https://doi.org/10.5114/oku/218000 (Case Report)

Received: 17.09.2025 Accepted: 28.09.2025

Analysis of Factors that Determine the Degree of Iatrogenic Impact of Surgery on the Ocular Surface in Glaucoma

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Abstract: **Introduction:** Primary open-angle glaucoma is a multifactorial chronic neurodegenerative disease. Although the pathogenesis of glaucoma is not fully understood, it is known that the level of intraocular pressure is interconnected with the death of retinal ganglion cells. Neither significant advances in the surgical treatment of glaucoma nor the development of new minimally invasive surgical interventions and a significant expansion of the arsenal of antihypertensive drugs have been able to stop its constant progress.
Case report: During the study, the influence of biomarkers LOX1, TGFb2, and pNF-H in the blood plasma of patients with primary open-angle glaucoma before surgery on the frequency of progression of glaucomatous optic neuropathy after anti-glaucomatous surgery was determined.
Results: The results obtained indicated a statistically significant dependence of the level of LOX1 in the blood plasma of patients with primary open-angle glaucoma before surgery on the frequency of progression of glaucomatous optic neuropathy after surgical antiglaucoma treatment.

Key words: glaucoma, pathogenetic factors, LOX1, progression, ultrasound, cavitation.

Introduction

Glaucoma is the leading cause of irreversible blindness worldwide and in Ukraine. Unfortunately, over the past 5 years, glaucoma has been the leading cause of visual disability in Ukraine. This negative situation is due to the asymptomatic course of the subclinical and early stages of the disease and several medical and social factors. The most common type in both the United States and Ukraine is primary open-angle glaucoma (POAG) [1]. Primary open-angle glaucoma is a multifactorial chronic neurodegenerative disease characterised by the acquired loss of retinal ganglion cells and subsequent atrophy of the optic nerve [2]. Although the pathogenesis of glaucoma is not fully understood, it is known that the level of intraocular pressure (IOP) is interrelated with the death of retinal ganglion cells. Neither significant advances in the surgical treatment of glaucoma nor the development of new minimally invasive surgical interventions and a significant expansion of the arsenal of antihypertensive drugs have been able to stop its constant progress [3].

Analysis of the literature of recent years shows that the number of necessary reoperations in glaucoma patients is about 50% [4]. However, the pathogenetic mechanisms leading to canal overgrowth have not yet been fully elucidated, and the development and implementation of modern devices (valves) does not solve the problem. We understand that any operation is an iatrogenic trauma for the patient, and we always hope to minimise this impact and expect that the result of the operation will be long-lasting and effective. Unfortunately, this is not always possible to achieve, and the formed filtration cushions often undergo scarring, which reduces the postoperative result and requires repeated interventions, this can negatively affect the surface of the eye, as well as accelerate the progression of the disease. Therefore, of course, we try to choose the gentlest method of treatment for the patient, which will allow us to postpone the destabilisation and progression of glaucoma.

The world literature suggests that increased IOP is the result of cellular and molecular changes in the trabecular meshwork (TM), which are caused by increased levels of transforming growth factor (TGF), in particular TGFb2, in the aqueous humour. TGFb2 expression is increased in the TM of POAG patients, which increases the contractile capacity of TM cells and promotes the formation of actin stress fibres, which increases the resistance to fluid outflow and thereby leads to increased IOP after surgery [5].

Previous studies indicate that another important factor that may affect the strength and elasticity of the TM is lysyl oxidase-1 (LOX1), a major component of fibrillar aggregates of the extracellular matrix (ECM), which is involved in tissue fibrogenesis in glaucoma patients who have undergone antiglaucomatous surgery [6].

Recently, there has been increasing evidence that neurofilaments (NFs) can influence the maintenance, regeneration, and plasticity of the neuronal cytoskeleton, and the dynamics and function of other cytoskeletal elements, including microtubules and actin filaments [7]. However, the role of the high-molecu-

ISSN 1505-2753

lar-weight neurofilament protein pNF-H in the induction of selective neuronal degeneration and chronic pathology is currently unknown.

