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# Trabeculectomy Tenon Advancement Technique May Reduce Bleb-Related Infections

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**Précis:** Trabeculectomy using the Tenon advancement technique with a fornix-based (FB) conjunctival flap showed avascular bleb formation less frequently and had a significantly lower risk of developing bleb-related infections than trabeculectomy with a limbus-based conjunctival flap.

**Purpose:** To determine whether the Tenon advancement technique for trabeculectomy with a FB conjunctival flap is effective in preventing bleb-related infections.

**Materials and Methods:** This was a single-center, nonrandomized retrospective cohort study of 998 eyes from 854 patients with glaucoma who underwent trabeculectomy with mitomycin C. Trabeculectomy procedures were categorized into 3 groups: limbus-based (LB, 296 eyes), FB without Tenon advancement (FBTA-, 167 eyes), and FB with Tenon advancement (FBTA+, 535 eyes). The cumulative incidence of bleb-related infections and the rate of surgical success during the 5-year postoperative follow-up period were analyzed using Kaplan–Meier survival analysis and Cox proportional hazards models. Intraocular pressure (IOP) reduction of <20% from baseline or additional glaucoma surgeries was deemed a surgical failure. Surgical success with or without IOP-lowering medications was evaluated according to different IOP criteria.

**Results:** Ten eyes developed bleb-related infections (8 eyes in the LB group and 1 eye in both the FBTA- and FBTA+ groups each). The cumulative probability of bleb-related infections in the LB, FBTA-, and FBTA+ groups was 4.8 ± 1.7% (± standard error), 0.8 ± 0.8%, and 0.3 ± 0.3%, respectively. The FBTA+ group had a significantly lower risk of bleb-related infections than the LB group (hazard ratio, 0.06; 95% confidence interval, 0.01 to 0.39; $P = 0.009$). The FBTA+ group did not have a higher risk of surgical failure.

**Conclusion:** The Tenon advancement technique for trabeculectomy using an FB conjunctival flap may be effective in preventing bleb-related infections without compromising surgical success.

**Key Words:** trabeculectomy, tenon advancement, fornix-based, limbus-based, bleb-related infections

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Trabeculectomy is a standard glaucoma surgery used to control intraocular pressure (IOP).[1,2] However, significant complications are associated with filtering blebs after trabeculectomy. In particular, a bleb-related infection that progresses to endophthalmitis is a representative long-term serious complication.[3–5] The adjunctive use of mitomycin C (MMC) has dramatically improved surgical success and therefore has become the standard procedure in trabeculectomy.[2,6,7] However, trabeculectomy with MMC tends to cause thin and avascular blebs.[8,9] Avascular blebs that develop with the use of MMC are pathologically characterized by attenuated conjunctival epithelium and loose, hypocellular subepithelial connective tissue, which reflects the toxicity of MMC.[10] Moreover, avascular blebs are risk factors for bleb leakage and bleb-related infections as late complications.[3,8,9] For these reasons, the ideal surgical procedure should suppress the avascularity of the bleb and reduce the risk of bleb-related infection. A fornix-based (FB) conjunctival flap develops a more diffuse and vascular bleb than a limbus-based (LB) flap.[11] However, no difference in the incidence of bleb-related infection between FB and LB flaps has been reported in previous studies.[12,13]

We developed the Tenon advancement technique as a surgical method to suppress avascular blebs. In this method, the Tenon's capsule was thinly stretched over the filtration site. The idea that the Tenon advancement may be effective in preventing avascular bleb formation and related complications was derived from our rabbit model of filtration surgery with MMC using a honeycomb-patterned film.[14] In the rabbit model, the film was effective in preventing avascular bleb development and conjunctival epithelial damage.[15] We postulate that the advancement of Tenon's capsule may have a similar effect in preventing avascular bleb formation by working as a barrier against conjunctival damage. We have been using the Tenon advancement technique since 2009. Recently, a noncomparative, 1-year prospective study reported a surgical technique similar to our method, named the "Tenon's layer reposition approach," and was effective in preventing bleb leaks.[16] However, the effect of this method on bleb-related infections has not been addressed. This study aimed to determine whether the Tenon advancement technique was effective in preventing bleb-related infections after trabeculectomy with MMC.

