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Predictors of intraocular pressure change after cataract surgery in patients with pseudoexfoliation glaucoma and in nonglaucomatous patients

Prediktori promene intraokularnog pritiska nakon operacije katarakte kod obolelih od pseudoeksfolijativnog glaukoma i kod bolesnika bez glaukoma

Bojana Markić, Milka Mavija, Saša Smoljanović-Skočić, Miljana Tepić Popović, Sanela Sanja Burgić

University of Banja Luka, Faculty of Medicine, Department of Ophthalmology, Banja Luka, Republic of Srpska, Bosnia and Herzegovina; University Clinical Center of the Republic of Srpska, Clinic for Eye Diseases, Banja Luka, Republic of Srpska, Bosnia and Herzegovina

Abstract

Background/Aim. The cataract surgery in eyes with and without glaucoma results in the sustained intraocular pressure (IOP) reduction but it is still unknown which glaucomatous patients will achieve clinically significant reduction. The preoperative IOP and some ocular biometric parameters have been shown as potential predictors of the postoperative IOP reduction. The aim of our prospective intervention study was to evaluate that relationship in medically controlled patients with the pseudoexfoliation glaucoma (PXG) and in the nonglaucomatous patients. **Methods.** Thirty-one PXG patients (31 eyes) and 31 nonglaucomatous patients (31 eyes), all with clinically significant cataract, were enrolled. The preoperative IOP, anterior chamber depth (ACD), axial length (AL), lens thickness (LT), lens position (LP) [LP = ACD + 0.5 LT], relative lens position (RLP) [RLP = LP / AL] and the pressure-to-depth ratio (PD ratio) [PD ratio = preoperative IOP/preoperative ACD] were evaluated as potential predictors of the IOP change in the 6th postoperative month. **Results.** In the 6th postoperative month, in the PXG group, the IOP reduction was -3.23 ± 3.41 mmHg (-17.67 ± 16.86%) from the preoperative value of 16.27 ± 3.08 mmHg and in the control group, the reduction was -2.26 ± 1.71 mmHg (-15.06 ± 10.93%) from the preoperative value of 14.53 ± 2.04 mmHg. In the PXG group, the significant predictors of the absolute and the percentage IOP reduction were the preoperative IOP, AL, and PD ratio. In the same group, RLP was shown as a significant predictor of absolute change in the IOP in multivariate analysis, and the percentage IOP change in both the univariate and the multivariate analyses. In the control group, the preoperative IOP and the PD ratio were the only significant parameters that could predict absolute change in the postoperative IOP. **Conclusion.** The cataract surgery leads to the IOP reduction both in the PXG and nonglaucomatous eye. Predictors monitored in this study are widely available and simply calculable parameters that can be potentially used in managing glaucoma.

Key words:
cataract surgery; glaucoma; intraocular pressure; ophtalmologic surgical procedures; postoperative complications.

Apstrakt

Uvod/Cilj. Operacija katarakte rezultira održivim sniženjem intraokularnog pritiska (IOP) u očima sa ili bez glaukoma, ali je još uvek nejasno kod kojih će se bolesnika sa glaukomom postići klinički značajna redukcija IOP. Preoperativni IOP i neki okularni biometrijski parametri su se pokazali kao potencijalni prediktori postoperativnog sniženja IOP. Stoga je cilj naše prospektivne intervencijske studije bio da ispitamo taj odnos kod medikamentozno lečenih bolesnika sa pseudoeksfolijativnim glaukomom (PXG) i kod onih bez glaukoma. **Metode.** Ispitan je 31 bolesnik sa PXG (31 oko) i 31 bolesnik bez glaukoma (31 oko), svi sa klinički značajnom kataraktom. Preoperativni IOP, dubina prednje očne komore (ACD), aksijalna dužina (AL), debljina sočiva (LT), pozicija sočiva (LP) [LP = ACD + 0.5 LT], relativna pozicija sočiva (RLP) [RLP = LP/ AL] i indeks pritisak-dubina (PD indeks) [PD indeks = preoperativni IOP/preoperativni ACD] su ispitani kao potencijalni prediktori promene IOP u 6. postoperativnom mesecu. **Rezultati.** U 6. postoperativnom mesecu u grupi sa PXG, sniženje IOP je iznosilo -3.23 ± 3.41 mmHg (-17.67 ± 16.86%) u odnosu na preoperativnu vrednost IOP od 16.27 ± 3.08 mmHg, a u kontrolnoj grupi, sniženje je iznosilo

Correspondence to: Bojana Markić, University Clinical Center of the Republic of Srpska, Clinic for Eye Diseases, 12 beba bb, 78 000 Banja Luka, Republic of Srpska, Bosnia and Herzegovina. E-mail: bojana.markic@gmail.com

-2.26 ± 1.71 mmHg (-15.06 ± 10.93%) u odnosu na preoperativnu vrednost IOP od 14.53 ± 2.04 mmHg. U grupi sa PXG, značajni prediktori apsolutnog i relativnog sniženja IOP su bili preoperativne vrednosti IOP, AL i PD indeksa. U istoj grupi, RLP se pokazao kao značajan prediktor apsolutne promene IOP u multivarijantnoj analizi, a procentualne promene IOP i u univarijantnoj i multivarijantnoj analizi. U kontrolnoj grupi, preoperative vrednostii IOP i PD indeksa su bili jedini značajni parametri koji su mogli da ukažu na apsolutnu promenu IOP posle operacije katarakte. **Zaključak.** Operacija katarakte dovodi do sniženja IOP kod obolelih od PXG i kod bolesnika bez glaukoma. Prediktori ovog sniženja su široko dostupni parametri, jednostavni za izračunavanje i potencijalno se mogu koristiti u donošenju odluka o lečenju glaukoma.

