Five-year Outcomes of Trabeculectomy Combined With Phacoemulsification Compared to Trabeculectomy Followed by Phacoemulsification: A Retrospective Cohort Study

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Abstract

Background: We aimed to compare the outcomes of trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification.

Methods: A total of 141 patients with open-angle glaucoma who underwent trabeculectomy followed by (n = 48) or combined with (n = 93) phacoemulsification were included. We analyzed the data collected in “The Collaborative Bleb-Related Infection Incidence and Treatment Study” (CBIITS), which was a prospective cohort study conducted in 34 clinical centers including 1,249 eyes. The main outcome was the cumulative probabilities of success based on IOP within 5 years. Surgical failure was defined as performance of an additional glaucoma surgery or fulfilling one of the following criteria: preoperative intraocular pressure (IOP) >21 mmHg (A), IOP >18 mmHg (B), or IOP >15 mmHg (C). The secondary outcomes were the cumulative probabilities of success, but data on phacoemulsification during the 5-year follow-up were censored, the risk factors for surgical failure, and Δ visual acuity.

Results: There was no significant difference in the cumulative probabilities of success of the main outcome. When data on phacoemulsification during the 5-year follow-up were censored, the probabilities of success in trabeculectomy followed by phacoemulsification were significantly higher for criteria A (p = 0.02), B (p < 0.01), and C (p < 0.01). Lower preoperative IOP, younger age, and trabeculectomy combined with phacoemulsification were associated with poorer outcome. Trabeculectomy followed by phacoemulsification had significantly worse Δ logMAR visual acuity at 6 and 12 months (p < 0.01).

Conclusion: The cumulative probabilities of success after trabeculectomy combined with or followed by phacoemulsification remained unchanged. Combining phacoemulsification adversely affects the cumulative probabilities of success after trabeculectomy. Visual acuity improvements noted in the early postoperative period after combining phacoemulsification disappeared within 5 years.

Introduction

Trabeculectomy has been the standard filtering surgery for patients with glaucoma due to uncontrollable intraocular pressure (IOP) [1]. When trabeculectomy is performed in patients with glaucoma, it is difficult to determine the best time to carry out a cataract surgery because the cataract frequently progresses after trabeculectomy [2-4] and because phacoemulsification is known to adversely affect the IOP control after trabeculectomy [5-7]. Recently, we also reported that phacoemulsification performed in patients with a history of trabeculectomy led to poorer surgical outcomes of trabeculectomy [8]. Additionally, the number of patients with glaucoma and cataract is increasing with the aging of society and growth of population worldwide [9]. In this situation, we are even more concerned about the best time to perform a cataract surgery because trabeculectomy combined with phacoemulsification also causes poorer IOP control than that of trabeculectomy alone [10, 11]. However, no studies conducted in large cohorts and over long periods have assessed the surgical outcomes between trabeculectomy followed by phacoemulsification and trabeculectomy combined with trabeculectomy.

The present study analyzed the data collected in “The Collaborative Bleb-Related Infection Incidence and Treatment Study” (CBIITS), which was a prospective cohort study conducted in 34 clinical centers including 1,249 eyes [12]. CBIITS investigated the incidence, severity, and prognosis of bleb-related infections following trabeculectomy with mitomycin C treatment for 5 years. Therefore, the present study aimed to compare the long-term outcomes between trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification and to identify the risk factors for surgical failure.

Methods

Patient selection

CBIITS is a multicenter, prospective cohort study that aimed to investigate the incidence of and risk factors for bleb-related infection. The investigators from Japan Glaucoma Society voluntarily participated in CBIITS in which a total of 34 clinical centers enrolled the participants. An institutional review board approval from each clinical center was obtained, respectively, and a written informed consent was obtained from all participants. The protocol conformed to the tenets of the Declaration of Helsinki. The postoperative ophthalmologic examinations were conducted every 6 months up to 5 years. CBIITS enrolled 1,249 eyes of 1,249 patients for 2 years, and the enrollment was completed on March 31, 2007. The study finally included 1,098 eyes treated with trabeculectomy.