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## MATERIALS AND METHODS

This single-center, retrospective cohort study was approved by the Medical Ethics Committee of Kanazawa University Hospital and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all the patients. We retrospectively reviewed the charts of consecutive patients with glaucoma who underwent trabeculectomy at Kanazawa University Hospital from April 2004 to December 2017 and collected data until 5 years after the trabeculectomy procedure.

Trabeculectomy procedures were categorized into 3 groups: limbus-based (LB) group, FB without Tenon advancement (FBTA-) group, and FB with Tenon advancement (FBTA+) group. LB, FBTA-, and FBTA+ were not selected randomly but rather chronologically in this order.

The IOP was measured with Goldmann applanation tonometry. The primary outcome of this study was the bleb-related infection as a late-onset complication, and, therefore, eyes with follow-up periods <6 months were excluded. Given that previous scarring in the filtration area could prevent the Tenon advancement or affect postoperative avascular bleb formation independently of surgical technique, only trabeculectomy performed in the virgin conjunctival area during the study period was eligible, and surgical bleb revision was excluded. If multiple trabeculectomies were performed in different virgin conjunctival areas during the study period, only the first surgery was eligible, and the follow-up period was terminated when the second surgery was performed. If both eyes of the same patient were eligible, both eyes were enrolled. Inclusion of the second eye increases statistical power in controlling the correlation between fellow eyes, given that two eyes are usually correlated strongly but not perfectly.[17]

### Surgical Techniques

During the study period, trabeculectomy was performed by 10 experienced surgeons. In the FB procedure, a traction suture is used on the upper peripheral cornea. After sub-tenon anesthesia, an FB conjunctival incision was made, followed by dissection between Tenon's capsule and sclera. A $3 \times 3$ mm to $4 \times 4$ mm square half-thickness scleral flap was created. MMC (0.4 mg/ml)-soaked sponges were applied to the sub-Tenon's space for 3 to 5 minutes and then washed out with saline. The application time depended on factors including the age of patients, scarring, and thickness of the Tenon's capsule in the dissecting area. After peripheral iridectomy, the scleral flap was sutured using 10-0 nylon sutures. The conjunctival flap was closed at the limbus using 10-0 nylon sutures. When the Tenon advancement technique was used, the retracted Tenon's capsule was pulled forward and sutured at the limbus together with the conjunctival flap, using 10-0 nylon sutures to create a thin sheet of Tenon's capsule underneath the conjunctiva. If the Tenon's capsule was thick and close to the limbus, it was stretched out to form a thin, uniform sheet, and the redundant part of the capsule that extends well beyond the limbus was excised. In older patients, the Tenon's capsule may be thin and retracted posteriorly. In these cases, the Tenon's capsule was separated from the sclera and the insertions of the rectus muscles to facilitate forward stretching of the capsule. Tenon advancement was defined as successful when the sheet of the Tenon's capsule completely covered the filtration area and the circumferential incision site of the limbus; if the Tenon's capsule could not be pulled forward to the limbus or was lost, these cases were reassigned to the FBTA- group (Fig. 1).

In the LB procedure, traction sutures and anesthesia were the same as in the FB procedure. After LB conjunctival incision, Tenon's capsule was incised, and the scleral surface was exposed to the limbus. The following surgical steps were the same as in the FB procedure, except 10-0 nylon sutures were used to close the conjunctival flap near the fornix.

### Bleb Morphology, Infection, and Other Surgical Complications

Bleb-related infections were staged according to the Collaborative Bleb-Related Infection Incidence and Treatment Study.[12] Stage I represents blebitis, and stage II denotes infection extending into the anterior chamber. Stage III infection involves the vitreous and retina.[18,19] Complications other than bleb-related infections include bleb leaks with a positive Seidel test, hyphema formed with a niveau, a shallow anterior chamber, and choroidal detachment extending greater than 1 quadrant. Hypotony maculopathy was defined as an IOP of less than 5 mm Hg and the presence of macular chorioretinal folds upon fundus examination. Complications were reported according to the postoperative period: the early period within 1 month and the late period thereafter. An avascular bleb included V0 (avascular white) and V1 (avascular cystic) based on the Indiana Bleb Appearance Grading Scale.[20] An avascular bleb was determined based on the findings 12 months postoperatively. In cases with a follow-up period of <12 months, bleb morphology at the last follow-up was adopted. The judgement of the avascular bleb was based on the subjective evaluation of photographs performed independently by 2 physicians who were masked to patient data (including surgical procedures), though masking the site of conjunctival incision was impossible. If the 2 raters made different decisions, judgement was finalized through discussion.