Ključne reči:
katarakta, ekstrakcija; glaukom; intraokularni pritisak; hirurgija, oftalmološka, procedure; postoperativne komplikacije.

Introduction

Glaucoma is the leading cause of irreversible blindness and the only treatment is lowering the intraocular pressure (IOP) to a level on which the disease does not progress [1]. The pseudoexfoliation glaucoma (PXG) is one of the most complicated forms of glaucoma for treatment because of the high IOP at the onset, poor response to medical therapy and faster progression. The PXG is characterized by the pathological production and accumulation of an abnormal extracellular fibrillar material mainly visible on the anterior lens capsule, the pupillary margin, corneal endothelium, lens zonules, trabecular meshwork and it often correlates with an increased incidence of cataract formation usually in the lens nucleus or center. A loss of zonules support and poor pupillary dilation make the cataract surgery challenging and with potential complications like vitreous loss, subluxation or luxation of the lens. Studies have shown that the cataract surgery leads to an IOP reduction in glaucomatous and nonglaucomatous eyes, and the IOP reduction effects vary, depending on the type of glaucoma and monitoring period [2]. However, a clinically significant IOP reduction does not occur in every patient [3, 4]. More recent studies are trying to identify the factors that can indicate which patients will achieve a clinically significant IOP reduction after a cataract surgery.

The preoperative value of IOP has been found to be a significant predictor of the IOP reduction after a cataract surgery. Patients with higher levels of preoperative IOP obtain greater postoperative IOP reduction [2, 3, 5]. Also, some ocular biometric parameters, such as anterior chamber depth (ACD), axial length (AL), lens thickness (LT), lens position (LP) [defined as: ACD + 0.5 LT], relative lens position (RLP) [defined as: LP/AL] and the pressure-to-depth ratio (PD ratio) [defined as: preoperative IOP/preoperative ACD] have been recognized as potential predictors of postoperative IOP reduction [2, 6–11].

To our knowledge, there have been no prospective studies which evaluated these clinical variables in the PXG patients. Accordingly, the aim of this study has been to determine if the preoperative values of IOP, ACD, AL, LT, LP, RLP and PD ratio are related to the postoperative IOP changes in the PXG patients and to compare these findings with those of nonglaucomatous patients.

Methods

Thirty-one (31 eyes) PXG patients and thirty-one (31 eyes) nonglaucomatous patients (controls), who underwent cataract surgery by phacoemulsification (PHACO) and posterior chamber intraocular lens (IOL) implantation at the Clinic for Eye Diseases of the University Clinical Center of the Republic of Srpska, Bosnia and Herzegovina, were included in this prospective intervention study between December 2016 and December 2018. The study was approved by the institutional Ethics Committee, conducted in accordance with the Helsinki Declaration and the informed consent was obtained from all the patients.

General exclusion criteria were: ocular trauma, inflammation, retinal disorder, nonglaucomatous optic neuropathy, long-term use of corticosteroids (systemic or topical), previous intraocular surgery or laser intervention, and any other type of glaucoma except PXG.

General inclusion criteria were: age ≥ 18 years, presence of clinically significant cataract, operative and postoperative course without complications and participation until the study completion.

All PXG patients were with previously diagnosed structural and functional glaucomatous changes, with the presence of pseudoexfoliation material (PXM) at the pupillary margin and/or the lens surface and treated with topical antiglaucomatous medications. The control group consisted of the nonglaucomatous patients referring to elective surgery of the senile cataract, with bilaterally gonioscopically determined angle openness classified as the Shaffer's and Tour's [12] grade 3 or 4 and with the bilateral IOP ≤ 21 mmHg.

The data we collected consisted of the patient's age, gender, the best corrected visual acuity (BCVA) measured by the Snellen's charts (decimal system), gonioscopy (the Shaffer's and Tour's [12] grade scale), the diurnal IOP curve test (the IOP measurement at 07:30, 13:30 and 19:30 with the Goldmann applanation tonometer), the number and type of glaucoma therapy. Eye selection criteria were based on worse BCVA.

The measurements of the biometric parameters ACD, LT and AL were obtained with non-contact optical biometer IOLMaster 500 (Carl Zeiss Meditec, Inc., Dublin, CA) and contact applanation the A-scan ultrasonic biometer (Tomey, AL-100 Biometer, Japan).

According to the following formulas, the calculations were as follows:

$IOP = (IOP_{07:30}+IOP_{13:30}+IOP_{19:30}) / 3$

$LP = ACD + 0.5\ LT$ [13]

$RLP = LP / AL$ [13]

PD ratio = preoperative IOP / preoperative ACD [9].