The institutional review board of Fukui University Hospital, Fukui, Japan, approved the present study, and 141 eyes of 141 patients with open-angle glaucoma who had participated in CBIITS were included. We notified and disclosed research information on the homepage to guarantee the opportunity for research participants to refuse. The enrolled patients were divided into two groups: trabeculectomy followed by phacoemulsification group and trabeculectomy combined with phacoemulsification group. “Trabeculectomy followed by phacoemulsification” referred to the performance of lens extraction with phacoemulsification during the 5-year follow-up period after trabeculectomy. In CBIITS, the local investigators at each center decided the indications for surgery, selection of operative procedure, operative technique, and application of postoperative medication or additional glaucoma treatment, either medically or surgically. However, trabeculectomy was usually performed with 0.04% mitomycin and fornix-based or limbus-based conjunctival incision.

In the present study, we included Japanese patients with open-angle glaucoma (primary open-angle glaucoma, exfoliation glaucoma, and glaucoma secondary to uveitis); at least 20 years of age; who underwent trabeculectomy with 0.04% mitomycin C; with phakic eyes; and who completed the 5-year follow-up without dropouts. We excluded the eyes that previously underwent glaucoma and vitreoretinal surgeries, experienced rupture during phacoemulsification, and with any postoperative intraocular surgeries except for glaucoma reoperation or phacoemulsification.

Main outcome measure

The primary outcome measure was the cumulative probabilities of success in the Kaplan–Meier survival curve analysis based on the IOP. The IOP was measured every 6 months at each center during the 5-year follow-up in CBIITS. In the present study, surgical failure was defined, before performing the data analysis, based on the following IOP levels with or without antiglaucoma medications: <20% reduction in preoperative IOP or IOP >21 mmHg (criterion A), IOP >18 mmHg (criterion B), or IOP >15 mmHg (criterion C). Additionally, surgical failure was declared in cases that required reoperation for glaucoma or had loss of light perception or low IOP (≤ 5 mmHg). Reoperation for glaucoma comprised bleb needling >6 months after trabeculectomy, bleb revision, or additional glaucoma surgery. Laser suture lysis or bleb needling within 6 months following trabeculectomy was not considered as surgical failure because it was a part of the postoperative management for trabeculectomy.

Secondary outcome measures

Secondary outcomes included the following three factors. The first factor was the cumulative probabilities of success in the Kaplan–Meier survival curve analysis with the criteria the same as those of the primary outcome, but the data on phacoemulsification during the 5-year follow-up were censored. The second factor was the risk factors for failure in the first secondary outcome. The third factor was Δ (the value of postoperative visual acuity minus that of preoperative visual acuity) visual acuity change during the 5-year follow-up. Visual acuity aggregated in the form of decimal visual acuity was converted to logarithm of minimum angle of resolution (logMAR) visual acuity in the statistical analysis.

Sample size

In a previous study [11], the cumulative probabilities of success after trabeculectomy followed by phacoemulsification appeared to be superior to those of trabeculectomy combined with phacoemulsification when data on phacoemulsification during the 5-year follow-up were censored. Therefore, we assumed proportional hazards and designed the sample size using the method of Lakatos et al. [13] to test the difference between the survival functions of the two groups. If the difference in surgical failure rate between the two groups was $\geq 25\%$ with a two-sided significance level of 0.05 and a power of 0.8, the estimated sample size of at least 105 eyes was considered as essential to detect a significant difference between the two groups.

Statistical analysis

SPSS version 26.0 (IBM Institute, Inc. Chicago, IL, USA) was used for statistical analysis. Univariate analyses were performed using Wilcoxon non-parametrical and chi-square tests for baseline characteristics. Wilcoxon non-parametrical test with Bonferroni correction was used to determine the Δ visual acuity between the two groups. The 5-year cumulative probabilities of surgical failure were analyzed using the Kaplan–Meier survival curves and log-rank test. The Cox proportional hazards regression model was used to determine the risk factors for surgical failure.