### Criteria for Surgical Success

The addition of glaucoma surgery or cyclophotocoagulation or less than 20% of IOP reduction from baseline was regarded as a surgical failure. The 3 criteria of IOP level for surgical success were as follows: (A) $5 \leq$ IOP $\leq 18$ mm Hg, (B) $5 \leq$ IOP $\leq 15$ mm Hg, and (C) $5 \leq$ IOP $\leq 12$ mm Hg. For each criterion, complete success without additional IOP-lowering medication and qualified success, regardless of the use of IOP-lowering medication, were determined. IOP values were collected at 1, 3, 6, 9, and 12 months and every 6 months thereafter for up to 60 months. Surgical failure was determined based on the data obtained $\geq 3$ months after surgery. Postoperative laser suture lysis and bleb needling, which were performed at the surgeon's discretion, were not considered failures.

### Statistical Analysis

Baseline patient characteristics, surgical complications, bleb morphology, and postoperative interventions were compared among the 3 groups using logistic regression or linear regression with cluster robust standard errors accounting for the correlation between fellow eyes for categorical and numerical variables.[17] The best-corrected visual acuity was converted into the logarithm of the minimal angle of resolution format (counting fingers, 2.3; hand movements, 2.6; light perception, 3.0; no light perception, 3.6).[21] The Kappa statistics were used to determine the