The surgery consisted of the standard clear corneal incision phacoemulsification by using the phaco-chop technique in all patients under topical anesthesia, using the Stellaris Vision Enhancement System (Bausch & Lomb) and the IOL (Akreos Adapt AO, Bausch & Lomb) was implanted in-the-bag. The antibiotic prophylaxis was provided as a subconjunctival and intracameral injection. Phacoemulsification parameter, Absolute phaco time was recorded at the end of each surgery.

The postoperative therapy included topical antibiotics/steroid 8 times daily during the first postoperative week, followed by 6 times daily, 4 times daily and 2 times daily in the next three weeks, respectively.

In order to avoid the effect of topical antiglaucoma therapy change on postoperative values of IOP, all the PXG patients postoperatively continued to use preoperatively administered antiglaucoma therapy, except for the prostaglandin analogs. After 1 month, the same prostaglandin analogs were resumed and the studied eyes were then back on the same glaucoma medication regimen.

The postoperative checkups were performed on the first and seventh day as well as in the 1st, 3rd and 6th month.

The clinical examinations, diagnostic measurements and all surgeries were performed by the same ophthalmologist (BM).

We compared the absolute IOP change and the IOP change percentage in the 6th postoperative month as the main outcomes for the predictors of interest.

Continuous variables were reported as the mean ± standard deviation (SD). The Mann-Whitney *U* test was used to assess differences between the groups for ordinal or continuous variables, and the χ^2 test for categorical variables.

We used the linear mixed-effects regression analysis in order to determine the correlation between the outcome variables and the preoperative factors, including the preoperative values of IOP, age, gender and biometric parameters (ACD, AL, LT, LP, RLP, PD ratio). The multivariate linear mixed-effects regression models were created in order to adjust to potential confounders, including gender, age and the preoperative values of IOP.

In all models assessing the PD ratio and the IOP change, the preoperative IOP value was not included because it is a part of the PD ratio calculation.

The regression coefficients (B), the coefficients of determination (r^2) and the statistical significance (*p*-value) were reported. *P* values ≤ 0.05 were considered significant. All the statistical analyses were performed using the SPSS software V.21 (SPSS, Inc., Chicago, IL, USA).

Results

The group of 31 patients with the PXG, and 31 patients with the senile cataract as the control group were included in this prospective study. The demographic characteristics, preoperative biometric measurements, preoperative IOP, postoperative IOP (measurements in the 1st, 3rd and 6th month) and the postoperative IOP changes of each group are shown in Table 1. According to the gender, there were no significant differences between the groups. The mean age was significantly higher in the PXG group. There was a significant difference between the two groups in patients' age (76 ± 6 years vs. 71 ± 7 years; $p < 0.01$), preoperative values of IOP (16.27 ± 3.08 mmHg vs. 14.53 ± 2.04 mmHg; $p < 0.01$), LT (4.65 ± 0.50 mm vs. 4.34 ±, 56 mm; $p < 0.05$), PD ratio (5.23 ± 0.25 vs. 4.77 ± 0.82; $p < 0.01$), the absolute IOP change in the 1st month (-2.96 ± 2.65 mmHg vs. -1.00 ± 1.73 mmHg; $p < 0.01$) and percentage IOP change in the 1st month (-16, 86 ± 13.05%; -6.54 ± 12.04%; $p < 0.01$), with all of the above

Table 1

Demographic characteristics and examined parameters in patients subjected to cataract surgery

Characteristics	PXG group (n = 31)	Control group (n = 31)	*p*
Gender (male/female), n (%)	20/11 (65/35)	15/16 (48/52)	0.153
Age (years), mean ± SD	76 ± 6	71 ± 7	< 0.01
Pre-op IOP (mmHg), mean ± SD	16.27 ± 3.08	14.53 ± 2.04	< 0.05
ACD (mm), mean ± SD	2.90 ± 0.34	3.07 ± 0.31	0.066
AL (mm), mean ± SD	23.80 ± 0.84	23.45 ± 0.93	0.213
LT (mm), mean ± SD	4.65 ± 0.50	4.34 ± 0.56	< 0.05
LP (mm), mean ± SD	5.23 ± 0.25	5.25 ± 0.32	0.490
RLP, mean ± SD	0.22 ± 0.01	0.22 ± 0.02	0.150
PD ratio, mean ± SD	5.66 ± 1.15	4.77 ± 0.82	< 0.01
Post-op IOP (mmHg), mean ± SD			
1st month	13.32 ± 2.34	13.53 ± 2.22	0.531
3rd month	13.19 ± 2.21	12.09 ± 2.03	0.099
6th month	13.04 ± 1.95	12.27 ± 1.89	0.147
Ab IOP change 1st month (mmHg), mean ± SD	-2.96 ± 2.65	-1.00 ± 1.73	< 0.01
% IOP change 1st month, mean ± SD	-16.86 ± 13.05	-6.54 ± 12.04	< 0.01
Ab IOP change 3rd month (mmHg), mean ± SD	-3.08 ± 2.73	-2.44 ± 1.76	0.426
% IOP change 3rd month	-17.57 ± 13.43	-16.40 ± 11.40	0.741
Ab IOP change 6th month (mmHg), mean ± SD	-3.23 ± 3.41	-2.26 ± 1.71	0.281
% IOP change 6th month, mean ± SD	-17.67 ± 16.86	-15.06 ± 10.93	0.356