Results

Baseline characteristics

Table 1 shows the baseline characteristics. A total of 48 eyes underwent trabeculectomy followed by phacoemulsification, whereas 93 eyes underwent trabeculectomy combined with phacoemulsification. Significant differences were observed in the number of secondary glaucoma due to uveitis ($p = 0.02$), preoperative logMAR visual acuity ($p < 0.01$), and the base of conjunctival flap ($p = 0.03$) between the two groups. Preoperative IOP (mean $\pm$ SD) was not significantly different between the trabeculectomy followed by phacoemulsification group (24.0 ± 10.1 mmHg) and trabeculectomy combined with phacoemulsification group (24.4 ± 8.0 mmHg; $p = 0.35$).

Table 1. Baseline characteristics

	TLE followed by Phaco	TLE combined with Phaco	p value
N	48	93	
Age (years)	64.5 $\pm$ 12.0	67.7 $\pm$ 9.95	0.197
Sex, male (%)	56.2	53.8	0.86
Sub-types of OAG			
POAG, n (%)	31 (65)	50 (54)	0.29
EXG, n (%)	8 (17)	7(8)	0.17
SG, n (%)	9 (19)	36 (39)	0.02 [†]
LogMAR VA	0.14 $\pm$ 0.28	0.48 $\pm$ 0.50	< 0.01 [*]
Base, fornix (%)	34.7	54.8	0.03 [†]
IOP (mmHg)	24.0 $\pm$ 10.1	24.4 $\pm$ 8.0	0.35
Glaucoma medication (n)	2.3 $\pm$ 1.1	2.7 $\pm$ 1.0	0.14
VF (MD)	-18.1 $\pm$ 7.31	-15.6 $\pm$ 11.1	0.40

TLE = trabeculectomy, Phaco = phacoemulsification, POAG = primary open-angle glaucoma, EXG = exfoliation glaucoma, SG = secondary glaucoma, Posner = Posner-Schlossman syndrome, LogMAR = logarithm of minimum angle of resolution, VA = visual acuity, IOP = intra ocular pressure, VF = visual field, MD = mean deviation

[†]Chi-square test ^{*} Wilcoxon non-parametrical test

Primary outcome

Results of the Kaplan–Meier survival curve analysis between the trabeculectomy followed by phacoemulsification group and the trabeculectomy combined with phacoemulsification group for criteria

A, B, and C are shown in Figure 1. No significant differences were observed between the trabeculectomy followed by phacoemulsification group and the trabeculectomy combined with phacoemulsification group in any criteria.

Secondary outcomes

Figure 2 shows that the trabeculectomy combined with phacoemulsification group had significantly lower cumulative probabilities of success for criteria A, B, and C ($p = 0.02$, $p < 0.01$, and $p < 0.01$, respectively) than the trabeculectomy followed by phacoemulsification group when data on phacoemulsification during the 5-year follow-up were censored. For criterion A, the cumulative probabilities of success of trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification at 5 years were 66.7% and 43.0% ($p = 0.02$), respectively. For criterion B, the cumulative probabilities of success of trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification at 5 years were 64.6% and 37.6% ($p < 0.01$), respectively. For criterion C, the cumulative probabilities of success of trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification at 5 years were 54.2% and 22.6% ($p < 0.01$), respectively.

Risk factors for surgical failure

Results of the Cox proportional hazards model are listed in Table 2, when data on phacoemulsification during the 5-year follow-up were censored. Trabeculectomy combined with phacoemulsification was consistently associated with poorer surgical outcomes for criteria A ($p = 0.01$), B ($p = 0.01$), and C ($p < 0.01$). Preoperative lower IOP was associated with poorer surgical outcomes for criteria A ($p < 0.01$) and B ($p = 0.04$). Younger age was associated with poorer surgical outcomes for criteria A ($p = 0.02$) and B ($p = 0.04$).