The use of new biochemical blood markers TGFb2, LOX1, and pNF-H to determine the risks of developing IOP decompensation determine the degree of iatrogenic impact of surgery on the ocular surface, and the progression of glaucomatous optic neuropathy after surgical antiglaucoma intervention in patients with POAG in the Ukrainian population is a solution to an urgent scientific and applied problem in modern ophthalmology, which can help us understand the course of POAG and changes in the ocular surface after surgery, and be a relevant target for the prevention and treatment of glaucoma.

Case report

Eighty-eight patients participated in the study. All patients were informed about the nature of the study and signed an informed consent form to participate. Patients were divided into 2 groups. The main group consisted of 56 patients with primary open-angle glaucoma. The gender and age characteristics of the patients in the main group were as follows: among thse examined were 26 men (46.4%) and 30 women (53.6%), aged from 41 to 88 years, whose average age was 61 ± 11 years.

The comparison group included 32 patients without glaucoma. The age of the patients ranged from 49 to 77 years, the mean age was 58 ± 9 years, there were 17 women in the control group (53.1%), and 15 men (46.9%). Both groups were compared by age and sex. The distribution of patients into groups is presented in Table I.

Indicator		Gender		Average age, years
		Men	Women	
Abs. / %	Main group, n = 56 (112 eyes)	26 / 46.4 %	30 / 53.6 %	61 ± 10
	Comparison group, N = 32 (64 eyes)	15 / 46.9 %	17 / 53.1 %	58 ± 11
	Level of significance of the difference, p	0.2		-

Tab. I. Distribution of patients into groups, n = 88 (176 eyes).

During the study, the levels of biomarkers TGFb2, LOX1, and pNF-H in the blood plasma of patients were determined. All patients in the main group had a history of minimally invasive antiglaucoma intervention, but in some patients after surgery the IOP level was stable, while in others the IOP level remained uncompensated. To determine the level of biomarkers in the blood plasma of patients, the enzyme-linked immunosorbent assay (ELISA) method was used. The results were statistically processed using the licensed software packages EZR (R–statistics) and Excel 2010 (Microsoft Corporation, USA). The level of significance of differences between observation groups was calculated using the Fisher test. The critical value of the level of significance was taken as equal to 0.05. ROC analysis was performed to determine the optimal threshold values. The basis of this analysis was the construction of ROC curves, which allow us to obtain quantitative characteristics of the sensitivity of diagnostic tests used at given levels of their specificity.

The main objective of the study was to determine the possible influence of the level of biomarkers LOX1, TGFb2, and pNF-H in the blood plasma of patients with primary open-angle glaucoma before surgery on the frequency of progression of glaucomatous optic neuropathy after anti-glaucomatous surgery. To implement the tasks of determining the optimal value of the threshold value of progression of glaucomatous optic neuropathy after surgery, ROC analysis was used.

First, we assessed the possibility of the influence of the value of the LOX1 level in the blood plasma of patients with POAG on the progression of glaucomatous optic neuropathy after antiglaucomatous surgery. Figure 1 presents the ROC curve of the logistic model.

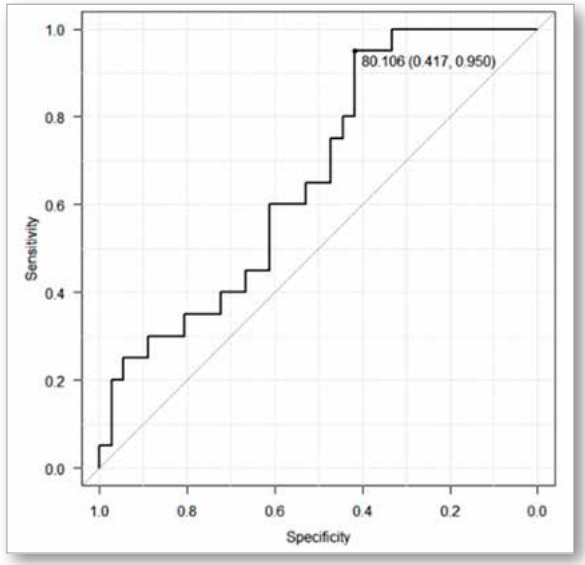

Fig. 1. ROC curve of the logistic model for predicting the frequency of POAG progression after antiglaucomatous surgery depending on the value of LOX1 in the blood of glaucoma patients. AUC = 0.664.