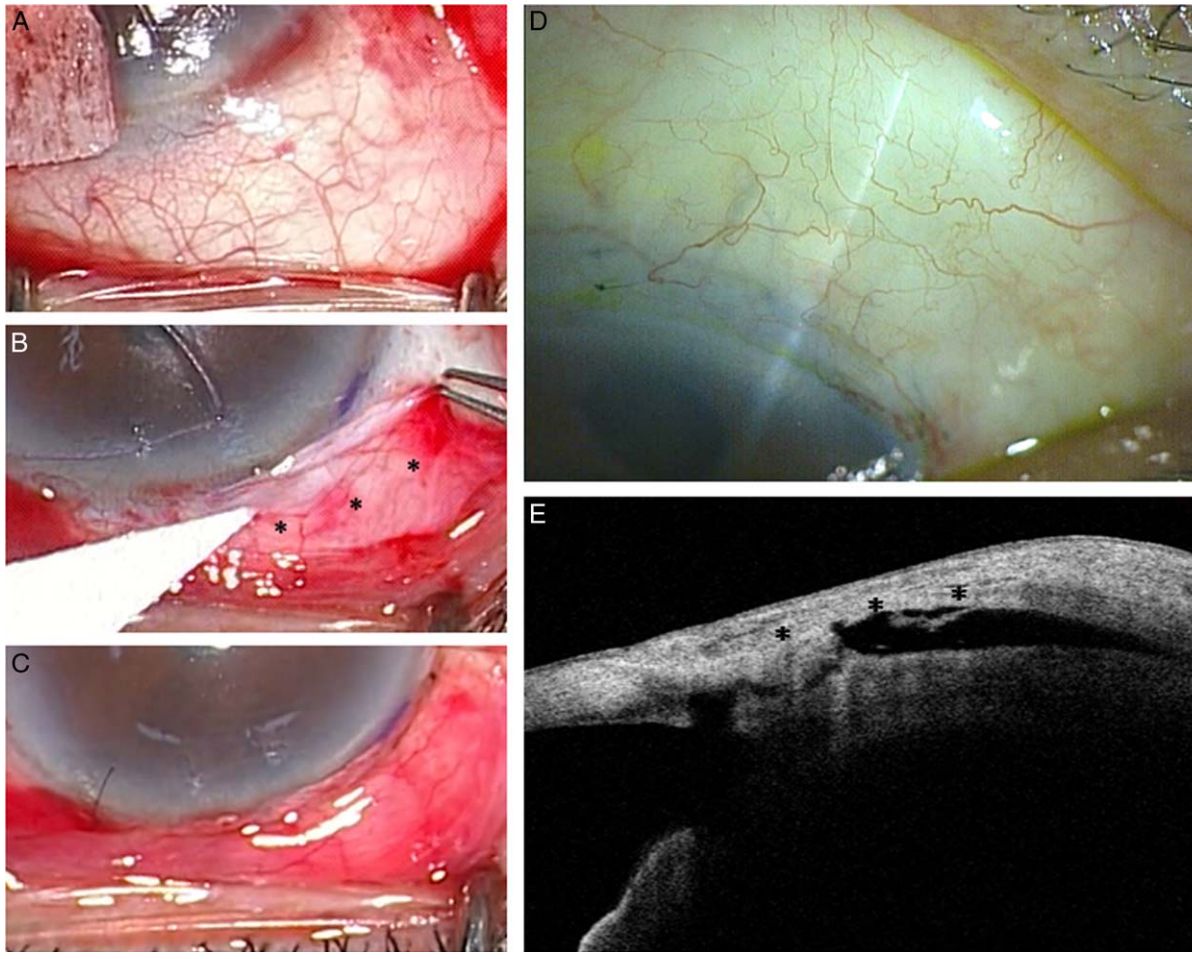


**FIGURE 1.** Intraoperative and postoperative images of eyes that underwent the Tenon advancement technique in trabeculectomy. A-C, Intraoperative images (surgeon's view). D, E, Postoperative images at 3 years. The intraocular pressure was 9 mm Hg. A, Before the conjunctival incision, the conjunctiva appeared thin, and the episcleral vessels were clearly visible. B, The retracted Tenon tissue (asterisks) is pulled and stretched forward to be sutured at the limbus together with the conjunctiva. C, Diffuse blebs formed at the end of the surgery. D, Diffuse vascular bleb 3 years postoperatively. E, Anterior-segment optical coherence tomography showing Tenon tissue lining the conjunctiva (asterisks) over the filtration space.

degree of agreement between physicians in their first assessment of avascular blebs.[22] The interpretation of the Kappa coefficients was based on the criteria of Landis and Koch.[23]

The Kaplan–Meier survival analysis was used to estimate the cumulative incidence of bleb-related infection and the cumulative rate of surgical success for the 3 groups in the first 5 years after surgery. For bleb-related infections, the hazard ratios (HRs) were compared among the 3 groups using multivariate Cox proportional hazards models with cluster robust standard errors accounting for the correlation between fellow eyes and propensity scores as a covariate to adjust the differences in baseline demographics.[24] Logistic regression analysis was performed to calculate the propensity score. For surgical success, the HR of the FBTA+ group or the FBTA- group in comparison with the LB group was calculated using a multivariate Cox proportional hazards model with cluster robust standard errors accounting for the correlation between fellow eyes and adjusting for baseline variables using propensity scores.

STATA software (version 17.0, StataCorp, College City, TX) was used for the analyses. The statistical significance level was set at $P < 0.05$. Correction using the Bonferroni method was performed for multiple comparisons.

## RESULTS

### Demographic Data

During the study period, 998 eyes from 854 patients who underwent trabeculectomy were included from the 1261 filtering procedures of 1219 eyes in 1029 patients. In total, 263 procedures were excluded. Ninety-four procedures were excluded because of the short follow-up period, 140 were excluded because of the use of Ex-PRESS (Alcon Laboratories, Fort Worth, TX) mini shunt, and 29 were excluded because they were the second or third surgery during the study period. In total, 20 eyes were excluded because the bleb revision was performed less than 6 months postoperatively. Bleb revision was performed in 5 eyes (1.7%), 7 eyes (4.0%), and 8 eyes (1.5%), in the LB, FBTA-, and FBTA+ groups, respectively. There were no significant differences between the LB and FBTA- groups, the LB and FBTA+ groups, orthe FBTA+ and FBTA- groups ($P = 0.34$, 1.0, 0.12, respectively). The Tenon advancement technique was

 

