main prognostic signs: AO duration, duration of IGT, IGT, PTI, LDL, and Vps Iy and Ved Iy, reflecting the blood flow velocity in the internal cerebral artery, which indirectly indicate the degree of narrowing of the cerebral arteries.

Thus, the analysis of the results of the examination of MS patients made it possible to construct a number of regression models that allow predicting the variants of MS. High informativity and reliability of the received models are confirmed by corresponding values of coefficients of determination and informativity, and also by a level of reliability. The obtained models were statistically significant, the determination coefficients were high – 0.79, 0.70, 0.74 for the corresponding variants of the MS in the first group; 0.61, 0.63, 0.63 – for corresponding variants in the second age group and 0.65, 0.65 and 0.62 – in the third age group.

It was established, for predicting the variants of MS prognostically important parameters are IGT, level of fasting glucose, TG, HDLP, immunoregulatory insulin (IRI), EF, waste circumference (WC), body mass index (BMI), HF, LF, left ventricular miocardial mass (LVMM), duration of AO, arterial pressure at rest (APSr.), arterial pressure in effort (APSeff.), pulse in night (Ps n), HF. These parameters with different regression coefficients are included in the regression equations, which characterizes the significance of these indicators for predicting the variants of MS – diabetic, hypertensive or combined.

A study of the incidence of complications of MS showed that in the age group of 20–40 years the incidence of MI was 1.9 %, and that of IS in 0.96 %, in the age group 41–60 years, respectively, 14.5 and 7.6 %; In the group of patients older than 60 years – MI was observed in 12.9 % of patients, IS in 6.7 % of cases.

It was established that prognostically important parameters for the prognosis of myocardial infarction were such characteristics as AO duration, IHD duration, duration of IGT, IGT, TG, HDL, PTI, HF, ST segment depression and APSr. For the prediction of the IS, the AO duration, the duration of the IGT, IGT, PTI, LDL, and also Vps Iy and Ved Iy have high information value.

It should be noted that to predict MI highly informative is the indicator such as ST segment depression, and in terms of IS prediction, the duration of manifestation of certain conditions, in particular AO and IGT, additionally highly informative in this group were Vps Iy and Ved Iy reflecting the blood flow velocity in the internal cerebral artery.

The conducted studies showed the heterogeneity of MS manifestations and its complications in different age groups, which are characterized by different prognostic parameters. Taking into account these, parameters will make it possible to predict both variants of the MS and its complications.

The data obtained by us agree with the results of a number of authors. Thus, in the study, [3] the authors evaluated the VAI index of visceral obesity as a diagnostic marker for MS and its potential for use in predicting the risk of developing cardiovascular complications of MS compared to other conventional anthropometric parameters (WC, BMI, WC/Hip circumference (HC), WC/Height, TG/HDL) . The study included 301 patients (148 men and 153 women). MS was detected in 108 respondents (35.9 %). Significant positive correlations were found between VAI and BP, fasting blood glucose level, LDL, negative relationship between VAI and adiponectin level. The obtained data testified that significant predictors for the diagnosis of MS were the ratio of WC/Height, TG/HDL and VAI (p<0.0001). Based on the results of multiple regression analysis, VAI, the ratio of WC/height and adiponectin level were independent risk factors for cardiovascular complications of MS, risk factors for the development of type 2 diabetes, VAI, TG/HDL ratio

and adiponectin level. The authors concluded that the possibility of using the visceral obesity index for predicting the risk of cardiovascular complications of the latter has been shown [3].

It is shown that MS is a factor predisposing to atrial fibrillation (AFib), a favourable background for the realization of risk factors for AFib. An example is a study by K. Umetani et al. [9]. The authors examined 592 patients without obvious structural changes in the heart. Multivariate regression analysis showed that MS is a significant risk factor for paroxysmal AFib, not related to the size of the left atrium (>44 mm) or age (>70 years). According to the researchers, the basis of a high risk of AFib in MS may be alimentary obesity [10]. In general, the view on the development of cardiovascular diseases and complications, as well as on cerebrovascular disorders through the prism of MS, is of great clinical importance, since on the one hand, this condition is reversible and, with appropriate treatment, it is possible to achieve the disappearance or decrease in the severity of its main manifestations, and on the other hand, it precedes the emergence of such pathological conditions and diseases as atherosclerosis, MI, IS, type 2 diabetes, AH – diseases, are currently the main causes of increased mortality [9, 12]. Affecting even one of the components of the MS, it is possible to achieve significant improvement by compensating for changes in other links of its pathogenesis [9].

