Original Article

Anterior segment parameters after trabeculectomy in pseudoexfoliation glaucoma versus primary open-angle glaucoma

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ABSTRACT

Background: The effects of trabeculectomy on anterior segment parameters have been widely investigated. However, the stabilization time for various glaucoma types after trabeculectomy remains debatable. We investigated the effect of mitomycin C-augmented trabeculectomy on ocular anterior segment parameters in primary open-angle glaucoma (POAG) and pseudoexfoliation glaucoma (PXG) during short-term follow-up using the Pentacam HR.

Methods: In this retrospective observational study, consecutive patients diagnosed with medically uncontrolled POAG or PXG who underwent MMC-augmented trabeculectomy were recruited. All individuals underwent detailed ocular examinations. All trabeculectomies were performed by a single surgeon using the same technique. Anterior segment parameters, including anterior chamber depth (ACD), anterior chamber volume (ACV), anterior chamber angle (ACA), and central corneal thickness (CCT) were measured using the Pentacam HR, along with intraocular pressure (IOP) using a Goldmann applanation tonometer, pre-operatively and at 1-week, 1-month, and 3-month post-operative visits.

Results: We included 80 patients with a median (range) age of 58.0 (41.0–86.0) years having a nearly similar sex ratio. The study groups were matched according to sex and age (both $P > 0.05$). The group-by-time interaction was significant for CCT and ACV (both $P < 0.05$) but not for IOP, ACD, and ACA (all $P > 0.05$). The mean (standard deviation [SD]) IOP, ACD, and ACA were comparable between groups (all $P > 0.05$) during the 3-month period; however, they changed significantly over time in both groups (all $P < 0.001$). The mean CCT and ACV were comparable between groups at each time point (all $P > 0.05$), except at the 1-month post-operative visit, at which the mean (SD) ACV was significantly lower in the PXG group ($P < 0.05$). We found a comparable mean (SD) CCT between paired visits in each group (all $P > 0.05$), except for the mean (SD) CCT at 3 months, which was significantly lower than that at the 1-month post-operative visit in the PXG group ($P < 0.05$). We found a comparable mean (SD) ACV between paired visits in each group (all $P > 0.05$); however, it was significantly lower at the 1-month post-operative versus the baseline visit in both groups and resumed a significantly higher value at the 1-month versus the 1-week visit and at the 3-month versus the 1-month visit in the PXG group (all $P < 0.05$).

Conclusions: We observed significant changes in IOP, ACD, and ACA over 3 months after post-augmented trabeculectomy in eyes with POAG and PXG; however, the majority of anterior segment parameters were comparable between the two groups. Further large-scale studies with longer follow-up periods should be conducted to verify the post-operative fluctuations in these parameters in POAG and PXG.

KEYWORDS

anterior eye segments, anterior chambers, Pentacam HR, open-angle glaucomas, exfoliation glaucoma, trabeculectomies, intraocular pressures, central corneal thickness, anterior chamber depth, anterior chamber volume, anterior chamber angle

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INTRODUCTION

Glaucoma is a chronic, irreversible, progressive optic neuropathy. Lowering the intraocular pressure (IOP) is the only feasible treatment approach, which can be achieved using topical or systemic medications, lasers, or surgical intervention. Trabeculectomy remains the reference standard surgical treatment for glaucoma [1]. The success rate of trabeculectomy can be influenced by various factors, including the surgical technique employed, dimensions and thickness of the flap created, density of the suture material utilized to secure the flaps, and degree of tension applied to the sutures [2, 3]. Moreover, glaucoma subtype is a determining factor for surgical success [4]. The outcomes of argon laser therapy and trabeculectomy were comparable between pseudoexfoliative glaucoma (PXG) and primary open-angle glaucoma (POAG) [5, 6]. However, the long-term success rate was significantly lower in eyes with PXG [6].

