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STUDY OF FACTORS THAT AFFECT THE STABILITY OF INTRAOCULAR PRESSURE AFTER SURGICAL ANTIGLAUCOMA INTERVENTION IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA

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Summary. *Primary open-angle glaucoma is a multifactorial chronic progressive neurodegenerative disease associated with characteristic structural damage to the optic nerve and associated visual dysfunction, in which intraocular pressure is a key factor. A number of studies in recent years have shown that the number of necessary repeated surgical interventions in glaucoma patients reaches more than 50%. However, to date, the pathogenetic mechanisms that lead to the overgrowth of the channels formed during the operation for the outflow of ocular fluid have not been fully elucidated, and the development and implementation of modern devices (valves) also does not solve the problem. The purpose of our work was to analyze and study risk factors that may affect the frequency of intraocular pressure decompensation in the postoperative period during antiglaucoma interventions and, accordingly, the rapid progression of glaucomatous optic neuropathy.*

Keywords: *primary open-angle glaucoma, intraocular pressure, LOX1, trabecular meshwork, surgery.*

Introduction. Analysis of domestic and foreign literature indicates that the problem of increasing the efficiency of diagnostics and treatment of patients with primary open-angle glaucoma (POAG) remains an urgent task of modern ophthalmology in Ukraine, since glaucoma is one of the main causes of primary disability. The severity of the course and the results of treatment of patients with glaucoma largely depend on the speed of diagnostics, quality and effectiveness of pathogenetically directed treatment [5]. It has been established that in patients with POAG, the structure and elasticity (function) of the trabecular meshwork (TM) are reduced, which leads to dysfunction and blockage of the main pathway for the



outflow of aqueous humor from the eye and can lead to increased outflow resistance, respectively, increased intraocular pressure (IOP) and, ultimately, the development of glaucoma [1]. The results of some studies indicate that the level of lysyl oxidase-1 (LOX1) increases in the aqueous humor of eyes of patients with POAG. As a result, the TM undergoes cellular and molecular changes that lead to IOP decompensation and rapid progression of the disease [2]. However, in the available domestic and foreign literature there are no data on the study of biochemical markers, namely LOX1, in the blood plasma of patients with POAG, as well as their impact on the possibility and frequency of IOP decompensation after surgical antiglaucoma intervention.

Analysis of previous studies and statement of the problem. Lysyl oxidase-1 is a member of the lysyl oxidase family of enzymes that catalyze the covalent cross-linking of collagen and elastin in connective tissues by oxidative deamination of lysine or hydroxylysine side chains. The formation of collagen or elastin cross-links leads to increased strength and structural integrity of connective tissue, which is essential for normal function [3]. Previous studies have shown increased expression and localization of LOX, LOX1, and LOX2 in tissues of patients with POAG. LOX1 has also been shown to be a major component of fibrillar aggregates of the extracellular matrix (ECM) and co-localizes with various components of elastic fibers. These results provide evidence for the involvement of LOX1 in the initial stages of abnormal fibrogenesis in tissues of patients with glaucoma. Alterations in the activation, processing, and/or substrate specificity of LOX1 may contribute to the abnormal aggregation of elastic fiber components into the characteristic fibrils of ocular tissues [4, 6].

Research goal and objectives. To study factors that influence the stability of intraocular pressure after surgical antiglaucoma intervention in patients with primary open-angle glaucoma.

Main part. The study included the main group of patients, 56 people (112 eyes) with POAG who underwent surgical antiglaucoma intervention (minimally invasive surgery - tunnel trabeculopuncture) to stabilize IOP. The comparison group included 32 patients (64 eyes) without glaucoma. The study included patients who underwent a comprehensive ophthalmological examination and treatment at the clinical facilities of the Department of Ophthalmology and Optometry of Postgraduate Education of the Institute of Postgraduate Education of the Bogomolets National Medical University. The study was conducted in compliance with the basic provisions of the Council of Europe Convention on Human Rights and Biomedicine, the World Medical Association Declaration of Helsinki on the Ethical Principles of Scientific Medical Research with Human Participation (1964, with subsequent amendments, including the 2000 version) and the current regulatory legal acts of Ukraine: "Fundamentals of the Legislation of Ukraine on Health Care" (1993), "On the Protection of Personal Data" (2010), "On Higher Education" (2017). All patients were fully informed about the nature of the study and signed an informed consent to conduct a diagnostic examination.

The results were statistically processed using the licensed software package EZR (R-statistics). The level of significance of differences between observation groups was calculated using Fisher's exact test.

