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Original Article

Long-Term Clinical Results of Trabectome Surgery in Turkish Patients with Primary Open Angle Glaucoma and Pseudoexfoliative Glaucoma

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Abstract

Objectives: The objectives of the study were to analyze the long-term results of trabectome surgery in Turkish patients with primary open angle glaucoma (POAG) and pseudoexfoliative glaucoma (PEXG) and to characterize the risk factors for failure.

Methods: This single-center retrospective non-comparative study included 60 eyes of 51 patients diagnosed with POAG and PEXG, who underwent trabectome alone or phacotrabeculectomy (TP) surgery between 2012 and 2016. Surgical success was defined as a 20% decrease in intraocular pressure (IOP) or IOP≤21 mmHg and no further glaucoma surgery. Risk factors for further surgery were analyzed with the Cox proportional hazard ratio (HR) models. The cumulative success analysis was undertaken with the Kaplan–Meier method based on the time to further glaucoma surgery.

Results: The mean follow-up period was 59.4±14.3 months. During the follow-up period, 12 eyes required additional glaucoma surgery. The mean pre-operative IOP was 26.9±6.8 mmHg. The mean IOP at the last visit was 18.8±4.7 mmHg (p<0.01). IOP decreased 30.1% from the baseline to the last visit. The average number of antiglaucomatous drug molecules used was 3.4±0.7 (range 1–4) preoperatively and 2.5±1.3 (range 0–4) at the last visit (p<0.01). The risk factors for further surgery requirement were determined as a higher baseline IOP value (HR: 1.11, p=0.03] and the use of a higher number of preoperative antiglaucomatous drug molecules (HR: 2.54, p=0.09). The cumulative probability of success was calculated as 94.6%, 90.1%, 85.7%, 82.1%, and 78.6% at three, 12, 24, 36, and 60 months, respectively.

Conclusion: The success rate of trabectome was 67.3% at 59 months. A higher baseline IOP value and the use of a higher number of antiglaucomatous drug molecules were associated with an increased risk of further glaucoma surgery requirement.

Keywords: Ab interno trabeculectomy, intraocular pressure, open angle glaucoma, pseudoexfoliative glaucoma, trabectome

Introduction

Glaucoma is an optic neuropathy characterized by specific optic disc findings reflecting retinal nerve fiber loss and certain visual field defects, in which intraocular pressure (IOP) is the only modifiable risk factor to slow down disease progression (1,2). Glaucoma is a challenging disease of the eye necessitating lifelong follow-up and the leading cause of irreversible vision loss worldwide (3).

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The treatment choices of glaucoma include medical therapy and surgical treatment (4). Among surgical options, trabeculectomy with an antimetabolite application remains the gold standard (5). Artificial drainage implants are among other filtering surgical options. These procedures are highly effective in lowering IOP but are not perfect therapeutic options due to their sight-threatening complications, such as prolonged hypotony, bleb-related endophthalmitis, cataract formation, suprachoroidal hemorrhage, and high rate of revision surgery (6-9).

Minimally invasive glaucoma surgery (MIGS) aims to lower IOP without leading to serious complications observed in filtering procedures. Saheb and Ahmed defined MIGS as a group of surgical interventions sharing common characteristics, including an ab interno approach with a clear corneal incision sparing the conjunctiva and sclera, minimal trauma to target tissues, lowering IOP, high safety profile without exposing the eyes to serious complications, and rapid recovery (10). In this regard, trabectome surgery (TS) with the Trabectome® device (Neomedix Corp., Tustin, CA, USA) is one of the MIGS procedures approved by the United States Food and Drug Administration in 2004.

In 2005, the first clinical results reported by Minckler et al. (11) showed the efficacy of TS in the treatment of open-angle glaucoma. Since then, many studies have shown the safety and efficacy of TS over six to 48 months. Recently, Mosaed et al. (12) and Esfandiari et al. (13) published the long-term results of TS over 90 months and 5-year follow-up periods, respectively.

In this study, we aimed to evaluate the long-term outcomes of TS in Turkish patients with primary open angle glaucoma (POAG) and pseudoexfoliative glaucoma (PEXG) and compare our results with the previous studies. We also aimed to delineate risk factors for failure.

