сосудистого генеза наблюдалось недостаточное снижение АД ночью в сравнении с пациентами группы 1. У большинства (58,9 %) пациентов, скорость нарастания $АД_{сист.}$ утром была увеличена, что свидетельствовало про вероятность негативного влияния на сосудистую систему в отсутствие явных признаков нагрузки АД даже на фоне антигипертензивной терапии у пациентов с начальными проявлениями ХИМ. Увеличение нагрузки систолическим АД ночью значимо влияло на риск структурного поражения головного мозга.

Ключевые слова: суточное мониторирование артериального давления, хроническая ишемия мозга, начальные проявления.

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according MRI, there was an insufficient reduction in blood pressure at night compared with patients in group 1. In the majority (58.9%) of patients the rate of rising of systolic blood pressure in the morning was increased, which indicated a possibility of negative influence on the vascular system in the absence of obvious signs of the burden of blood pressure even at the background of antihypertensive therapy in patients with initial manifestations of chronic cerebral ischemia. Increased load by systolic blood pressure at night significantly affected the risk of structural damage of the brain.

Keywords: ambulatory blood pressure monitoring, chronic cerebral ischemia, the initial stages of the disease.

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PREDICTION OF ARTERIAL HYPERTENSION DEVELOPMENT IN PATIENTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS USING LOGISTIC REGRESSION

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The article presents some possibilities of the method of evaluating the development of arterial hypertension (AH) in patients with newly diagnosed type 2 diabetes mellitus through the development of a mathematical model for predicting AH occurrence by the levels of statistically proven biochemical and anthropometric indicators.

Key words: type 2 diabetes mellitus, arterial hypertension, mathematical prediction

The study is a fragment of the research project "Pathology of the Respiratory, Cardiovascular and Digestive Systems in Patients with Diabetes Mellitus and Obesity: Features of Pathogenesis, Diagnosis and Treatment", state registration No. 0116U004505.

Type 2 diabetes mellitus (DM) is a global medical and social problem, since its development and progression are associated with a considerable number of disability cases, as well as an increase in mortality rates due to its cardiovascular complications worldwide [4]. Numerous prospective studies have demonstrated that in type 2 DM without co-existent AH, the risk of developing ischaemic heart disease (IHD) and cerebral stroke is 2-3 times higher and the risk of developing renal failure is 15-20 times higher as compared to the population without DM. The coexistence of DM and AH increases the risk of developing such complications twofold even in satisfactory control of glycemia and dyslipidemia [1, 2, 7, 9].

The purpose of the study was to develop a mathematical model for predicting the occurrence of cardiovascular complications, namely AH, in patients with newly diagnosed type 2 DM by the levels of statistically proven biochemical and anthropometric indicators.

Materials and methods. There were examined 40 patients with newly diagnosed type 2 DM without cardiovascular pathology at baseline. All the patients underwent complete physical examination, laboratory, clinical and instrumental examinations, enzyme immunoassay testing.

All the patients underwent an anthropometric evaluation. To diagnose obesity and its degree, there were used the World Health Organization (WHO) classification criteria and the determination of body mass index (BMI) by the following formula: BMI = body weight (kg) / height (m^2) [8]. The diagnosis of type 2 DM was made according to the recommendations of the WHO experts.

The concentration of total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol was determined using the peroxidase method by means of Cholesterol liquicolor reagent kits (Human Diagnostics, Germany); the concentration of triglycerides (TG) was determined using the enzymatic colorimetric method by means of Triglycerides GPO method reagent kit (Human Diagnostics, Germany); the concentration of LDL cholesterol was determined using the enzymatic colorimetric method by means of Human diagnostic kits (Human Diagnostics, Germany).

Enzyme immunoassay testing (a solid-phase enzyme linked immunosorbent assay) included the determination of serum insulin and leptin levels using the commercial ELISA kits (DRG Diagnostics, Marburg, Germany), the determination of serum resistin levels using the commercial ELISA kits

(BioVendor, Czech Republic), the determination of serum C-peptide levels by ELISA using a commercial assay kit (Monobind Inc., CA, USA), the determination of serum soluble platelet selectin (sP-selectin) levels using a commercially available ELISA kit (Bender MedSystems GmbH, Vienna, Austria), tumor necrosis factor-α (TNF-α) levels using the commercially available ELISA kits (Diaclone, France). Serum level of glycated haemoglobin (HbA_1C) was determined using a highly sensitive cation-exchange high-performance liquid chromatography method by means of a semi-automatic analyzer the D-10 and reagent kits (Bio-Rad, USA).

In our research work, we have analyzed 16 factors, namely the patients' age, BMI, the waist-to-hip ratio (WHR), the levels of leptin, resistin, sP-selectin, IL-2, IL-6, TNF-α, HbA_1C, insulin, C-peptide, TC, LDL cholesterol, HDL cholesterol, non-esterified fatty acids (NEFA) which, according to the literature and own observations, could affect AH development in patients with type 2 DM [5 – 6]. Information on these factors was analyzed immediately after the detection of type 2 DM and if the patient did not suffer from any cardiovascular pathology. Then, after a certain period of time (12 months), health status of patients included in the study was analyzed for the occurrence of cardiovascular pathology.