The results show that in patients with POAG, the cut-off level of LOX1 in plasma ≥ 80.106 ± 27.3 pg/ml is a possible risk factor for progression of glaucomatous optic neuropathy in the postoperative period, with a sensitivity of 95.0% and a specificity of 41.7% (Fig. 1). The area under the ROC curve AUC = 0.664 (95% CI 0.52 – 0.808) p <0.05.

Second, we analysed the dependence of progression of glaucomatous optic neuropathy after antiglaucomatous surgery in patients with POAG on the level of TGFb2 in the plasma of these patients before surgery. Figure 2 shows the ROC curve of the logistic model.

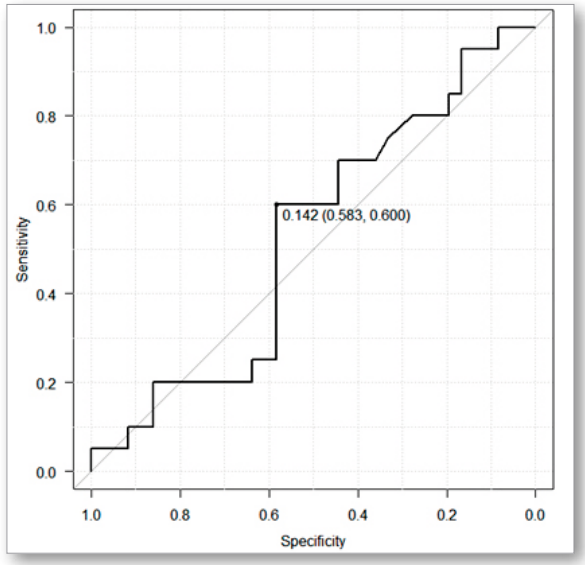

Fig. 2. ROC curve of the logistic model predicting the frequency of POAG progression after antiglaucomatous surgery depending on the value of TGFb2 in the blood of glaucoma patients. AUC = 0.526.

The results show (Fig. 2) that there is no correlation between the progression of glaucomatous optic neuropathy in patients with POAG after antiglaucomatous surgery and the level of TGFb2 in the blood plasma of patients. Area under the ROC curve AUC = 0.526 (95% CI 0.368 - 0.683), p >0.05.

Third, we analysed the dependence of the frequency of progression of glaucomatous optic neuropathy after antiglaucomatous surgery in patients with POAG on the level of pNF-H in the blood plasma of these patients. Figure 3 presents the ROC curve of the logistic model.

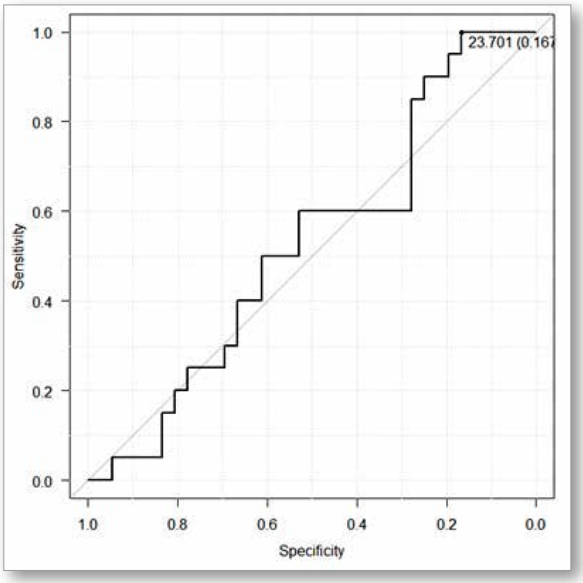

Fig. 3. ROC curve of the logistic model predicting the frequency of POAG progression after antiglaucomatous surgery depending on the value of pNF-H in the blood of glaucoma patients. AUC = 0.525.