Methods

This is a retrospective-single center non-comparative study that aimed to investigate whether TS was successful in the long term and determine factors influencing success or leading to failure. This study was approved by the local ethics committee with the registration number HNEAH-KAEK-2021/1 and adhered to the tenets of the Declaration of Helsinki as revised in 2013.

The study included all patients aged above 40 years, who had POAG and PEXG of any stage with or without previous surgical or laser intervention for glaucoma treatment and underwent trabectome surgery alone (TA) or combined with phacoemulsification trabectome phacotrabectome (TP) between 2012 and 2016 in a single tertiary center. Data were collected from the patient files and hospital records. Patients with less than 6 months of follow-up and those with missing or incomplete medical records were not included in the study. Patients with any secondary glaucoma (other than PEXG), angle closure glaucoma, congenital or juvenile glaucoma, those with a history of complicated cataract surgery, vitrectomy, or keratoplasty, and those with inflammatory eye diseases, retinal detachment, diabetic retinopathy, senile macular degeneration, retinal vascular diseases, aphakia, degenerative myopia, or nanophthalmos were not included in the study. Demographic data, including age and gender, eye laterality, best-corrected visual acuity using the logMAR system, lens status, type of glaucoma, glaucoma stage according to the Hodapp-Parrish-Anderson criteria (14) using the Goldmann visual field analysis Swedish Interactive Threshold Algorithm Standard 30–2 (Humphrey Visual Field Analyzer, Carl Zeiss Inc., Dublin, CA, USA), central corneal thickness (CCT) measured by Pentacam (rotating Scheimpflug camera; Oculus, Wetzlar, Germany), IOP measured using Goldmann applanation tonometry, number of antiglaucomatous drug molecules used, type of surgery, and any previous surgery were noted.

Outcome measures assessed at the sixth month and last visit included IOP, number of glaucoma drug molecules used, additional glaucoma or ocular surgery requirement and time from index to additional surgery, visual acuity, and any additional ocular pathology affecting visual acuity. Surgical success was defined as a drop in IOP by 20% or IOP ≤21 mmHg and no further glaucoma surgery. Patients that died and those that were lost to follow-up were also noted.

All the operations were performed by a single well-experienced glaucoma surgeon (Y.Y.). Surgery was performed under topical anesthesia through a 1.7 mm clear corneal temporal incision, using a modified Swan-Jacobs surgical gonioscopy lens (Ocular Instruments, Bellevue, WA, USA). To achieve the best visualization angle, the head was rotated 30-40°counterclockwise and the microscope was tilted 30–40° clockwise toward the surgeon. Using viscoelastic, the trabectome tip was advanced, and nasally ≈60–100° strip of the inner wall of the trabeculum and Schlemm's canal was removed. Routine anterior chamber antibiotic prophylaxis was applied. In the combined procedure, TS was performed first. All the patients were instructed to use antibiotics for 10 days and steroid and pilocarpine treatment for one month.

Statistical Analysis

Data were evaluated using the statistical package program of IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). For all the tests, $p<0.05$ was considered statistically significant. Frequency, percentage, mean±standard deviation, median, and range values were used to describe the data. Compliance with a normal distribution was investigated with the Kolmogorov-Smirnov and Shapiro–Wilk tests. Normally distributed (parametric) paired groups were compared using correlated-samples t-test, while paired groups without a normal distribution (non-parametric) were compared using the Wilcoxon test. The odds ratio was used to quantify the strength of the association between two parameters. The Kaplan–Meier survival plots were constructed to assess the long-term survival rates. The Cox proportional hazard model was used to identify risk factors for failure. A mixed-effects model with a compound symmetry covariance structure and four parameters was used to evaluate the inter-eye correlation effect of repeated measurements in both eyes of nine patients included in the study.

Results

A total of 60 eyes of 51 patients were included in the study. Of the 60 operations performed, 43 (71.7 %) were TA and 17 (28.3%) were TP. Half of the operations (n=30, 50%) were operated on the right eyes, and the remaining half on the left eyes. Of the patients, 23 (45.1%) were female and 28 (54.9%) were male. The mean age was 67.9 years (range, 21–85 years). The mean follow-up time was 59.4±14.3 months. The baseline characteristics of the operated eyes are shown in Table 1.