Studies have revealed the impact of trabeculectomy on anterior segment parameters [7, 8]. However, the stabilization time for changes in these parameters after trabeculectomy is a matter of debate [9]. Assessment of the anterior segment and bleb traditionally relies on slit-lamp examination; however, the use of imaging modalities that offer quantitative and comparable values is of growing importance [10]. The digital methods used for this purpose include the IOLMaster (Zeiss, Germany), AC-Master (Zeiss, Germany), Scheimpflug imaging Pentacam HR (Oculus, Wetzlar, Germany), and the slit-lamp pachymeter by Jaeger (Haag-Streit, Switzerland) [11]. The Pentacam HR provides measurements that correlate highly with those measured with different devices, and it features a higher interobserver agreement and a shorter learning curve than other devices [12].

In this study, we evaluated the effect of mitomycin C (MMC)-augmented trabeculectomy on anterior segment parameters in POAG and PXG during a short-term follow up using Pentacam HR.

METHODS

In this retrospective observational study, we recruited patients with the diagnosis of POAG or PXG who underwent MMC-augmented trabeculectomy in the Ophthalmology Department, Harran University Faculty of Medicine, Sanliurfa, Turkey, between January 2018 and January 2023. The study protocol was approved by the Ethics Committee of Harran University Faculty of Medicine. All procedures complied with the standards of the Ethics Committee of Harran University Faculty of Medicine Clinical Research and the ethical principles of the Declaration of Helsinki regarding human experimentation. All the participants provided written informed consent.

Individuals who had a confirmed diagnosis of POAG or PXG unresponsive to medical treatment, IOP ≥ 21 mmHg, and the presence of glaucomatous optic neuropathy and visual field changes, and who underwent MMC-augmented trabeculectomy, were consecutively recruited. The presence of gray-white exfoliation material at the pupillary border, iris, iridocorneal angle, or anterior lens capsule in eyes with PXG was confirmed using slit-lamp biomicroscopy (Topcon SL-D701, Tokyo, Japan) [6]. We excluded eyes with a history of intraocular surgery, laser treatment for glaucoma, or trauma; those with a compromised cornea, uveitis, or glaucoma other than POAG or PXG; and those with posterior segment pathologies. Patients with insufficient image quality were excluded from the analysis.

All individuals underwent detailed ocular examinations, including measurement of best-corrected distance visual acuity using a Snellen chart (NIDEK chart projector, CP670; Nidek Co., Gamagori, Japan), anterior and posterior segment examination using slit-lamp biomicroscopy, IOP measurement using a Goldmann applanation tonometer AT 900 (Haag-Streit), and indirect gonioscopy examination using a Goldmann three-mirror lens (Volk Optical, Inc., Mentor, OH, USA).

Anterior segment parameters, including anterior chamber depth (ACD), anterior chamber volume (ACV), anterior chamber angle (ACA), and central corneal thickness (CCT) were measured using the Pentacam HR, along with intraocular pressure (IOP) using a Goldmann applanation tonometer AT 900, pre-operatively and at 1-week, 1-month, and 3-month post-operative follow-up visits.

All trabeculectomies were performed by a single surgeon (M.T.) using the same technique [13]. Post-operatively, topical antibiotics (ofloxacin; Floxal EDO, Dr. Mann Pharma GmbH, Germany) five times daily, topical steroids (dexamethasone; Dexa EDO, Dr. Mann Pharma GmbH) five times daily, and mydriatic eye drops (cyclopentolate; Zyclolat EDO, Dr. Mann Pharma GmbH) three times daily for 6 weeks were administered and adjusted using an individualized approach. All previous anti-glaucoma medications were discontinued.

Statistical analysis was conducted using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA). All variables were tested for normality of data distribution, and continuous variables with or without normal distribution are presented as mean (standard deviation [SD]) or median (minimum and maximum), respectively. Categorical variables are presented as frequencies and percentages. Age and sex ratios between the groups were compared using the Mann–Whitney U and Chi-square tests, respectively. Anterior segment parameters (CCT, ACD, ACV, and ACA) and IOP of the two groups at all time points were compared using repeated-measures analysis involving group effects, time effects, and group-by-time interactions. All P-values < 0.05 were considered statistically significant.

RESULTS

Of the 80 included patients, with a median (range) age of 58.0 (41.0–86.0) years, 39 (48.8%) were men and 41 (51.2%) were women. There were no significant differences in patient characteristics between the groups (both $P > 0.05$) (Table 1).