Table 2. Hazard ratio analyzed using the multivariate cox proportional hazards regression models

Factor	Criteria					
	A		B		C	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Age (years)	0.97 (0.95–0.99)	0.02*	0.98 (0.95–0.99)	0.04*	0.98 (0.96–1.00)	0.07
Sex F / M	1.24 (0.75–2.07)	0.41	1.01 (0.62–1.64)	0.96	0.98 (0.64–1.50)	0.93
Preoperative IOP per mmHg	0.94 (0.91–0.98)	< 0.01*	0.96 (0.93–0.99)	0.04*	1.00 (0.96–1.03)	0.71
Conjunctival incision (Fornix-based/limbus-based)	0.93 (0.55–1.55)	0.77	0.96 (0.58–1.58)	0.86	1.06 (0.69–1.64)	0.80
Subtypes of OAG						
EXG / POAG	0.58 (0.26–1.29)	0.18	0.67 (0.31–1.47)	0.65	1.07 (0.50–2.31)	0.86
SG / POAG	0.71 (0.28–1.77)	0.46	0.79 (0.32–1.95)	0.61	0.99 (0.42–2.32)	0.98
TLE combined with phaco	2.31 (1.22–4.38)	0.01*	2.26 (1.22–4.18)	0.01*	2.23 (1.30–3.82)	< 0.01*
The number of glaucoma medication	1.04 (0.80–1.35)	0.77	1.06 (0.82–1.35)	0.68	1.12 (0.90–1.40)	0.31

HR = hazard ratio, F = female, M = male, IOP = intraocular pressure, OAG = open-angle glaucoma, POAG = primary, OAG = open-angle glaucoma, EXG = exfoliation glaucoma, SG = secondary glaucoma due to uveitis, Posner = Posner-Schlossman syndrome, TLE = trabeculectomy, Phaco = phacoemulsification

*Log-rank test

Δ Visual acuity change

The 5-year Δ visual acuity changes of trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification are shown in Figure 3. The Δ visual acuity in the trabeculectomy followed by phacoemulsification group and trabeculectomy combined with phacoemulsification group were 0.13 ± 0.25 and -0.16 ± 0.47 at 6 months ($p < 0.01$), 0.20 ± 0.46 and

-0.15 ± 0.53 at 12 months ($p < 0.01$), 0.06 ± 0.29 and -0.03 ± 0.60 at 36 months ($p = 0.12$), and 0.11 ± 0.41 and 0.07 ± 0.76 at 60 months ($p = 0.40$), respectively.

Discussion

The present study found no significant differences in the cumulative probabilities of success between the trabeculectomy followed by phacoemulsification group and the trabeculectomy combined with phacoemulsification group. By contrast, when the data on phacoemulsification performed during the 5-year follow-up were censored, significant differences were observed for criteria A, B, and C between the two groups. The potential risk factors in the Cox proportional hazards model revealed that trabeculectomy combined with phacoemulsification is an independent contributor to the surgical failure: for criterion A, RR of 2.31 ($p = 0.01$); for criterion B, 2.26 ($p = 0.01$); and for criterion C, 2.23 ($p < 0.01$) (Table 2).