Analysis of clinical risk factors for IOP decompensation showed that in the main group of patients with POAG, among 56 patients, the frequency of IOP decompensation was 28% and did not differ by gender ($p=0.789$). In addition, there was no dependence of the frequency of IOP decompensation after surgical antiglaucoma intervention on age ($p=1.000$). However, the lack of IOP stabilization increased with the duration of POAG disease and was higher in the age group with disease duration of more than 5 years ($p<0.05$). At the same time, the dependence of the occurrence of IOP decompensation on the size of the anterior-posterior segment of the eye (APS) and the presence of a history of phacomorphic syndrome was not determined ($p>0.05$). In addition, it was found that a statistically significant increase in the frequency of IOP decompensation was in patients with POAG and a history of dry eye disease ($p<0.05$). It should be noted that when comparing the relationship between the frequency of IOP decompensation and the level of intraocular pressure before surgery, a statistically significant correlation was established. Patients with a preoperative IOP value of 21 mmHg and above had a higher risk of IOP decompensation after surgery ($p<0.05$).

The next stage of our study was to determine the dependence of the frequency of IOP decompensation after surgical antiglaucoma intervention on the level of the biochemical marker LOX1 in the plasma of patients with POAG. ROC analysis was performed to determine the optimal values of the threshold values for the absence of IOP stabilization after surgery. The basis of this analysis is the construction of ROC curves, which allow obtaining a quantitative characteristic of the sensitivity of diagnostic tests used at given levels of their specificity. The dependence of the lack of IOP stabilization in patients with POAG on the level of LOX1 in blood plasma was analyzed. Figure 1 shows the ROC curve of the logistic model predicting the risk of IOP decompensation in patients with POAG after surgery from the level of LOX1 in blood plasma in these patients before surgery.

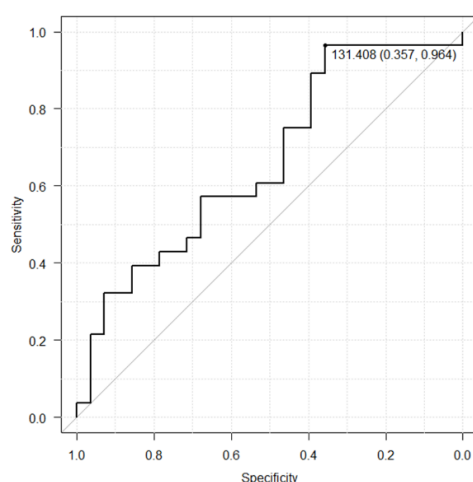


Fig. 1. ROC curve of the logistic model predicting the risk of IOP decompensation in patients with POAG after surgery based on the value of LOX1.

AUC = 0.662

Analysis of the results showed that in patients with no IOP stabilization, the cut-off value was $\geq 131.408 \pm 27.8$ pg/ml with a sensitivity of 96.4% and a specificity of 35.7% (Fig. 1). The area under the ROC curve AUC = 0.662 (95% CI 0.518 - 0.806) $p<0.05$, indicating



a high quality of the test. Thus, the results of the analysis indicate a statistically significant effect of the level of LOX1 in the blood plasma of patients with POAG on the frequency of IOP decompensation after their surgical intervention ($p < 0.05$). It should be noted that the study of LOX1 levels in the blood plasma of patients in the comparison group, without POAG, established a cut-off value of $\geq 63.634 \pm 20.3$ pg/ml with a sensitivity of 84.4%, specificity of 41.7%. The area under the ROC curve $AUC = 0.634$ (95% CI 0.51 – 0.758) $p < 0.05$, which was evidence of high test quality.

The next stage of our research was to analyze and determine the most significant indicators that affect the risk of IOP decompensation and, based on this, create a model for predicting the development of IOP decompensation after surgical antiglaucoma intervention in patients with POAG. The Stepwise method of variable inclusion/exclusion was used to select the minimum set of factor features associated with the original variable. When constructing a three-factor model for analyzing the causes of IOP destabilization, the dependence of the risk of destabilization on the most significant factor characteristics was revealed. Table 1 shows the results of estimating the model coefficients.

Table 1

Indicator	Model coefficient value	Significance level of the difference of the coefficient from 0, p	HR indicator (95% CI)
Const	-2.9 ± 1.03	0.004	-
IOP level before surgery (A)	4.04 ± 1.1	0.0002	57.0 (6.7-488)
Duration of the disease (B)	0.03 ± 0.8	With a disease duration of more than 5 years, the frequency of IOP decompensation increased	
LOX1 level in blood plasma (C)	-0.16 ± 0.82	At plasma LOX1 levels above 131.408 pg/ml, the incidence of IOP decompensation increased.	