Of the operated eyes, 45 (75%) had POAG and 15 (25%) had PEXG. Fourteen (23.3%) had early, 20 (33.3%) had moderate, and 26 (43.3%) had severe glaucomatous visual field changes. The mean CCT was 536.1 (443–617) microns.

A history of trabeculectomy surgery was present in 11 (18.3%) eyes, trabeculectomy and selective laser trabeculoplasty (SLT) in two (3.3%), and only SLT in one (1.7%).

During the follow-up period, two patients died, and one patient with bilateral TS did not adhere to follow-up. Therefore, the last visit data were available for 56 (93.3%) eyes.

No serious complication related to TS was seen in the long term, but early post-operative hyphema which resolved within the 1st week was nearly universal, seen in 90% of eyes.

The mean pre-operative IOP was 26.9±6.8 mmHg, the mean post-operative sixth-month IOP was 18.3±4.9 mmHg ($p<0.01$), and the mean last-visit IOP was 18.8±4.7 mmHg ($p<0.01$). Accordingly, compared to the baseline, IOP decreased by 31.9% and 30.1% at the sixth month and last visit, respectively.

The mean number of antiglaucomatous drug molecules used was 3.42±0.7 (range, 1–4), 1.9±1.42 (range, 0–4), and 2.5±1.34 (range, 0–4) preoperatively, at the 6th month, and at the last visit, respectively ($p<0.01$). At the final visit, eight (13.3%) eyes were not receiving any antiglaucomatous drug, and only one of these eyes had undergone additional glaucoma surgery.

The mean best-corrected visual acuity was 0.41±0.49 logMAR (range, 0–2) preoperatively and 0.61±0.75 logMAR at the last visit ($p=0.02$). During the follow-up, other ocular pathologies, including senile macular degeneration, diabetic

Table 1. Baseline characteristics of the operated patients

Baseline characteristics	
Age (years)	
Mean±SD Median(range)	67.9±11.7 69.5 (21–85)
Gender	
Female	23 (45.1%)
Male	28 (54.9%)
Eye	
Right	30 (50%)
Left	30 (50%)
CCT (micron)	
Mean±SD	536.1±37
Median(range)	531 (443-617)
Lens	
Phakic	32 (53.3%)
Pseudophakic	28 (46.7%)
logMAR	
Mean±SD	0.41±0.49
Median (range)	0.25 (0.00-2)
Antiglaucomatous drug molecules	
Mean±SD	3.42±0.76
Median (range)	4 (1-4)
Baseline IOP (mmHg)	
Mean±SD	26.9±6.8
Median(range)	27 (12-48)
Glaucoma stage	
Early	14 (23.3%)
Moderate	20 (33.3%)
Severe	26 (43.3%)
Glaucoma type	
POAG	45 (75%)
PEXG	15 (25%)
Surgery	
TA	43 (71.7%)
TP	17 (28.3%)
Prior surgery	
Trabeculectomy	11 (21.2%)
Trabeculectomy+SLT	2 (3.3%)
SLT	1 (1.7%)

POAG: Primary open-angle glaucoma; PEXG: Pseudoexfoliative glaucoma; TA: Trabectome alone; TP: Trabectome with phacoemulsification; CCT: Central corneal thickness; SLT: Selective laser trabeculoplasty.

maculopathy, and branch retinal vein occlusion developed in five eyes, leading to vision loss. During the follow-up five eyes required phacoemulsification surgery and were treated appropriately.

According to the surgical success criteria (20% decrease in IOP or IOP ≤21 mmHg and no further glaucoma surgery), the success rate was determined as 82.1% at the 6th month and 67.3% at the last visit.

At the final visit, 29 (70%) eyes with POAG and eight (57.1%) eyes with PEXG met the success criteria. The decrease in IOP was 32.2% in the POAG group and 23.3% in the PEXG group. The eyes that had undergone TA surgery had a 31.8% IOP decrease from the baseline, and 27 (69.2%) met the success criteria at the last visit. In the TP surgery group, the IOP decreased by 25% at the last visit compared to the baseline, and 10 (62.5%) patients met the success criteria. We did not perform a further subgroup analysis due to the small sample size or unequal distribution of cases in subgroups.