No prospective studies have been conducted in a large cohort with a long follow-up period to investigate the outcome of trabeculectomy combined with phacoemulsification. Ogata et al. prospectively reported that trabeculectomy combined with phacoemulsification ($n = 25$) resulted in inadequate IOP reduction compared with trabeculectomy alone ($n = 25$) at 1 year [10]. In another retrospective study, trabeculectomy combined with phacoemulsification had a lower cumulative probability of success than trabeculectomy alone for 4 years among older patients with open-angle glaucoma [11]. In a retrospective study, Donoso et al. showed that the surgical survival curve of trabeculectomy combined with phacoemulsification with intraoperative administration of 5-fluorouracil had no significant difference with that of trabeculectomy followed by phacoemulsification with intraoperative administration of 5-fluorouracil [14]. Results of the present study were consistent with those of previous studies, showing that trabeculectomy combined with phacoemulsification has no significant difference in the cumulative probabilities of success based on the IOP compared with trabeculectomy followed by phacoemulsification or has lower cumulative probabilities of success compared with trabeculectomy alone. In contrast to trabeculectomy alone, combined phacoemulsification increases the risk of blood-aqueous barrier collapse. The flare value after phacoemulsification returns to normal only after 6 months, but the flare value after trabeculectomy returns to normal only after 4 weeks [15]. Additionally, various fibrogenic cytokines, such as monocyte chemotactic protein-1 and interleukin-8, are secreted after phacoemulsification [16, 17]. The prolonged inflammation eventually leads to bleb scarring [18].

Although significantly better outcomes of Δ logMAR visual acuity were exhibited in the trabeculectomy combined with phacoemulsification group compared with those in the trabeculectomy followed by phacoemulsification group at 6 and 12 months after surgery, the difference in Δ logMAR visual acuity disappeared 12 months after surgery. In the trabeculectomy combined phacoemulsification group, visual acuity improved within a short-term follow-up after surgery due to the performance of cataract extraction. Similarly, Lockhead J et al [11]. reported a mean gain in the number of lines in the Snellen visual acuity chart from baseline after trabeculectomy combined with phacoemulsification for patients with open-angle glaucoma with at least 1-year follow-up compared with trabeculectomy alone. Park HJ et al [6].

also demonstrated that the mean visual acuity beyond the first postoperative month was significantly better than that at baseline after trabeculectomy combined with phacoemulsification. Similar to phacoemulsification alone, trabeculectomy combined with phacoemulsification also caused an improvement in visual acuity [19, 20]. Moreover, trabeculectomy alone for phakic eyes triggered the occurrence of lens opacification after surgery [2-4,21]. The deterioration of visual acuity within 12 months after surgery in the trabeculectomy followed by phacoemulsification group seemed to be due to the progression of cataract. A total of 33 of the 48 eyes in the trabeculectomy followed by phacoemulsification group underwent phacoemulsification within 36 months. Therefore, the mean value of Δ logMAR visual acuity was restored at 36 months after trabeculectomy. The difference in lens opacity between the two groups possibly lead to the significant outcomes of Δ logMAR visual acuity in the trabeculectomy combined with phacoemulsification group within 12 months. Interestingly, Δ logMAR visual acuity at 60 months was almost equal between the two groups because of the gradual deterioration of visual acuity in the trabeculectomy combined with phacoemulsification group. As shown in Figure 2, the surgical outcomes of the trabeculectomy combined with phacoemulsification group were significantly worse than those of the trabeculectomy followed by phacoemulsification group when data on phacoemulsification during the 5-year follow-up were censored. Compared with those in trabeculectomy alone, the uncontrolled postoperative IOPs in combined phacoemulsification might have resulted in the gradual deterioration of visual acuity for 5 years.

Multivariate analysis using Cox proportional hazards model identified two additional risk factors for surgical failure: younger age and lower preoperative IOP. Younger age has been considered a risk factor for trabeculectomy failure in many previous studies [22-25]. Vigorous healing response frequently occurs in individuals with a younger age, possibly due to a thicker Tenon's capsule [26]. A >20% IOP reduction in eyes with lower preoperative IOP is difficult to achieve without hypotony [8, 27].