The group-by-time interaction was significant for CCT and ACV (both $P < 0.05$), but not for IOP, ACD, or ACA (all $P > 0.05$) (Table 2). In the overall analysis of IOP, ACD, and ACA during the 3-month period, the mean (SD) values were comparable between the groups (all $P > 0.05$); however, they changed significantly over time in both groups (all $P < 0.01$) (Table 2).

The mean values for CCT and ACV were comparable between the groups at each time point (all $P > 0.05$), except at the 1-month post-operative visit, in which the mean (SD) ACV was significantly lower in the PXG (148.8 [16.4] mm^3) than in the POAG group (155.2 [23.0] mm^3) ($P < 0.05$) (Table 3).

Table 1. Demographic characteristics of study groups

Variables	Overall (n = 80)	POAG (n = 41)	PXG (n = 39)	*P*-value
Age (y), Median (Range)	58.0 (41.0 to 86.0)	56.0 (41.0 to 85.0)	58.0 (42.0 to 86.0)	0.145
Sex (Men / Women), n (%)	39 (48.8) / 41 (51.2)	19 (46.3) / 22 (53.7)	20 (51.3) / 19 (48.7)	0.827

Abbreviations: POAG, primary open angle glaucoma; PXG, pseudoexfoliation glaucoma; n, number of operated eyes; y, years; %, percentage. Note: POAG, indicates group of participants with diagnosis of POAG who underwent mitomycin C-augmented trabeculectomy; PXG, indicates group of participants with diagnosis of PXG who underwent mitomycin C-augmented trabeculectomy.

Table 2. Comparison of variables between study groups at different time points

Variables	Timepoint	Groups		*P*-values		
		POAG (n = 41)	PXG (n = 39)	Group effect	Time effect	Group-by-time interaction
IOP (mmHg), Mean ± SD	Preoperative	36.2 ± 4.5	37.5 ± 4.4	0.395	**< 0.001**	0.979
	1-week postoperative	12.5 ± 1.9	12.8 ± 1.8			
	1-month postoperative	15.3 ± 2.4	15.5 ± 2.1			
	3-month postoperative	17.1 ± 2.6	17.5 ± 2.0			
CCT (μm), Mean ± SD	Preoperative	532.2 ± 27.4	526.8 ± 19.8	0.482	**< 0.001**	**< 0.001**
	1-week postoperative	537.3 ± 28.0	536.8 ± 19.1			
	1-month postoperative	533.7 ± 29.4	527.4 ± 19.2			
	3-month postoperative	530.8 ± 28.8	519.5 ± 20.9			
ACD (mm), Mean ± SD	Preoperative	2.8 ± 0.4	2.7 ± 0.3	0.781	**< 0.001**	0.159
	1-week postoperative	2.6 ± 0.3	2.6 ± 0.3			
	1-month postoperative	2.7 ± 0.3	2.7 ± 0.3			
	3-month postoperative	2.8 ± 0.3	2.7 ± 0.3			
ACV (mm^3), Mean ± SD	Preoperative	158.4 ± 23.2	153.6 ± 16.5	0.058	**< 0.001**	**0.005**
	1-week postoperative	148.2 ± 23.5	141.0 ± 16.4			
	1-month postoperative	155.2 ± 23.0	148.8 ± 16.4			
	3-month postoperative	156.9 ± 23.1	151.6 ± 16.6			
ACA (degree), Mean ± SD	Preoperative	35.7 ± 4.0	35.1 ± 3.4	0.639	**< 0.001**	0.397
	1-week postoperative	31.0 ± 4.0	30.9 ± 3.6			
	1-month postoperative	34.1 ± 3.9	34.2 ± 3.6			
	3-month postoperative	34.9 ± 3.9	34.7 ± 3.5			

Abbreviations: POAG, primary open angle glaucoma; PXG, pseudoexfoliation glaucoma; n, number of operated eyes; IOP, intraocular pressure; mmHg, millimeter of mercury; SD, standard deviation; CCT, central corneal thickness; μm, micrometer; ACD, anterior chamber depth; mm, millimeter; ACV, anterior chamber volume; mm^3, cubic millimeter; ACA, anterior chamber angle. Note: *P* values < 0.05 are shown in bold; POAG, indicates group of participants with diagnosis of POAG who underwent mitomycin C-augmented trabeculectomy; PXG, indicates group of participants with diagnosis of PXG who underwent mitomycin C-augmented trabeculectomy.