The method of logistic regression was used to establish the reliability of the influence of the aforementioned factors on the development of AH in patients with newly diagnosed type 2 DM but without this complication who were under our observation for a year. This statistical method allows identifying factors that have prognostic value for AH development in their combination among all the biochemical and anthropometric indicators being recorded in a patient when detecting type 2 DM. Logistic regression is applied to detect the relationship between one dependent variable and one or more independent variables, as well as to predict the value of one dependent variable (e.g. AH occurrence) based on the value of other (independent) variables. This method is used if dependent variable can take on two values only which completely corresponds to our tasks [3]. This statistical method allows identifying factors that have prognostic value for AH development in their combination among all the biochemical and anthropometric indicators being recorded in a patient when detecting type 2 DM. Logistic regression is applied to detect the relationship between one dependent variable and one or more independent variables, as well as to predict the value of one dependent variable (e.g. AH occurrence) based on the value of other (independent) variables. This method is used if dependent variable can take on two values only which completely corresponds to our tasks [3].

The stepwise logistic regression method with the inclusion of signs was applied and approximately 50 iterations (the process of applying mathematical operation repeatedly using different data which allows us to gradually approach the correct result) were performed in every analysis to create the most accurate model.

With the use of regression analysis, there were identified risk factors for AH development.

The evaluation (Z) of AH development is carried out by the formula:

$$Z = K + \beta_1 x_1 + \beta_2 x_2 + \dots \beta_n x_n, \qquad (1)$$

where K is a constant,

β_i are coefficients of each factor,

x_i are factor values.

Accordingly, the following formula is used to evaluate the development of AH:

Z = 2.81*BMI + 0.458*resistin + 0.012*sP-selectin + 0.311*IL-6 + 0.1228*TNF-α – 0.995* LDL cholesterol – 106.87

If the result is less than 50%, it is assessed as a "minimal risk" for AH development; if the result is greater than 50%, it is assessed as a "high risk" for AH development.

The probability of AH occurrence (p) depending on the selected factors is calculated by the formula:

$$p = \frac{1}{1+e^{-z}} * 100\% \qquad (2)$$

where e = 2.72... is the base for natural logarithms.

Results of the study and their discussion. We have determined which factors among 16 analyzed affect the probability of AH development and what effect has their combination in patients with newly diagnosed type 2 DM.

The values of regression coefficients of selected factors are presented in Table 1.

Table 1

Results of regression coefficients towards probability of AH development in patients with newly diagnosed type 2 DM according to the method of logistic regression

No	Factors	Symbol	Regression coefficient (β_i)
1.	BMI, kg/m^2	A	2.810
2.	Resistin, ng/ml	B	0.458
3.	sP-selectin, ng/ml	C	0.012
4.	IL-6, pg/ml	D	0.311
5.	TNF-α, pg/ml	E	0.122
6.	LDL cholesterol, mmol/l	F	0.995
	Constant β_0		-106.87

The reliability of the calculated coefficients was verified using the Wald method; the reliability of the model was verified using the Chi-Square test. Chi-Square value of 13.003 indicates a reliable model with error probability of 4.3% (p=0.043).

Nagelkerke R Square value of 0.95 allows us to assert that in all the patients with newly diagnosed type 2 DM, the combined effect of 6 factors analyzed determinates the development of AH in 95%, while in 5 %, AH occurrence is determined by other factors being not included in the regression model.

Accordingly, we can state that among 16 factors analyzed, six factors, namely the levels of resistin, sP-selectin, IL-6, TNF-α, LDL cholesterol and BMI may provoke AH development in patients with newly diagnosed type 2 DM i.e. the higher the values of factors analyzed, the higher probability of AH occurrence.

Having applied the results obtained using the method of logistic regression to the formula, we have obtained Z value for the determination of the probability of AH development (1.1):

$$Z = 2.81*A+0.458*B+0.012*C+0.311*D+0.122*E-0.995*F-106.87 \quad (1.1),$$

where: A – BMI, kg/m^2;
B – resistin, ng/ml
C – sP-selectin, ng/ml;
D – IL-6, pg/ml;
E – TNF-α, pg/ml;
F – LDL cholesterol, mmol/l.

We present some cases of the prediction of AH development in patients with newly diagnosed type 2 DM.

Clinical case 1. A 43-year-old patient A. presented with newly diagnosed type 2 DM. According to examination results, BMI was 34.0 kg/m^2, resistin level was found to be 4.11 ng/ml, sP-selectin level was 280.21 ng/ml, IL-6 concentration was 0.78 pg/ml, TNF-α level was found to be 2.47 pg/ml, LDL cholesterol level was 3.24 mmol/l.

