

## MEDICAL SCIENCES

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### A MATHEMATICAL MODEL OF PREDICTING THE RISK OF TREATMENT FAILURE IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA

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#### **Abstract**

The article is aimed at elaborating a multi-factorial mathematical model of the treatment efficiency of primary open-angle glaucoma. The scope of investigation includes analyzing the functional parameters of the vision in 127 patients with primary open-angle glaucoma and selecting the significant indicators for evaluating the effectiveness of its treatment. The study revealed four characteristic factors associated with the risk of treatment failure: Method of Treatment, NFL, Vrim, PSD. This set of indicators determined the basis for developing the model of predicting the risk of treatment failure. The sensitivity of the elaborated model was 74.5% (95% CI 60.4% - 85.7%), its specificity was 69.1% (95% CI 56.7% - 79.8%)

**Keywords:** treatment, functional parameters, vision.

#### **Introduction**

The topicality and complexity of the scientific problems concerning the treatment of primary glaucoma is predetermined by both complicacy of the pathogenetic mechanisms of disease development and frequent use of the symptomatic approach to its

prevention and treatment instead of the pathogenetic one. [2]. The number of patients with primary glaucoma are predicted to increase to 79.6 million people by 2020, 74% of them will have primary open angle glaucoma (POAG). In the light of the contemporary understanding primary open-angle glaucoma is considered to be a multi-factorial disease with a threshold effect leading to the glaucomatous optic neuropathy [1]. The development of POAG is closely connected with the microstructural changes revealing at different levels due to violation of many involution and biomechanical processes, mechanisms of blood circulation and vascular autoregulation, acceleration of neural cells apoptosis and decreasing the natural level of neuroprotection [3]. Nowadays the metabolic factors of glaucoma development are insufficiently studied, and the concept of metabolic pathogenesis of glaucomatous optic neuropathy is in the research stage. In the case of glaucoma the destruction of retinal ganglion cells and optic nerve is a slow process, and the phenomenon of parabiosis of axons and nerve fibers is prolonged and reversible. In this regard, neuroprotection should be recognized as one of the promising areas of prevention and treatment of glaucomatous optic neuropathy [4,5]. We have previously reported the experimental and clinical substantiation of applying the neuroprotective therapy in the complex treatment of POAG [6,7]. ]. Despite numerous studies, the problem of assessing both the progression of glaucomatous optic neuropathy in patients with POAG and the effectiveness of treatment remains unresolved. It has predetermined the purpose of our investigation.

### **Material and Methods**

The study of the functional parameters of the organ of vision carried out in 127 patients with POAG. The first group was formed by the patients with POAG of stages I-II and normal intraocular pressure (IOP) (19 patients received conventional treatment and complex neurotropic drugs, 22 patients received only conventional treatment). The second group consisted of the operated POAG patients with normal IOP (21 patients received conventional treatment and complex neurotropic drugs, 20 patients received only conventional treatment). The third group involved the patients with primary open angle glaucoma and IOP normalized by applying the local hypotensive therapy (20 patients received conventional treatment and complex neurotropic drugs, 25 patients received only conventional treatment). The method of treatment of POAG elaborated by us includes traditional treatment and complex

neurotropic therapy (non-competitive antagonist of glutamate NMDA-receptors and nootropics P. O.). To reveal the risk factors for treatment failure in patients with primary open-angle glaucoma and assess their orientation and degree of influence the study used the methods of constructing and analyzing the logistic regression models.

In the course of the analysis 20 indicators were examined as the factorial markers concerned with the construction of mathematical models: Degree of Severity, Method of Treatment, Vision, IOP, Optic Disc, NFL (nerve fiber layer thickness), NFLS (nerve fiber layer thickness in the upper part), NFLI (nerve fiber layer thickness in the lower sector), NFLt (nerve fiber layer thickness in the temporal sector), NFLn (nerve fiber layer thickness in the nasal sector), Vrim (volume neuroretinal rim), Srim, MD (mean deviation), PSD (pattern standard deviation), Phosphite, Rheography, Duration of the Low Recovery, Vmax (maximum fast filling speed), Average Speed of the Slow Filling, Disk Mean. The factors most closely correlated with the risk of treatment failure were revealed in the course of selecting the most significant indicators with the use of the of step-by-step elimination method. As a result of the analysis four factorial markers were selected: Method of Treatment (X1), NFL (nerve fiber layer thickness) (X2), Vrim (volume neuroretinal rim) (X3), PSD (pattern standard deviation) (X4). The model of predicting the risk of treatment failure was constructed with the established set of the factorial indicators. The adequacy of the prognostic model was assessed by using the method of constructing the ROC curves of the model (Figure).

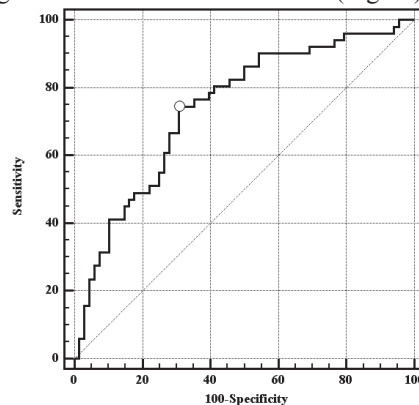


Fig. – The ROC curve of the model of predicting the risk of treatment failure (0 marks the optimal values of sensitivity and specificity of the model)

**Results and their discussion**

The analysis found that the area under the ROC-curve was  $AUC = 0,74 \pm 0,05$ , the model is adequate ( $p < 0,001$ ). At the selected optimal threshold of acceptance / rejection of the model sensitivity was 74.5% (95% CI 60.4% - 85.7%), its specificity was 69.1% (95% CI 56.7% - 79.8%). The results indicate a high relevance of the selected factorial indicators: Method of Treatment, NFL, Vrim, PSD - for predicting the risk of treatment failure. The results of analyzing the model coefficients are shown in Table.

**Table 1. The Coefficients of the Four Factor Model of Predicting the Risk of Treatment Failure (the Logistic Regression Model)**

The Factorial Indicator	The Coefficients of the Prediction Model, $b \pm m$	The Level of the Significance of the Difference between Coefficient and 0, p	The OR Marker (95% CI OR)
Method of Treatment	$-1,8 \pm 0,4$	$< 0,001$	0,17 (0,07 - 0,39)
NFL	$0,01 \pm 0,02$	0,52	-
Vrim	$-2,9 \pm 3,2$	0,36	-
PSD	$0,06 \pm 0,07$	0,36	-

The analysis of the coefficients of the logistic regression model reveals that the use of neurotropic drugs significantly ( $p < 0,001$ ) reduces the risk of treatment failure (when adjusting for all risk factors),  $OR = 0.17$  (95% CI 0.07 - 0.39) .

**Conclusions**

1. For the first time the effectiveness of the treatment of POAG was assessed by constructing the multi-factorial mathematical prognostic model.
2. The four factorial indicators associated with the risk of treatment failure were selected: Method of Treatment, NFL, Vrim, PS); the sensitivity of the model was 74.5% (95% CI 60.4% - 85.7%), its specificity was 69.1% (95% CI 56.7% - 79.8%).

3. The inclusion of neurotropic drugs in the complex treatment of POAG significantly ( $p < 0,001$ ) reduces the risk of treatment failure (when adjusting for all risk factors), OR = 0.17 (95% CI 0.07 - 0.39).

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