During the follow-up period, 12 (21.4%) eyes required additional glaucoma surgery, namely, trabeculectomy with mitomycin C (n=8), Ahmed glaucoma valve implantation (n=2), trabeculectomy and SLT (n=1), and only SLT (n=1). The mean interval between index TS and additional glaucoma surgery was 22.6±21.9 months (range, 1–63 months).

The Kaplan–Meier survival analysis of further glaucoma surgery requirement showed a mean survival of 70.8±3.6 months. The cumulative probability of success was determined as 94.6%, 90.1%, 85.7%, 82.1%, and 78.6% at three, 12, 24, 36, and 60 months, respectively. Figure 1 presents the Kaplan–Meier survival plots indicating the time of additional glaucoma surgery in cases of failure.

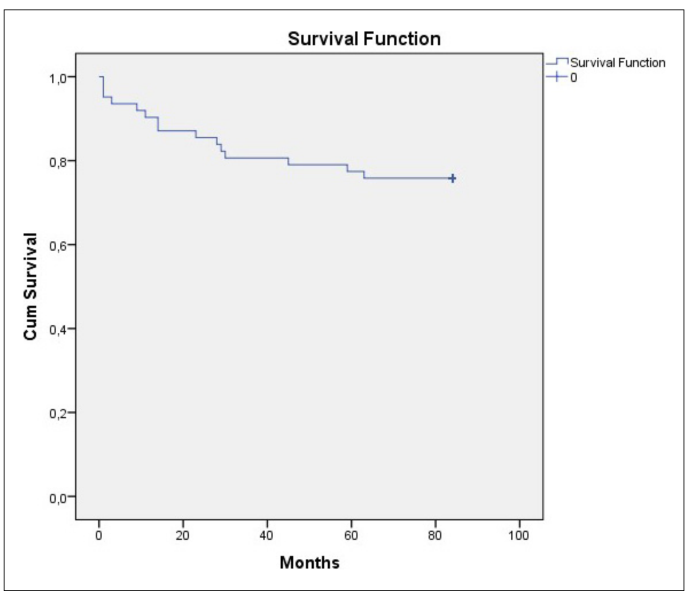

Figure 1. Kaplan–Meier survival plots of further glaucoma surgery requirement. Cum survival: Cumulative survival.

The Multivariate Cox regression analysis was stratified by age, preoperative IOP, number of pre-operative antiglaucomatous drug molecules used, CCT, and glaucoma type. The risk factors for further surgery requirement were determined as a higher baseline IOP value (hazard ratio [HR]: 1.11, p=0.03) and the use of a higher number of pre-operative antiglaucomatous drug molecules (HR: 2.55, p=0.09) (Table 2).

Half of failures in the POAG group and only 25% of those in the PEXG group occurred within the 1st year after TS. The odds ratio of early failure was 3.0 in the POAG group (95% confidence interval: 0.21–42.6).

Discussion

The Trabectome® device uses high frequency-microelectrocautery with simultaneous infusion and aspiration to ablate the inner wall of the trabeculum and Schlemm's canal, providing the aqueous fluid with a direct access to collector channels (11). In a prospective study evaluating 101 eyes over 30 months, Minckler et al. (15) reported an 84% success rate and high safety profile.

In 2014, Mosaed et al. (12) published a large data pool obtained from the Trabectome Study Group Database, including 5,436 patients followed up for 90 months. The average IOP reduction was 29% (from 23.0±7.9 mmHg to 16.5±3.8 mmHg), and the number of antiglaucomatous drug molecules used was reduced from 2.6±1.3 to 1.6±1.3 (38%). In the same study, the survival rate was reported to be 60% for all the cases, 76% for the patients that underwent combined surgery, and 50% for those that underwent TA. Secondary glaucoma surgery was required by 7% of the patients. The authors noted that their study was limited in that it was not clear how many eyes were still included in the 90th-month data.