In addition comparing the values of the levels of the LOX1 indicator in the blood plasma of patients with glaucoma (the main group) and patients without glaucoma (the comparison group) gave interesting results. Analysis of the obtained results shows that the level of the LOX1 indicator in the blood plasma is not only decisive for patients with glaucoma, but it can also be a marker for determining the frequency of IOP destabilisation and the frequency of progression of glaucomatous optic neuropathy after surgical antiglaucoma intervention. The value of LOX1 in the blood plasma cut-off ≥ 63.634 ± 20.3 pg/ml is a risk factor for the development of glaucoma debut with a sensitivity of 84.4% and specificity of 41.7%. Area under the ROC curve AUC = 0.634 (95% CI 0.51–0.758) p <0.05.

In our opinion, the moderate level of specificity of the test may be associated with several factors: first, with a small number of patients who were included in the study, and second, with the fact that glaucoma is a multifactorial disease, and the level of LOX1 in blood plasma is one of the additional possible pathogenetic factors of the disease development but not the only unified factor of glaucoma development. Thus, patients who have a LOX1 value in blood plasma ≥ 63.634 ± 20.3 pg/ml should be classified as a high-risk group for glaucoma development and require more attention from ophthalmologists and dynamic monitoring.

Results

Recently, many mechanisms have been identified that are crucial in the pathogenesis of glaucoma; however, none of them characterises the disease sufficiently, and the multifactorial aetiology of glaucoma remains, unfortunately, a fundamental problem today that requires the search and development of new treatment strategies [8].

When the first-line treatment of glaucoma, i.e. medical therapy, fails, doctors resort to laser treatment, and when the latter fails to lower IOP to the desired target level, surgery is performed. Surgical treatment plans may vary depending on the type of glaucoma and the individual patient. Surgical options, such as trabeculectomy and tubular shunt implantation, are usually considered when other treatments do not produce the desired results [9].

Recently, minimally invasive glaucoma surgery (MIGS) has become very popular due to its less invasive nature and increased safety. As a rule, MIGS are aimed at various ways of reducing IOP, providing an effective reduction in intraocular pressure with increased safety. However, despite significant advantages, the effect of reducing IOP after surgical anti-glaucomatous intervention is often levelled. As shown by studies in recent years, the percentage of regression of the result of IOP stabilisation after surgical treatment in patients with POAG can reach more than 50% [4]. Despite modern technologies and innovative surgical materials, the filtration pads of the conjunctiva and Tenon's membrane formed during surgery are scarred, and the pores and holes formed in the trabecular meshwork are clogged with pigment, newly formed vessels, and synechiae.

There is currently no unified standardised glaucoma surgery, and even surgeries of the same type performed by the same surgeon vary from patient to patient.

The use of ultrasonic phacoemulsifiers and ultrasonic scalpels in cataract surgery has opened a new era for minimally invasive eye surgery and the ability to perform the procedure with an incision of less than 1.0–1.2 mm without collateral traumatic damage to the eye tissues [10].

However, the use of ultrasonic cavitation in the surgical treatment of glaucoma has not yet found its proper application. Although, as previous studies show, the use of an ultrasonic scalpel to clean the trabecular meshwork of the anterior chamber angle due to the secondary effects accompanying the phenomenon of ultrasonic cavitation has certain prospects [11].

Today, it is well known that there is a fairly high percentage of positive results after anti-glaucomatous operations, especially with minimally invasive surgery and, especially, when the surgical intervention was performed in the early stages of the glaucoma process [9]. Our study was devoted to elucidating pathogenetic factors that may affect the duration of IOP stabilisation in the postoperative period in the surgical treatment of POAG, and accordingly lead to progression or stabilisation of the glaucoma process.

Our results indicated a statistically significant relationship between the level of LOX1 in the blood plasma of patients with POAG before surgery and the frequency of progression of glaucomatous optic neuropathy after surgical antiglaucoma treatment.