PXG – pseudoexfoliation glaucoma; Pre-op – preoperative; IOP – intraocular pressure; ACD – anterior chamber depth; AL – axial length; LT – lens thickness; LP – lens position; RLP – relative lens position; PD ratio – the ratio of Pre-op IOP and ACD; Post-op – postoperative; Ab – absolute; SD – standard deviation.

variables being larger in the PXG group. Postoperatively, in both groups, compared to the preoperative IOP values, the reduction of the IOP was observed in each measurement time point. The absolute and the percentage reduction of the IOP in the 6th month in the PXG group was -3.23 ± 3.41 mmHg (-17.67 ± 16.86%), and in the control group, -2.26 ± 1.71 mmHg (-15.06 ± 10.93%). There was no statistically significant difference between the groups for either the absolute or the percentage IOP reduction (Table 1).

The linear mixed-effects regression models were used to show the association between the absolute IOP change in the 6th month and gender, age, preoperative IOP value and ocular biometric parameters for both groups (Table 2).

In the univariate mixed-effects models, for both groups, the preoperative IOP value was found to be a significant predictor of the absolute IOP reduction. In the PXG group, in the univariate and multivariate models, the AL and PD ratio were associated with the significant absolute IOP change 6 months after the cataract surgery, and the RLP in the multivariate model. In the control group, PD ratio was the significant predictor of the absolute IOP change both in the univariate and multivariate analyses (Table 2). The predictability of the potential predictors was shown through the coefficient of determination and according to the r^2 value, in the PXG group, in the univariate model, the preoperative IOP (r^2 = 47.3%) was the best predictor of the absolute IOP change, followed by the PD ratio and the AL (r^2 = 18.3% and 12.5%, respectively). In the multivariate model, in the PXG group, among significant predictors, the AL, RLP and PD ratio were the best predictors of the absolute IOP change (r^2 = 57.7%, 51.9% and 14.7%, respectively). In the control group, the best predictor was the preoperative IOP (r^2 = 22.5%), followed by the PD ratio (r^2 = 16.3% in the univariate and r^2 = 13.7% in the multivariate analyses) (Table 2).

Table 3 shows the association between the percentage IOP change in the 6th postoperative month and gender, age, preoperative IOP and ocular biometric parameters for the PXG and control groups, using the linear mixed-effects regression models. The coefficient of determination was also explored.

In the univariate analysis, in the PXG patients, the significant predictors of the percentage IOP change were the preoperative IOP and in the univariate and multivariate analyses, the AL, RLP and PD ratio. Among the significant predictors in the univariate model, the preoperative IOP, followed by the AL, PD ratio and RLP (r^2 = 26.7%, 14.7%, 12.6% and 10.5%, respectively) had the best predictability of the percentage IOP change. In the multivariate model, the order of the best predictability among the parameters was as follows: AL, RLP, PD ratio (r^2 = 37.9%, 35.2% and 8.8%, respectively).

Neither the univariate nor the multivariate analysis identified statistically significant predictors of the percentage IOP change in the 6th postoperative month in the control group (Table 3).

Discussion

The majority of studies, mainly the retrospective ones, examining the effect of a cataract surgery on the IOP reduction, have been conducted in patients with primary open angle glaucoma (POAG), primary angle-closure glaucoma (PACG), and nonglaucomatous patients, and only a few in patients with PXG [2, 14]. A possible explanation for this is the lower PXG incidence compared to other glaucoma forms, as well as its wide variations in incidence and prevalence among different countries globally and in different geographical areas within the same country [15]. Although there has been no organized data collection at the Clinic for Eye Diseases of the Republic of Srpska University Clinical Center so far, our clinical observation is that there is a significantly higher number of patients with pseudoexfoliation syndrome (PXS) and the PXG in the municipalities of Šipovo and Mrkonjić Grad compared to patients from other municipalities in the Krajina region. According to the data from the operative protocol of the Clinic for Eye Diseases in Banja Luka, out of 100 patients who undergo a cataract surgery, 11% also suffer from the PXG. This data significantly differs from the data of the study by Kovač et al. [15], where the PXG was present in 6.5% of the totally 674 patients planned for the cataract surgery. This discrepancy is undoubtedly influenced by the sample size, but certainly also by the geographical areas with the higher PXG incidence and their distance from the medical centers where the cataract surgery is performed, which is the case here.

Our research was inspired by the need to advance our day-to-day clinical practice in the PXG patient treatment. Aware of the diurnal IOP fluctuations [16], and in order to obtain the most recent values for IOP and PD ratio parameters, the IOP daily curve was performed preoperatively and at each measurement time point postoperatively.