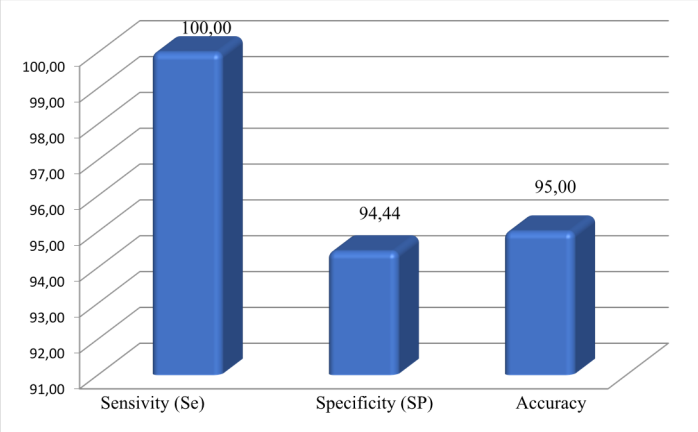

Fig. 1. Criteria for diagnostic accuracy of the proposed model for predicting AH development according to the method of logistic regression

Having carried out the necessary calculations according to the formula (1.1), Z value for the risk of AH development was found to be "-2.23" and the individual risk of AH development was 9.67%.

Thus, we obtained a low value for the probability of AH development, i.e. in appropriate pathogenetic therapy, this patient would not develop AH. Further observation for 12 months demonstrated that this patient did not develop any symptoms of AH, i.e. our model was correct.

Clinical case 4. A 60-year-old patient B. presented with newly diagnosed type 2 DM. According to examination results, BMI was 35.28 kg/m^2, resistin level was found to be 1.98 ng/ml, sP-selectin level was 220.82 ng/ml, IL-6 concentration was 4.81 pg/ml, TNF-α level was found to be 10.22 pg/ml, LDL cholesterol level was 1.38 mmol/l.

Having carried out the necessary calculations according to the formula (1.1), Z value for the risk of AH development was found to be "0.002" and the individual risk of AH development was 50.05%.

Thus, we obtained high values for the probability of unfavorable prognosis, i.e. in standard therapy, this patient would develop AH. Further observation for 12 months demonstrated that this patient developed the symptoms of AH which coincided with our prognosis.

We have analyzed information on all the patients of the study group to determine the diagnostic accuracy of the proposed model for predicting AH development (Fig.1). The probability of developing AH within a year in preliminary predicted high risk of AH occurrence, i.e. test sensitivity was found to be 100.0%; the probability of the negative result in unfavorable prognosis, i.e. test specificity was found to be 94.44%; the accuracy (the proportion of true positive and true negative test results) was 95.00%.

The probability that the patient would develop AH in positive prognosis, i.e. the positive predictive value was 66.7%; the probability that the patient would not develop AH in unfavorable prognosis, i.e. the negative predictive value was 100.0%.

When analyzing the results obtained, it can be stated that the model for predicting AH development elaborated in this study has 100% sensitivity, i.e. if the prognosis results indicate that the patients is at high risk of AH development – in standard therapy, unfavorable results should be expected. This information is of great practical importance from the medical, social and economic point of view, since it allows the doctor to start the prevention of these diseases even before the onset of their manifestations.

Conclusion

At the same time, the results of specificity of the prognostic models obtained being over 94% indicate that in appropriate pathogenetic therapy, AH development should not be expected.

Mathematical prediction allows detecting patients at high risk of developing unfavorable outcomes. Timely treatment and constant control over risk factors allow selecting an effective pathogenetic method of treatment and reduce the risk of developing cardiovascular complications in patients with type 2 DM.

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Реферати

ПРОГНОЗУВАННЯ РОЗВИТКУ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ У ХВОРИХ ІЗ ВПЕРШЕ ВИЯВЛЕНИМ ДІАБЕТОМ 2 ТИПУ ЗА ДОПОМОГОЮ ЛОГІСТИЧНОЇ РЕГРЕСІЇ

Урбанович А.М., Костіцька І.О., Жураківська О.Я.

У статті представлено деякі можливості методу оцінки розвитку артеріальної гіпертензії (АГ) у хворих на вперше виявлений цукровий діабет 2 типу шляхом розробки математичної моделі прогнозування виникнення АГ за рівнями статистично доведених біохімічних та антропометричних показників.

Ключові слова: цукровий діабет 2 типу, артеріальна гіпертензія, математичне прогнозування.

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ПРОГНОЗИРОВАНИЕ РАЗВИТИЯ АРТЕРИАЛЬНОЙ ГИПЕРТОНИИ У ПАЦИЕНТОВ С ВПЕРВЫЕ ДИАГНОСТИРОВАННЫМ ДИАБЕТОМ 2 ТИПА С ИСПОЛЬЗОВАНИЕМ ЛОГИСТИЧЕСКОЙ РЕГРЕССИИ

Урбанович А.М., Костицкая И.А., Жураковская О.Я.

В статье представлены некоторые возможности метода оценки развития артериальной гипертонии (АГ) у пациентов с впервые диагностированным сахарным диабетом 2 типа путем разработки математической модели прогнозирования возникновения АГ по уровням статистически подтвержденных биохимических и антропометрических показателей.

Ключевые **слова:** сахарный диабет 2 типа, артериальная гипертензия, математическое прогнозирование.

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