Conclusion

The studies have shown the heterogeneity of the manifestations of MS and its complications in different age groups, which are characterized by different prognostic parameters. Taking these parameters into account will make it possible to predict both variants of the MS flow and its complications.

Assessment of the frequency of complications of MS during the observed period (five years) – myocardial infarction and ischemic stroke (IS) in different age groups showed that in the general group of patients MI developed in 12.9 % of patients, IS in 6.7 % of cases. The differences are significant (at $p < 0.05$) with respect to the age group of 20–40 years.

A significant increase in the frequency of MI and IS from the age of the patients was revealed. So, in the age group of 20–40 years during the observed period, the IM rate was 1.9 %, IS was observed in 0.96 % of the patients. In the group of patients aged 41 to 60 years, the incidence of MI was 14.5 %, the incidence of IS was 7.6 %. The values of these indicators were significantly higher than the corresponding indices in the first age group ($p < 0.05$). There was an increase in the incidence of MI and IS in patients older than 60 years, which were noted respectively in 20.1 % and 10 % of patients, the values of these parameters were higher than of young patients ($p < 0.05$), but did not differ significantly from those in patients of the second group.

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In general, the results obtained confirm that for effective prevention and treatment of patients with MS, it is necessary to have information on the nature of the course of this syndrome, which can be solved to some extent by predicting MS variants and their complications based on the use of factor analysis.

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DYNAMICS OF CLINICAL-FUNCTIONAL PARAMETERS IN PATIENTS WITH STABLE CORONARY HEART DISEASE AFTER THE REVASCULARIZATION TAKING INTO ACCOUNT THE PROGRAMS OF RESTORATIVE TREATMENT

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Restorative treatment of patients with stable coronary heart disease is an important component of a comprehensive approach after the revascularization procedures. Our studies performed have shown that the dynamics of clinical-functional parameters in such patients depend on the applied programs of the restorative treatment. The use of standard therapy and restorative treatment programs has improved the quality of life by increasing physical activity, reducing angina pectoris attacks, increasing the treatment satisfaction and attitude towards illness. The developed author's program of "Clinical-psychological rehabilitation of cardiologic patients by optimization of the internal picture of health" in combination with standard treatment and suggestive therapy, has contributed to the positive dynamics of clinical, functional, psychological components and positive impact on the long-term consequences of the disease course.

Key words: coronary intervention, suggestive therapy, picture of health, rehabilitation.

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ДИНАМІКА КЛІНІКО-ФУНКЦІОНАЛЬНИХ ПОКАЗНИКІВ ХВОРИХ НА СТАБІЛЬНУ ШЕМИЧНУ ХВОРОБУ СЕРЦЯ ПІСЛЯ ПРОВЕДЕННЯ РЕВАСКУЛЯРИЗАЦІЇ ІЗ УРАХУВАННЯМ ПРОГРАМ ВІДНОВНОГО ЛІКУВАННЯ

Відновне лікування хворих на стабільну шемічну хворобу серця є важливою складовою комплексного підходу після проведення ревазуляризаційних процедур. Проведені нами дослідження показали, що динаміка показників у таких хворих залежить від застосованих програм відновного лікування. Застосування стандартного лікування та програми відновного лікування сприяло покращенню якості життя шляхом збільшення об'єму фізичних навантажень, зменшення нападів стенокардії, зростання задоволення лікуванням та відношення до хвороби. Розроблена авторська програма «Клініко-психологічної реабілітації кардіологічних хворих шляхом оптимізації внутрішньої картини здоров'я» у поєднанні із стандартним лікуванням та сугестивною терапією, сприяла позитивній динаміці клінічних, функціональних, психологічних складових та позитивному впливу на віддалені наслідки перебігу захворювання.

Ключові слова: коронарне втручання, сугестивна терапія, картина здоров'я, реабілітація.

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The diseases of the cardiovascular system are among the causes of disability and mortality [3, 9]. According to WHO forecasts up to 2030, the number of deaths because of diseases of the circulatory system will increase up to 25 million [5]. In Ukraine, cardiovascular diseases kill about 500,000 people a year, and in Europe – more than 4 million people. Over the past thirty years in our country, there has been an increase in cardiovascular diseases 3.5-fold, while the mortality rate has increased by 46 % [2].