Our study results show that the cataract surgery led to the IOP decrease in both PXG patients treated with medicaments and in nonglaucomatous patients. In patients with PXG, the reduction was recorded as early as in the first postoperative month and showed a tendency towards further reduction in the third and sixth month. In nonglaucomatous patients, the IOP decrease was the biggest in the third month, and the effect of the decrease began to weaken in the sixth month (Table 1; the absolute and the percent changes in IOP).

In the 6th postoperative month in the PXG group, the absolute IOP reduction was -3.23 ± 3.41 mmHg (-17.67 ± 16.86%), and in nonglaucomatous patients, -2.26 ± 1.71 mmHg (-15.06 ± 10.93%), with no significant difference between the groups.

According to the report of American Academy of Ophthalmology (AAO), among 5 studies that included only PXG patients (3 with level II evidence and 2 with level III evidence; totally 132 patients) and examining the effect of phacoemulsification on IOP, only 3 studies were prospective (totally 58 patients) [2]. The sample size in these five studies ranged from 4 to 51 patients and depending on the study, the follow-up period was 12 to 60 months. For the total sample

Table 2

Association between various predictors of absolute intraocular pressure (IOP) change after cataract surgery (using absolute IOP change at 6 months as the dependent variable)

Predictor	PXG group						Control group					
	Univariate			Multivariate			Univariate			Multivariate		
	B ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)
Gender	1.03 ± 1.02	0.318	0.1				0.17 ± 0.62	0.830	3.3			
Age	0.11 ± 0.10	0.298	0.4				-0.03 ± 0.04	0.499	1.8			
Pre-op IOP	-0.73 ± 0.14	< 0.01	47.3				-0.42 ± 0.13	< 0.01	22.5			
ACD	-1.25 ± 1.53	0.421	1.2	-0.86 ± 1.20	0.482	41.3	0.10 ± 1.04	0.920	3.4	0.03 ± 0.93	0.974	20.4
AL	-1.41 ± 0.63	< 0.05	12.5	-1.48 ± 0.50	< 0.01	57.7	-0.38 ± 0.33	0.269	0.9	0.14 ± 0.38	0.711	20.8
LT	1.86 ± 0.97	0.065	8.8	1.44 ± 0.74	0.065	49.7	0.43 ± 0.56	0.448	1.4	0.38 ± 0.52	0.475	22.0
LP	1.42 ± 1.96	0.476	1.7	1.68 ± 1.73	0.340	44.1	0.75 ± 0.98	0.451	1.4	0.59 ± 0.91	0.522	21.7
RLP	7.66 ± 4.03	0.068	8.5	6.81 ± 3.04	< 0.05	51.9	2.56 ± 1.90	0.189	2.6	0.86 ± 1.86	0.648	21.1
PD ratio	-1.11 ± 0.41	< 0.01	18.3	-1.13 ± 0.47	< 0.05	14.7	-0.91 ± 0.35	< 0.05	16.3	-0.96 ± 0.36	< 0.05	13.7

PXG – pseudoexfoliation glaucoma; Pre-op IOP – preoperative intraocular pressure; ACD – anterior chamber depth; AL – axial length; LT – lens thickness; LP – lens position; RLP – relative lens position; PD ratio – the ratio of preoperative IOP to ACD; *B* – regression coefficient; SE – standard error; r^2 – coefficient of determination.

Table 3

Association between various predictors of percentage intraocular pressure (IOP) change after cataract surgery (using % IOP change at 6 months as the dependent variable)

Predictor	PXG group						Control group					
	Univariate			Multivariate			Univariate			Multivariate		
	B ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)	*B* ± SE	*p*	r^2 (%)
Gender	-2.04 ± 5.52	0.714	3.3				1.90 ± 3.98	0.637	2.6			
Age	0.44 ± 0.57	0.447	1.5				-0.32 ± 0.28	0.265	1.7			
Pre-op IOP	-2.98 ± 0.90	< 0.01	26.7				-1.76 ± 0.94	0.072	7.7			
ACD	-0.61 ± 8.54	0.944	3.8	1.04 ± 7.89	0.896	19.8	-0.03 ± 6.64	0.997	3.4	-1.04 ± 6.43	0.873	6.6
AL	-7.81 ± 3.34	< 0.05	14.7	-8.44 ± 3.25	< 0.05	37.9	-2.12 ± 2.15	0.331	0.1	1.03 ± 2.60	0.695	7.0
LT	5.71 ± 5.69	0.325	0.0	5.16 ± 5.11	0.323	23.1	2.41 ± 3.60	0.508	1.9	2.92 ± 3.62	0.427	8.8
LP	8.55 ± 10.37	0.417	1.2	13.38 ± 10.62	0.220	24.9	3.62 ± 6.29	0.569	2.3	3.30 ± 6.29	0.604	7.5
RLP	43.52 ± 21.09	< 0.05	10.5	43.83 ± 18.68	< 0.05	35.2	13.67 ± 12.27	0.275	0.9	4.51 ± 12.91	0.725	6.9
PD ratio	-5.00 ± 2.26	< 0.05	12.6	-5.67 ± 2.56	< 0.05	8.8	-3.74 ± 2.37	0.126	4.7	-4.15 ± 2.41	0.097	4.1