Table 3. Intergroup comparisons of CCT and ACV between POAG and PXG groups at different time points

Timepoint	CCT	ACV
	P-value	*P*-value
Preoperative	0.540	0.200
1-week postoperative	0.190	0.059
1-month postoperative	0.293	**0.013**
3-month postoperative	0.112	0.139

Abbreviations: CCT, central corneal thickness; ACV, anterior chamber volume; POAG, primary open angle glaucoma; PXG, pseudoexfoliation glaucoma. Note: *P*-value < 0.05 is shown in bold; POAG, indicates group of participants with diagnosis of POAG who underwent mitomycin C-augmented trabeculectomy; PXG, indicates group of participants with diagnosis of PXG who underwent mitomycin C-augmented trabeculectomy.

Table 4. Intragroup comparisons of CCT and ACV between two timepoints in POAG or PXG group

Two timepoints	CCT		ACV	
	POAG, *P*-value	PXG, *P*-value	POAG, *P*-value	PXG, *P*-value
Preoperative vs. 1-week postoperative	0.478	0.469	0.293	0.053
Preoperative vs. 1-month postoperative	0.602	0.050	**0.030**	**< 0.001**
Preoperative vs. 3-month postoperative	0.401	0.070	0.341	0.220
1-week postoperative vs. 1-month postoperative	0.561	0.041	0.086	**0.009**
1-week postoperative vs. 3-month postoperative	0.458	0.074	0.393	0.182
1-month postoperative vs. 3-month postoperative	0.826	**0.001**	0.046	**0.001**

Abbreviations: CCT, central corneal thickness; ACV, anterior chamber volume; POAG, primary open angle glaucoma; PXG, pseudoexfoliation glaucoma. Note: *P*-values < 0.05 are shown in bold; POAG, indicates group of participants with diagnosis of POAG who underwent mitomycin C-augmented trabeculectomy; PXG, indicates group of participants with diagnosis of PXG who underwent mitomycin C-augmented trabeculectomy.

We found a comparable mean (SD) CCT between paired visits of each group (all $P > 0.05$), except at 3 months (519.5 [20.9] μm), when it was significantly thinner than in the 1-month visit (527.4 [19.2] μm) in the PXG group ($P < 0.05$) (Table 4). We found a comparable mean (SD) ACV between paired visits in each group (all $P > 0.05$), except at the 1-month post-operative visit (155.2 [23.0] mm^3 in POAG and 148.8 [16.4] mm^3 in PXG), when it was significantly lower than in the baseline visit (158.4 [23.2] mm^3 in POAG and 153.6 [16.5] mm^3 in PXG) in both groups, and was significantly higher at the 1-month (148.8 [16.4] mm^3) versus the 1-week (141.0 [16.4] mm^3) visit and at the 3-month (151.6 [16.6] mm^3) versus the 1-month (148.8 [16.4] mm^3) visit in the PXG group (all $P < 0.05$) (Table 4).

DISCUSSION

Comparison of anterior segment parameters, IOP, and CCT in short-term post-MMC-augmented trabeculectomy between eyes with POAG and PXG revealed no significant differences at multiple postoperative time points, except for a significantly lower ACV in the PXG group at 1 month compared with that of the POAG group that was comparable at 3-month visit. However, during the 3-month period, the IOP, ACD, and ACA significantly changed over time in each group. Furthermore, ACV was significantly reduced in both groups at 1 month compared with baseline and showed a significant increase in subsequent follow-up measurements compared with that of the preceding visits in the PXG group.