In 2019, Esfandiari et al. (13) reported the 5-year outcomes of a combined TP case series including 93 patients. The authors determined the cumulative probability of success as 67.5% at the 5th year. Risk factors for failure were reported to be lower baseline IOP, younger age, and higher

Table 2. Cox proportional hazard regression model

	Hazard ratio	p
Age	0.985 (0.942–1.031)	0.515
Preop IOP	1.113 (1.010–1.226)	0.030
Preop antiglaucomatous drug molecules	2.552 (0.843–7.721)	0.097
CCT	1.013 (0.993–1.032)	0.196
Glaucoma Type	0.961 (0.236–3.914)	0.956

IOP: Intraocular pressure; CCT: Central corneal thickness; Preop: Preoperative.

CCT. Exfoliative glaucoma was associated with a higher success rate. IOP dropped from 20±5.6 to 15.6±4.6 mmHg at 5 years.

In 2019, Avar et al. (16) reported the 3.5-year outcomes of 81 trabectome cases, in which IOP decreased by 28% and 26% in those with POAG and PEXG, respectively. In the same study, the Cox proportional hazard model showed that the risk of failure nearly doubled in the POAG cases compared to the PEXG group.

In 2020, Kono et al. (17) published the long-term results of 305 trabectome cases, using IOP ≤21 mmHg and ≥20% IOP reduction as criterion A; IOP ≤18 mmHg and ≥20% IOP reduction as criterion B, and IOP ≤16 mmHg and ≥20% IOP reduction as criterion C. At 72 months, the success probabilities for all the cases were determined as 44%, 35%, and 17% for criteria A, B, and C, respectively. The baseline IOP dropped from 29.2±9.8 mmHg to 16.4±5.8 mmHg at 72 months. There was no significant difference between the glaucoma types in terms of success probability at 72 months when criterion A was considered. The authors also emphasized that the combined procedure significantly reduced the failure risk, whereas POAG and previous SLT history significantly increased this risk. Further glaucoma surgery was required by 44.6% of the eyes.

In a report by Minckler et al., (18) including a retrospective case series of 1,127 trabectome surgical procedures (738 TA and 366 TP), IOP was found to decrease by 39% at 24 months. Failure defined as additional glaucoma surgery was observed in 100 of the 738 (14%) TA cases. In another clinical cohort outcome study, Pahlitzsch et al. (19) included 268 POAG and 98 PEXG cases and reported a success rate of 80.5% and 80.8%, respectively, using the criteria of IOP ≤21 mmHg or ≥20% IOP reduction. The authors found no significant difference in IOP reduction between the PEXG and POAG groups at 36 months. They reported that for the POAG and PEXG groups, the rates of additional surgery requirement were 17.9% and 16.3% after a mean follow-up period of 457 and 355 days, respectively.

In the current study, we found that TS was successful in reducing the baseline IOP from 26.9±6.8 mmHg to 18.8±4.7 mmHg ($p<0.01$) over a mean follow-up of 59 months. During this period, the mean IOP decreased by 30.1%, and the mean number of antiglaucomatous drug molecules used decreased from 3.42±0.7 to 2.5±1.34 ($p<0.01$). These results are consistent with the previous reports in the literature.

In the current study, accepting the surgical success criterion as a 20% drop in IOP or IOP ≤21 mmHg without additional glaucoma surgery requirement, we determined the success rate as 67.3% at the last visit. During the follow-up period, 21.4% of the eyes required additional glaucoma surgery. Therefore, in our study, the rate of additional surgery requirement was relatively higher than the rate reported by Mosaed et al. (12) and lower than that of Kono et al. (17) In our study, the Kaplan–Meier analysis of the time to additional surgery showed a mean survival of 70.8±3.6 months (Fig. 1). The cumulative probability of success was determined as 94.6%, 90.1%, 85.7%, 82.1%, and 78.6% at months 3, 12, 24, 36, and 60, respectively. This is important in terms of providing real life data and showing the benefits of TS.