IOP – intraocular pressure; PXG – pseudoexfoliation glaucoma; Pre-op – preoperative; ACD – anterior chamber depth; AL – axial length; LT – lens thickness; LP – lens position; RLP – relative lens position; PD ratio – the ratio of preoperative IOP to ACD; *B* – regression coefficient; SE – standard error; r^2 – coefficient of determination.

of 132 patients, the preoperative IOP was 20.7 ± 4.4 mmHg and in the follow-up period of 34.2 ± 20.8 months the IOP reduction of -4.1 mmHg (-20.0%) occurred. The largest IOP reduction was found in one study and was -13.6 mmHg (-43.0%) in the follow-up period of 12 months. The sample included 16 patients with uncontrolled PXG with the preoperative IOP value of 32.0 mmHg. A significant IOP reduction of -11.6 mmHg (-51.0%) was also found in one study in 4 patients who experienced secondary angle closure due to the zonular weakness. In the other three analyzed studies, the IOP reduction ranged from -1.1 mmHg (-6.0%) to -5.6 mmHg (-27.0%) [2].

Elgin et al. [17] determined, after a one-month period, the IOP reduction from the preoperative value of 18.3 ± 2.5 mmHg to the postoperative value of 15.2 ± 1.2 mmHg in 29 patients with PXG.

Jimenez-Roman et al.[18] retrospectively examined cataract surgery impact on IOP in 44 medically controlled patients with PXG, and with respect to the preoperative IOP (17.00 ± 2.75 mmHg) in the 6th postoperative month, the IOP reduction of -3.65 mmHg (-20.3%) was observed, which remained unchanged in the 12th month.

Abdelghany et al. [19] have recently conducted a prospective study on the impact of a cataract surgery on the IOP changes, ganglion cell complex, and peripapillary retinal nerve fibers layer in medically controlled patients with PXG. Eighty five patients were divided into two groups. The first group consisted of 40 patients with PXG and cataract who underwent cataract surgery. The control group consisted of 45 non-operated patients with PXG and no cataract. The controls were performed in the 3rd, 6th, 12th and 18th month. The preoperative IOP was significantly different between the groups (20.42 ± 0.90 mmHg in the pseudophakic group and 16.62 ± 1.00 mmHg in the control group), which may be due to cataract presence and changes in lens thickness. Compared with the preoperative IOP, a significant reduction in IOP was found postoperatively during each control, where the biggest one was in the third month (15.35 ± 1.03 mmHg), and the reduction effect gradually weakened till the end of the research in the 18th month (17.00 ± 2.75 mHg). In the 6th month, the reduction was -5.02 mmHg. Numerous studies have identified the IOP reduction in the nonglaucomatous patients after the cataract surgery by extracapsular extraction and phacoemulsification, ranging from 1.1 mmHg to 4.0 mmHg [3, 5, 19, 20].

In a study by Hsu et al. [21] on the cataract surgery impact on IOP in 75 nonglaucomatous patients (75 eyes), in the fourth postoperative month, the IOP reduction of -2.03 ± 2.42 mmHg (-12.74%) was noticed versus the preoperative value of 14.5 ± 3.05 mmHg.

Based on the above, we conclude that our results are consistent with the previous studies suggesting an IOP decrease after the cataract surgery in the PXG patients and nonglaucomatous patients, as well as the extent of its reduction.

In our study, regression analysis in the univariate model for both groups has shown the significant negative correlation of the preoperative IOP (PXG group: B = - 0.73 ± 0.14; p < 0.01; Control group: B = - 0.42 ± 0.13; p < 0.01) and its absolute postoperative reductions in the 6th month in the sense that the preoperatively higher IOP values are associated with the greater postoperative reductions, which is consistent with the results of other studies [2, 3, 5]. In our sample, this would mean that if the IOP is preoperatively increased by 1 mmHg (relative to the average IOP for the observed group), the absolute postoperative reduction will be greater by the additional 0.73 ± 0.14 mmHg in the PXG patients and in nonglaucomatous patients by the additional 0.42 ± 0.13 mmHg (Table 2). For the percentage IOP change in the 6th month, this was only the case for the PXG group (B = -2.98 ± 0.90; p < 0.01), whereas in the control subjects, this parameter had no significance (B = -1.76 ± 0.94; p = 0.072) (Table 3).

Since the preoperative IOP higher values tend to result in its greater absolute reduction compared to the lower basal values, we also examined the relative (percentage) IOP change in our study, because the percentage change may be similar in eyes with different initial IOP measurements.

The preoperative IOP values in our study proved to be a significant predictor of both the absolute and the percentage postoperative IOP changes in the PXG patients with predictive ability of r^2 = 47.3% and r^2 = 26.7%, respectively, and in the control group only for the absolute change with predictive ability of r^2 = 22.5% (Tables 2 and 3).

Pradhan et al. [22] examined the impact of the cataract surgery on the IOP in 77 patients (70 POAG; 4 POAG suspect; 3 with ocular hypertension) and found that the preoperative IOP indicates a change in the postoperative IOP values in the range of 13% to 20% and that these percentages depend on the number of the preoperative IOP measurements (one preoperative IOP measurement, prediction of 13% change in the postoperative IOP; the average value of two measurements, prediction 17%; the average value of three measurements, prediction 15%; the average value of up to four measurements, prediction 20%). It is worth mentioning that in that study, the preoperative IOP data were collected up to five years prior to cataract surgery and reflect the long-term fluctuations in the IOP. Also, the regression analysis was performed only with respect to the absolute but not to the percentage IOP change.