Balsak and Ekinci [14] followed 54 eyes with POAG that underwent combined phacoemulsification with 5-fluorouracil-augmented trabeculectomy, up to 6 months post-operatively, and found a significant increase in ACD and ACA compared with baseline values, while CCT remained unchanged [14]. Similarly, we observed an overall significantly increasing trend in these parameters, yet the positive effect of combined phacoemulsification in their study was inevitable. A prospective study [9] using Pentacam HR in 38 phakic eyes with POAG that underwent 5-fluorouracil-augmented trabeculectomy revealed a significant decrease in ACA, ACD, and ACV with an increase in CCT at the 1-week post-operative visit, followed by a significant increase in ACA, ACD, and ACV and a decrease in CCT at the 1-month visit. Thereafter, all parameters remained comparable to baseline values for up to 6 months post-operatively. The study revealed stabilization of anterior segment parameters after the 1-month early post-operative visit, when they returned to their baseline values [9]. In our study, the eyes in the POAG group showed a decrease in ACD and ACA values up to the 1-week post-operative visit, followed by an increase in subsequent visits up to 3 months post-operatively. However, CCT and ACV remained unchanged, except for a significant decrease in ACV at 1 month, which achieved a comparable value at 3 months. These findings imply short-term fluctuations in the anterior segment parameters following augmented trabeculectomy in eyes with POAG. However, the trend of changes in posterior segment parameters measured using optical coherence tomography in patients with the same type of glaucoma, POAG, who underwent MMC-augmented trabeculectomy has revealed a different pattern [13].

Elgin et al. [15] included 19 eyes with POAG and 20 eyes with PXG that underwent 5-fluorouracil-augmented trabeculectomy. Using an optical biometer, CCT and ACD, along with other parameters, were measured at baseline and at 1 and 3 months post-operatively. Eyes in both groups revealed a significantly shallower ACD at 1 and 3 months post-operatively; however, CCT remained unchanged in eyes with POAG, with a significant increase observed at the 1-month follow-up in the PXG group, which returned to its baseline value at the 3-month visit. However, no significant difference was found between the groups in pre-operative or 1- and 3-month post-operative mean values for all parameters [15]. Consistent with that study, in our similar post-operative period, we found comparable anterior segment parameters between the study groups, except for the ACV, which was significantly lower in the PXG group than in the POAG group at the 1-month post-operative visit which returned to its baseline value at the 3-month visit.

Eyes with pseudoexfoliation syndrome with or without PXG were found to have thinner CCT than controls [16]. Doganay et al. [17] used Pentacam HR in participants without a history of ocular surgery, including 80 eyes of 50 patients with pseudoexfoliation syndrome, 80 eyes of 57 patients with PXG, and 80 eyes of healthy controls, and found no statistically significant difference in ACD, ACV, ACA, and CCT between the study groups, except for a significantly shallower ACD in PXG versus healthy eyes [17]. Ozkan Aksoy et al. [18] used Galilei, a dual Scheimpflug analyzer imaging system, to compare CCT, ACV, ACA, and ACD along with other anterior segment parameters in participants without a history of ocular surgery, including 47 eyes of 38 patients with PXG, 30 eyes of 15 patients with primary angle-closure glaucoma (PACG), and 60 eyes of 30 healthy controls. Although eyes with PACG had significantly lower values for ACV, ACD, and ACA than the other study groups, these parameters were comparable between eyes with PXG and those of healthy controls [18]. Considering these findings [16-18], the observed changes in the anterior segment parameters among eyes with PXG could have been caused by surgical intervention; however, this justification is not infallible. Therefore, future comparative longitudinal studies, including eyes with PXG with and without a history of augmented trabeculectomy, could confirm or refute this reasoning.

A study [19] using Scheimpflug-based imaging in eyes with a wide spectrum of diagnoses of angle closure observed a significant reduction in the ACA of eyes with PACG at 3 months after peripheral iridotomy, despite experiencing a significant early increase at 1 month. This observation may indicate the effect of glaucoma type on anterior segment parameters, irrespective of the type of surgical intervention [19]. In a follow-up study of eyes that underwent 5-fluorouracil-augmented trabeculectomy, Diagourtas et al. [20] measured ACD using IOLMaster at multiple visits. Most of the included eyes had POAG or PXG and experienced a significant reduction in ACD at all follow-up visits, except for the last follow-up at 8 weeks. The authors did not compare ACD in the subgroups of eyes with PXG and POAG, as this was not the aim of their study [20]. In the current study, we observed significant changes in ACD and ACA in eyes with PXG and POAG after augmented trabeculectomy. Because the above studies [19, 20] did not compare the parameters between these two types of glaucoma, a direct comparison of our outcomes with their results is not prudent.