Although we did not perform a subgroup analysis according to the glaucoma types, we detected half of the failures in the eyes with POAG within the 1st year. We also determined POAG has an odds ratio of 3.0 (95% confidence interval: 0.21–42.6) for early failure compared to PEXG. In a report by Kono et al., (17) no significant difference was found in success probability according to the glaucoma type at 72 months. In contrast, Avar et al. (16) reported significantly better survival in PEXG than in POAG over a mean follow-up of 3.5 years. Esfandiari et al. (13) also found PEXG to be associated with a higher chance of success. Discrepancies in reports may be related to the differences in follow-up duration, considering that the reports indicating better results for PEXG had shorter follow-up periods (19-23). Since PEXG is associated with fibrillary protein deposition in the trabeculum, (24) it may have an initially better response to surgical operations bypassing trabecular resistance. This may be the reason better outcomes are reported in patients with PEXG in the short term.

In our study, the multivariate Cox regression analysis stratified by age, baseline IOP, number of antiglaucomatous drug molecules used, glaucoma type, and CCT showed an increased risk of further surgery requirement in the presence of a higher baseline IOP (HR: 1.11, $p=0.03$) and use of a higher number of antiglaucomatous drug molecules (HR: 2.55, $p=0.09$). Patients with a higher baseline IOP value are expected to have a higher IOP reduction after TS. Many studies suggest that a higher baseline IOP value is associated with a higher IOP reduction after TS (13,25). An increased baseline IOP value reflects the aggressiveness of glaucoma. Similar to our study, a recent report published by Kono et al. (17) also indicated an association between a high baseline IOP value and a significant increase in failure risk. However, Esfandiari et al. (13) found that a lower baseline IOP value, younger age, and higher CCT were risk factors for failure. In the study of Esfandiari et al., all the cases underwent TP surgery, and the mean baseline IOP was 20.0±5.6, which was lower compared to both our study and that of Kono et al. (17) This suggests that the data of Esfandiari et al. (13) may have been biased by the floor effect in normotensive eyes.

Some authors reported that combined TP had no additional effect on IOP reduction, but it resulted in a bias in patient selection toward the earlier stages of glaucoma (25,26). According to a study by Dang et al., (27) patients undergoing TP have a relatively stable glaucoma without the need for pressure reduction, but they do have a motivation to reduce medication. Dang et al. (27) also stated that with the coarsened exact matching method, phacoemulsification performed during the same session with TS did not contribute to IOP reduction. Although Esfandiari et al. [13 included only TP cases; they reported a 5-year success probability rate of 67.5%. Similarly, our success rate was 67.3% at 59 months.

In this study, higher CCT was not found to be a risk factor for further surgery requirement. However, Esfandiari et al. (13) reported an association between a thicker cornea and risk of failure. Thicker corneas may reflect ultrastructural and biomechanical properties that may interfere with trabecular and more distal outflow facility of aqueous humor (28-30). Further studies are needed to provide a better understanding of this relationship.

The limitations of our study are the retrospective design, low number of patients, and inadequate follow-up data, especially in the intermediate period. Moreover, we included both patients with POAG and PEXG that underwent either TA or TP at different glaucomatous stages, and some had a history of the previous glaucoma surgery. Nevertheless, our study offers an objective view concerning what to expect in patients undergoing TS in the long term. To the best of our knowledge, this is the first study reporting the long-term results of TS in Turkish patients.

Conclusion

We achieved a 67.3% success rate with TS over a mean follow-up period of 59 months. The probability of success was 78.6% at 60 months when additional surgery requirement was accepted as a criterion for failure. A higher baseline IOP value and use of a higher number of antiglaucomatous drug molecules significantly increased the failure rate in the long term. These data can assist clinicians in appropriate patient selection and provide an idea about the long-term outcomes of candidates for TS.

Disclosures

Ethics Committee Approval: This study was approved by the local ethics committee with the registration number HNEAH-KAEK-2021/1.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Conception: Y.U., C.B.; Design – Y.U., C.B.; Supervision – M.S., Y.U.; Resource – D.C., Y.U.; Materials – D.C., Y.U.; Data Collection and/or Processing – Y.U., C.B., D.C.; Analysis and/or Interpretation – Y.U., C.B., M.S.; Literature Search – Y.U.; Writing – Y.U., C.B.; Critical Reviews – Y.U., C.B., D.C., M.S.

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