Figure 2 shows the ROC curve of the logistic three-factor model for analyzing the causes of IOP destabilization from the most significant factor characteristics. The area under the ROC curve $AUC = 0.83$ (95% CI 0.716 - 0.944).

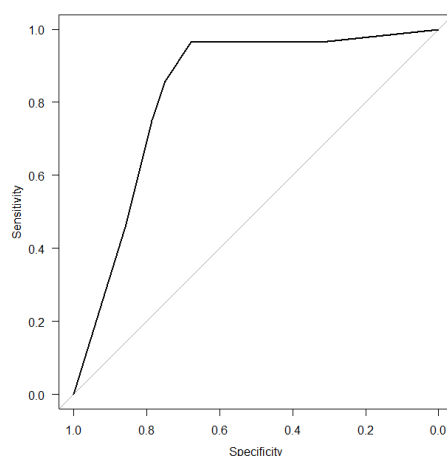


Fig. 2. ROC curve of the logistic three-factor model for analyzing the causes of IOP destabilization. Area under the ROC curve $AUC = 0.83$ (95% CI 0.716 - 0.944)

Based on the obtained dependence, a mathematical model for predicting IOP destabilization after surgical antiglaucoma intervention in patients with POAG was calculated:

$$K = -2.9 + 4.04 \times A + 0.03 \times B + (-0.16) \times C \quad (1)$$

where:

A – IOP level before surgery (mmHg): 0.001 – up to 20 mmHg; 1 – 21 mmHg and above;

B – disease duration (in years): 0.001 – up to 5 years; 1 – 5 years and above;

C – LOX1 level in blood plasma (pg/ml): 0.001 – up to 131.408 pg/ml; 1 – 131.408 pg/ml and above;

Conclusions. The results obtained indicate that the most significant factors influencing the frequency of IOP destabilization after surgical antiglaucoma intervention are the level of IOP before surgery, the duration of the disease and the level of LOX1 in the blood plasma in patients with POAG. The risk of developing IOP decompensation in patients with POAG increases with an increase in the level of IOP before surgery above 21 mm Hg, with the duration of the disease before surgery more than 5 years and the level of LOX1 in the blood plasma before surgery $\geq 131.408 \pm 27.8$ pg/ml. The results obtained in the study will open new ways of personalized management of patients with glaucoma. These results will help ophthalmologists calculate the risks of developing IOP decompensation in patients with POAG. This will help analyze the existing risk factors of the disease in the patient before surgery and plan the optimal and effective plan of surgery and management of the postoperative period, which will increase the effectiveness of treatment, the patient's quality of life and slow down the possible progression of glaucomatous optic neuropathy in the future.

References:

- [1] Karimi, A., Crouch, D. J., Razaghi, R., Crawford Downs, J., Acott, T. S., Kelley, M. J., Behnsen, J. G., Bosworth, L. A., & Sheridan, C. M. (2023). Morphological and biomechanical analyses of the human healthy and glaucomatous aqueous outflow pathway: Imaging-to-modeling. *Computer methods and programs in biomedicine*, 236, 107485. <https://doi.org/10.1016/j.cmpb.2023.107485>
- [2] Kumari, S., Panda, T. K., & Pradhan, T. (2017). Lysyl Oxidase: Its Diversity in Health and Diseases. *Indian journal of clinical biochemistry* : IJCB, 32(2), 134–141. <https://doi.org/10.1007/s12291-016-0576-7>
- [3] Laczko, R., & Csiszar, K. (2020). Lysyl Oxidase (LOX): Functional Contributions to Signaling Pathways. *Biomolecules*, 10(8), 1093. <https://doi.org/10.3390/biom10081093>
- [4] Sethi, A., Wordinger, R. J., & Clark, A. F. (2013). Gremlin utilizes canonical and non-canonical TGF β signaling to induce lysyl oxidase (LOX) genes in human trabecular meshwork cells. *Experimental eye research*, 113, 117–127. <https://doi.org/10.1016/j.exer.2013.05.011>
- [5] Tang, Y., Pan, Y., Chen, Y., Kong, X., Chen, J., Zhang, H., Tang, G., Wu, J., & Sun, X. (2021). Metabolomic Profiling of Aqueous Humor and Plasma in Primary Open Angle Glaucoma Patients Points Towards Novel Diagnostic and Therapeutic Strategy. *Frontiers in pharmacology*, 12, 621146. <https://doi.org/10.3389/fphar.2021.621146>
- [6] Vallet, S. D., Guérout, M., Belloy, N., Dauchez, M., & Ricard-Blum, S. (2019). A Three-Dimensional Model of Human Lysyl Oxidase, a Cross-Linking Enzyme. *ACS omega*, 4(5), 8495–8505. <https://doi.org/10.1021/acsomega.9b00317>