Having received negative results regarding the lack of correlation between TGFb2 and pNF-H levels in the blood plasma of patients with POAG with the results of IOP levelling after surgical antiglaucoma intervention and the lack of influence on the further progression of glaucomatous optic neuropathy, we still consider this direction to be very promising for further research. In our opinion, the negative result may be associated with the very specific design of our study. For the most part, we included in the main group glaucoma patients who suffered damage after surgical antiglaucoma intervention. Perhaps, in the future, it would be more appropriate to determine TGFb2 and pNF-H markers in another category of patients, for example, those who had POAG but had no history of glaucoma surgery. We also believe that for further research, the number of patients in the main group should be expanded, or patients with other types of glaucoma should be included, for example, secondary, pseudoexfoliative, etc. Since determination of TGFb2 and pNF-H levels in the intraocular fluid of the anterior chamber by foreign colleagues revealed their

positive correlation with the glaucoma process, these markers can be very useful for monitoring the glaucoma process.

Conclusions

Clinical management of glaucoma requires individualisation, taking into account the needs of the individual patient, the experience of the treating ophthalmologist, and the socio-economic environment.

Ocular surgery can cause increased intraocular pressure through various mechanisms. Without appropriate treatment, this can lead to irreversible glaucomatous damage to the optic nerve and potentially irreversible vision loss.

The study of LOX1 levels in the blood plasma of patients with POAG before surgery has a prognostic role in determining the risks of IOP levelling after surgical antiglaucoma intervention and further progression of glaucomatous optic neuropathy.

Disclosure
Conflict of interests: none declared
Funding: no external funding
Ethics approval: Not applicable.

References:

1. Allison K, Patel D, Alabi O:. *Epidemiology of Glaucoma: The Past, Present, and Predictions for the Future*. Cureus. 2020; 12(11): e11686.
2. Tang Y, Pan Y, Chen Y, et al.: *Metabolomic Profiling of Aqueous Humor and Plasma in Primary Open Angle Glaucoma Patients Points Towards Novel Diagnostic and Therapeutic Strategy*. Front Pharmacol. 2021; 12: 621146.
3. Harasymowycz P, Birt C, Gooi P, et al.: *Medical Management of Glaucoma in the 21st Century from a Canadian Perspective*. J Ophthalmol. 2016; 2016: 6509809.
4. Gedde SJ, Feuer WJ, Lim KS, et al.: *Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 5 Years of Follow-up*. Ophthalmology. 2022; 129(12): 1344–1356.
5. Tovar-Vidales T, Clark AF, Wordinger RJ:. *Transforming growth factor-beta2 utilizes the canonical Smad-signaling pathway to regulate tissue transglutaminase expression in human trabecular meshwork cells*. Exp Eye Res. 2011; 93(4): 442–451.
6. Schlötzer-Schrehardt U, Zenkel M:. *The role of lysyl oxidase-like 1 (LOXL1) in exfoliation syndrome and glaucoma*. Exp Eye Res. 2019; 189: 107818.
7. Yan Z, Liao H, Chen H, et al.: *Elevated Intraocular Pressure Induces Amyloid-β Deposition and Tauopathy in the Lateral Geniculate Nucleus in a Monkey Model of Glaucoma*. Invest Ophthalmol Vis Sci. 2017; 58(12): 5434–5443.
8. Fernández-Durango R, Fernández-Martínez A, García-Feijoo J, et al.: *Expression of nitrotyrosine and oxidative consequences in the trabecular meshwork of patients with primary open-angle glaucoma*. Invest Ophthalmol Vis Sci. 2008; 49(6): 2506–2511.
9. Wagner IV, Stewart MW, Dorairaj SK:. *Updates on the Diagnosis and Management of Glaucoma*. Mayo Clin Proc Innov Qual Outcomes. 2022; 6(6): 618–-635.
10. Roberts HW, Day AC, O'Brart DP:. *Femtosecond laser-assisted cataract surgery: A review*. Eur J Ophthalmol. 2020; 30 (3): 417–429.
11. Sharhorodskyi S, Luhovskyi OF: *Research into the possibility of using effects accompanying the phenomenon of ultrasonic cavitation in a scalpel for the treatment of glaucoma*. Mechanics and Advanced Technologies. 2024; 8 (4): 397–404.

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