Moghimi et al. [23] examined 33 nonglaucomatous patients with PXS and found a moderate IOP decrease of 3.3 mmHg (18%) three months after the cataract surgery (the preoperative IOP: 18.1 ± 3.4 mmHg) with a predictive ability of the preoperative IOP of r^2 = 39% for its postoperative change.

According to a study by Shingleton et al. [24], the prediction of the preoperative IOP value for the postoperative IOP change in people with PXS was 40%.

The slightly higher percentage of predictability of the preoperative IOP obtained in our study for the absolute IOP change in the PXG group (r^2 = 47.3%) may reflect the analysis of the three preoperative IOP measurements in the daily IOP curve test and “improve” the result of a prediction of the postoperative IOP change relative to a single measurement. The statistical phenomenon of "regression to the mean value", which is a consequence of an inadequate number of the basic preoperative IOP measurements, was minimized thanks to a daily curve test conducted preoperatively in our study.

The exact mechanisms of the IOP reduction after cataract surgery are still not clear.

So far, in patients with the preoperatively narrow iridocorneal angle, shallow anterior chamber, and greater natural lens thickness, cataract surgery results in major changes in the anterior segment configuration, resulting in clinically significant reduction and a good long-term IOP control [25]. Thanks to these observations, cataract surgery or clear lens extraction are the procedures that have often become the first choice or an integral part of treating the narrow-angle glaucoma [26].

Several theories have hypothesized about the occurrence of the postoperative IOP reduction in people with open angle, whether with POAG, PXG, or healthy subjects.

When it comes to people with the PXS or PXG, according to one theory, the removal of a portion of the anterior lens capsule during capsulorhexis also removes the source of pseudoexfoliation material [27]. A correlation between the intraoperatively used fluid volume and the postoperative IOP change was also found, regarding the higher flow, greater IOP reduction, which supports the idea that surgery increases the clearance of the exfoliative material and pigmentary debris from the anterior eye segment and trabeculum [2, 27, 11]. The removal of the natural lens leads to the anterior ocular chamber deepening (enlargement of the aqueous humor "reservoir") and the displacement of the ciliary body backward and, consequently, its smaller compression into the trabeculum and Schlemm's canal, thereby improving draining. Some other theories are that the chamber angle deepening, low grade inflammatory response caused by the delivered ultrasound energy and the trabecular meshwork microscopic remodeling lead to the aqueous increased draining [24]. Whatever the mechanism, the question is if any other way, except for the preoperative IOP measurement, is possible for determining which patient will benefit from the cataract surgery in terms of achieving a clinically significant IOP reduction? This is especially important for glaucoma patients who have low IOP (low-teen) by the medical or the laser therapy, but the disease progression is still present. In such patients, it is not easy to make a decision about a filtering operation known to be frequently accompanied by a range of serious intraoperative or postoperative complications and frequent failure.

In this regard, numerous biometric parameters are observed as possible IOP change predictors after cataract surgery. Recently, papers have been published, where in order to obtain biometric measurements, the optical coherence tomography for the anterior eye segment (AS-OCT) has been used, but due to the cost of the equipment, such diagnostics is unavailable for most public health institutions, especially in the economically underdeveloped countries. In our study, we have analyzed the parameters whose values are easily obtained as a part of the patient's preoperative preparation for the cataract surgery using optical biometry and ultrasound A-scans available at all centers where the cataract surgery is performed. Also, most of the research has so far been done using such equipment, so that our results can be compared with those of other authors.

The results of the biometric measurements obtained from our subjects indicate an average shallower anterior chamber in the PXG group relative to the control group (PXG ACD: 2.90 ± 0.34 mm; control ACD: 3.07 ± 0.31 mm; $p = 0.066$), which is in line with the results of other studies [17, 28]. The probable reason for this is the increased zonular laxity in patients with PXG and lens anteposition. The lens thickness also plays a significant role in this, and was on average higher in the PXG group (PXG LT: 4.65 ± 0.50 mm; control LT: 4.34 ± 0.56 mm; $p < 0.05$). The LP parameter, represented by the sum of ACD and half LT, is expected to be uniform between the groups given that the ACD is higher in the control group. As the AL parameter is also uniform across groups, so is the same case for the RLP parameter represented by the LP and AL relationship. The preoperatively higher IOP and the lower ACD resulted in the significantly higher PD ratio in the PXG group compared to the control group (PXG PD ratio: 5.66 ± 1.15; control PD ratio: 4.77 ± 0.82; $p < 0.01$) (Table 1). Examining the correlation of the absolute postoperative IOP change in the 6th month and the biometric parameters, in the PXG group univariate model, a significant inverse correlation was present for the parameters AL ($B = -1.41 \pm 0.63$; $p < 0.05$) and PD ratio ($B = -1.11 \pm 0.41$; $p < 0.01$). When in the multivariate analysis parameters such as gender, age and the preoperative IOP were added, a significant correlation between the absolute postoperative IOP change and parameters AL ($B = -1.48 \pm 0.50$; $p < 0.01$), RLP ($B = 6.81 \pm 3.04$; $p < 0.05$) and PD ratio ($B = -1.13 \pm 0.47$; $p < 0.05$) was found. Parameters AL and PD ratio had small predicative value for the absolute postoperative IOP change (r^2 = 12.5%; r^4 = 18.3%, respectively) in the univariate model. In the multivariate model, AL and RLP had standard predictability (r^2 = 57.7%; r^2 = 51.9%, respectively), while PD ratio parameter had low predictability (r^2 = 14.7%) (Table 2).