This study had some limitations. First, as this was a cohort study, the participants were not randomly divided into two groups. Actually, the rate of fornix-based conjunctival flap was significantly higher in the trabeculectomy combined with phacoemulsification group. However, the Cox proportional hazards model showed that the surgical outcomes were not dependent on the base of the conjunctival flap. The incidence of secondary glaucoma due to uveitis was significantly higher in the trabeculectomy combined with phacoemulsification group. Eyes with uveitis were associated with cataract [28, 29]. The high incidence of cataract in uveitic glaucomatous eyes might have caused the selection bias. Second, phacoemulsification, trabeculectomy, and trabeculectomy combined with phacoemulsification were not standardized. The technique used to perform these procedures depends on the discretion of each center. Hence, further prospective randomized studies should be conducted to resolve these limitations.

In conclusion, the present study showed no significance in the cumulative survival of success after trabeculectomy followed by phacoemulsification and trabeculectomy combined with phacoemulsification for patients with open-angle glaucoma. However, trabeculectomy combined with phacoemulsification appeared to have lower cumulative probabilities of success compared with trabeculectomy alone. When the data on phacoemulsification during the 5-year follow-up were censored,

younger age, lower preoperative IOP, and trabeculectomy combined with phacoemulsification were risk factors for surgical failure. The Δ logMAR visual acuity in trabeculectomy followed by phacoemulsification was significantly higher in the early postoperative period compared with that in trabeculectomy combined with phacoemulsification. However, the Δ logMAR visual acuity had no significant differences between the two groups regardless of the timing of phacoemulsification.

Abbreviations

CBIITS: The collaborative bleb-related infection incidence and treatment study; IOP: Intra ocular pressure; LogMAR: Logarithm of minimum angle of resolution

Declarations

Ethics approval and consent to participate

The institutional review board of Fukui University Hospital, Fukui, Japan approved this study, and informed consent was obtained from all the patients participating in CBIITS study.

Consent for publication

Not applicable.

Competing interests

None declared.

Funding

Not applicable.

Author's contributions

SA: planning the study, data analysis, writing the first draft, and finalization of the manuscript. KI, YO, and YT: data collection, data analysis, and writing the first draft. MI: planning the study, data analysis, writing the first draft, and finalization of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

Figure 1

Comparison of the Kaplan–Meier survival curve analysis results between the trabeculectomy followed by the phacoemulsification group and trabeculectomy combined with phacoemulsification group for criteria A, B, and C. There were no significant differences between the trabeculectomy followed by the phacoemulsification group and the trabeculectomy combined with phacoemulsification group in all criteria. The data were compared using a log-rank test. Trab = trabeculectomy; Phaco = phacoemulsification

Figure 2

Comparison of the Kaplan–Meier survival curve analysis results between the trabeculectomy followed by phacoemulsification group and the trabeculectomy combined with phacoemulsification group for criteria A, B, and C, when the data on phacoemulsification performed during the 5-year follow-up were censored. The probabilities of success for criteria A, B, and C in the trabeculectomy followed by phacoemulsification group and trabeculectomy combined with phacoemulsification group were 66.7% and 43.0% for criterion A ($p = 0.02$), 64.6% and 37.6% for criterion B ($p < 0.01$), and 54.2% and 22.6% for criterion C ($p < 0.01$), respectively. The data were compared using a log-rank test. Trab = trabeculectomy; Phaco = phacoemulsification

Figure 3

Comparison of the $\Delta \log\text{MAR}$ visual acuity change between the trabeculectomy followed by phacoemulsification group and trabeculectomy combined with phacoemulsification group. Trabeculectomy followed by phacoemulsification had a higher value of $\Delta \log\text{MAR}$ acuity at 6 and 12 months (6 months, $p < 0.01$; 12 months, $p < 0.01$). The data (mean $\pm$ standard deviation) were compared using the Wilcoxon non-parametrical test with Bonferroni correction. Trab = trabeculectomy; Phaco = phacoemulsification; LogMAR = logarithm of minimum angle of resolution; VA = visual acuity; Δ = the value of postoperative logMAR VA minus that of preoperative logMAR VA