In a review of 25 studies involving 690 participants [21] with various types of glaucoma at the immediate post-trabeculectomy visit, a significant reduction in ACD followed by gradual deepening and approximation to baseline values on day 14 was reported [21]. This may indicate that the effect of trabeculectomy on anterior segment parameters is not long-lasting and does not depend on the type of glaucoma, as we observed. Further studies with subgroup analyses may provide more robust inferences.

However, Husain et al. [22], in a prospective cohort study with 5 years of follow-up after trabeculectomy, found a continuous reduction in ACD and axial length compared with baseline values at all follow-up visits, with a mean decrease of 0.11 mm and 0.16 mm, respectively. Eyes with POAG had higher odds of fluctuation in both parameters than those with PACG [22]. We believe that other undetermined factors may have influenced these observed discrepancies in the post-trabeculectomy anterior segment parameters and deserve further investigation.

Karasheva et al. [23], in a prospective study of 45 eyes mostly having POAG or PXG that underwent trabeculectomy with or without antimetabolites, measured ACD using IOLMaster and found almost no changes in ACD at all post-operative visits. They indicated that the ACD was almost unchanged for all measurements, and that the mean variability in ACD measurements was 0.061 mm. They found no significant correlation between post-operative IOP reduction and ACD for pooled data of study participants. No subgroup analysis of the observed changes was performed among the different glaucoma types [23]. In the current study, in the PXG group, the mean ACD at baseline and at the post-operative visits was constantly at 2.7 mm, except at 1 week, when the measurement was 2.6 mm. Tekan et al. [24] used Sirius, a Scheimpflug-based imaging system, and found significant increases in ACD, ACA, and ACV in 53 eyes with POAG or PXG that underwent combined phacoemulsification and gonioscopy-assisted transluminal trabeculotomy at 3 months post-operation. The study did not compare the outcomes of eyes with POAG and PXG, and only pooled data were assessed [24]. Up to the 3-month post-augmented trabeculectomy visit, we observed significant changes in IOP, ACD, and ACA in both groups. Furthermore, ACV was significantly reduced in both groups at 1 month and resumed a significant increase in subsequent follow-ups compared with the preceding visit in the PXG group.

This comparative follow-up study did not detect a significant difference in the anterior segment parameters between eyes with POAG and PXG pre-operatively or in the short-term post-operative follow-up using the sophisticated Pentacam HR imaging system. Considering that a similar surgical technique was performed by a single experienced glaucoma surgeon, the results of this comparison may be considered reliable. However, the study failed to measure functional changes along with anatomical variations in the study participants, and comparing the long term post-operative trends in these two parameters could provide a valuable practical outcome. In addition, the short-term follow-up, lack of healthy controls, and failure to include glaucomatous eyes without a history of surgical intervention are other limitations of our study. Further large-scale studies addressing these limitations are necessary to validate these preliminary results. Moreover, machine learning models have recently been used to predict the success rate of trabeculectomy [25]. We propose using a similar approach by exploiting artificial intelligence for predicting anterior segment parameters in the short- and long-term post-trabeculectomy in various types of glaucoma, especially in eyes with POAG and PXG.

CONCLUSIONS

We observed significant changes in IOP, ACD, and ACA over 3 months following augmented trabeculectomy in the POAG and PXG groups; however, most anterior segment parameters were comparable between the two types of glaucoma. A practical point could be the time effect rather than the effect of glaucoma type on post-operative fluctuations in these parameters; however, this justification is not infallible. Further large-scale studies are required to test this hypothesis.

ETHICAL DECLARATIONS

Ethical approval: The study protocol was approved by the Ethics Committee of Harran University Faculty of Medicine. All procedures complied with the standards of the Ethics Committee of Harran University Faculty of Medicine Clinical Research and the ethical principles of the Declaration of Helsinki regarding human experimentation. All the participants provided written informed consent.
Conflict of interest: None.

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