Examining the correlation between the percentage postoperative IOP change in the 6th month and the biometric parameters in the PXG group, both in the univariate and multivariate models, it was significant for the parameters: AL, RLP and PD ratio. The parameters AL (r^2 = 37.9%) and RLP (r^2 = 35.2%) had the highest prediction value for the percentage IOP change in the multivariate model, while for the same parameters it was low in the univariate analysis. The predictability of the PD ratio was low in both univariate and multivariate models (Table 3).

For the control group, no parameter in the analysis model was found to be significant to indicate the percentage postoperative IOP change (Table 3).

A systematic review of the peer-reviewed literature shows that the largest number of studies addressing biometric parameters as possible predictors of the postoperative IOP change have been performed in PACG, POAG and nonglaucomatous patients. Since one of the inclusion criteria in our research was the degree of angle openness according to Shaffer's grade 3 or 4, our results are more appropriate to compare with the previous studies in this field that included patients with POAG, in the absence of published studies with PXG subjects. Thus, a significant correlation between the AL parameter and the absolute and percentage reduction of the postoperative IOP was also found by Yoo et al. [29] in individuals with suspected POAG but not in patients with POAG. Hsu et al.[21], Coh et al. [8], Bilak et al.[30] and Moghimi et al.[7] found this correlation in nonglaucomatous patients in both the univariate and multivariate analyses. The above studies did not calculate the prediction calculations for the AL parameter.

The PD ratio parameter was first introduced by Issa et al.[9] who found that in nonglaucomatous patients, the higher PD ratio was followed by the greater postoperative absolute reduction in IOP and indicated it as a strong predictor of this reduction (r^2 = 73.0%). The significant predictability of 34.1% for the PD ratio in nonglaucomatous patients was also established by Dooley et al. [10]. Hsu et al. [21] confirmed its significance as a predictor of both the absolute (r^2 = 52.9%) and the percentage (r^2 = 39.0%) postoperative IOP reductions in the nonglaucomatous patients, and Coh et al. [8] in patients with POAG.

The RLP is a parameter dependent on the thickness of the natural lens, its anteposition, the depth of the anterior chamber, and the total length of the bulb. Its role as a predictor of IOP change is significant in individuals with a narrow angle, and can be potentially used in individuals with an open angle.

Hsu et al. [21] found no association between RLP and the postoperative IOP changes in the multivariate analysis in nonglaucomatous patients. Examining nonglaucomatous patients and patients with POAG, neither Coh et al.[8] found a significant association between RLP and the postoperative absolute or percentage IOP reduction in either the univariate or multivariate analyses. In contrast, DeVience et al. [31] found the significant association between RLP and the postoperative IOP reduction in nonglaucomatous patients in the univariate analysis, but without calculating the prediction for RLP.

Our results show that the RLP is of limited use when viewed separately, but when other possible predictors, such as the preoperative IOP, age and gender are added, it can be helpful to a clinician in recognizing in which direction the postoperative change in IOP in patients with PXG may be expected.

Our research has several limitations. We did not subdivide glaucomatous patients by glaucoma stage that some studies have found to be related to the postoperative IOP change [29]. Patients with Shaffer's angle grade 3 and 4 were included in the study, so we did not have the data on IOP changes in patients with PXG and with a secondary narrow or closed angle. Leaving patients postoperatively on the same medication regimen as they had had preoperatively, we obtained data on change in IOP indicating the true impact of cataract surgery on IOP, but also we are aware of the hypotensive effect of medications on the IOP measurement results. It follows that the most accurate data on the impact of cataract surgery in patients with PXG could be obtained if the trial was performed in patients who had undergone the preoperative wash-out period since the antiglaucoma therapy, which is almost inapplicable to patients with PXG. Alternatively, the newly diagnosed patients may be examined without initiating medication or laser treatment, which will be feasible in some future studies.

Conclusion

Through the prospective study, we have found that cataract surgery results in a moderate decrease in IOP in both medically controlled patients with PXG and in nonglaucomatous patients. The occurrence and extent of this reduction may be indicated by clinical variables readily available by standard ophthalmic diagnostic equipment. In the PXG group, the preoperative IOP, AL, and PD ratio proved to be significant predictors of both the absolute and the percentage changes in IOP, whereas the RLP parameter proved to be a significant predictor of only the percentage IOP change. Of all the parameters tested, the preoperative IOP and the PD ratio stood out in the control group as the only significant predictors only of the absolute change in IOP.

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