**TABLE 1.** Comparisons of Baseline Patient Characteristics Between 3 Types of Conjunctival Flaps

| | LB | FBTA- | FBTA+ | Total | *P* |
|---|---|---|---|---|---|
| Number of patients/eyes | 262/296 | 154/167 | 470/535 | 854/998 | |
| Age (y), mean, SD (range) | 65.7, 12.8 (12–89) | 65.6, 14.1 (25–89) | 67.3, 12.3 (17–91) | 66.5, 12.8 (12–91) | 1.0*, 0.35†, 0.62‡ |
| Sex (eyes, Female/Male) | 104/192 | 56/111 | 230/305 | 390/608 | 1.0*, 0.13†, 0.13‡ |
| Laterality (eyes, right/left) | 148/148 | 84/83 | 263/272 | 495/503 | 1.0*, 1.0†, 1.0‡ |
| Diabetes mellitus | 75 (25.3%) | 52 (31.1%) | 108 (20.2%) | 235 (23.6%) | 0.65*, 0.36†, 0.02‡ |
| Hypertension | 115 (38.9%) | 66 (39.5%) | 204 (38.1%) | 385 (38.6%) | 1.0*, 1.0†, 1.0‡ |
| Glaucoma types | | | | | |
| POAG | 120 (40.5%) | 55 (32.9%) | 248 (46.4%) | 423 (42.4%) | 0.42*, 0.44†, 0.015‡ |
| XFG | 72 (24.3%) | 34 (20.4%) | 133 (24.9%) | 239 (24.0%) | 1.0*, 1.0†, 0.74‡ |
| NVG | 22 (7.4%) | 40 (24.0%) | 41 (7.7%) | 103 (10.3%) | <0.001*, 1.0†, <0.001‡ |
| UG | 33 (11.2%) | 16 (9.6%) | 41 (7.7%) | 90 (9.0%) | 1.0*, 0.39†, 1.0‡ |
| Others | 49 (16.6%) | 22 (13.2%) | 72 (13.5%) | 143 (14.3%) | 1.0*, 0.82†, 1.0‡ |
| Follow-up periods (mo) after trabeculectomy, mean, SD (range) | 39.2, 21.8 (6–60) | 40.4, 20.8 (6–60) | 37.3, 20.0 (6–60) | 38.4, 20.7 (6–60) | 1.0*, 0.74†, 0.33‡ |
| Preoperative IOP (mm Hg), mean, SD (range) | 28.0, 10.5 (13–75) | 29.8, 10.7 (14–60) | 25.7, 9.4 (12–60) | 27.1, 10.1 (12–75) | 0.29*, 0.009†, <0.001‡ |
| Preoperative antiglaucoma medication scores, mean, SD (range) | 3.3, 1.1 (0–5) | 3.2, 0.9 (0–5) | 3.8, 1.0 (0–7) | 3.6, 1.0, (0–7) | 1.0*, <0.001†, <0.001‡ |
| Preoperative spherical equivalent, mean, SD (range) | −2.9, 4.3 (−27 to 8.6) | −2.4, 3.3 (−10.8 to 9.6) | −3.0, 3.5 (−20.6 to 11.1) | −2.8, 3.7 (−27.0 to 11.1) | 0.59*, 1.0†, 0.23‡ |
| Preoperative best-corrected visual acuity (logMAR), mean, SD (range) | 0.54, 0.70 (−0.08 to 3.0) | 0.50, 0.65 (−0.08 to 2.6) | 0.32, 0.54 (−0.08 to 3.0) | 0.42, 0.62 (−0.08 to 3.0) | 1.0*, <0.001†, 0.008‡ |
| Preoperative cataract surgery | 92 (31.1%) | 74 (44.3%) | 255 (47.7%) | 421 (42.2%) | 0.02*, <0.001†, 1.0‡ |
| Preoperative trabeculectomy | 24 (8.1%) | 14 (8.4%) | 31 (5.8%) | 69 (6.9%) | 1.0*, 0.68†, 0.74‡ |
| Preoperative trabeculotomy | 37 (12.5%) | 31 (18.6%) | 123 (23.0%) | 191 (19.1%) | 0.27*, 0.002†, 0.71‡ |
| Preoperative pars plana vitrectomy | 13 (4.4%) | 8 (4.8%) | 36 (6.7%) | 57 (5.7%) | 1.0*, 0.54†, 1.0‡ |
| Combined cataract surgery | 12 (4.1%) | 7 (4.2%) | 0 | 19 (1.9%) | 1.0*, NA†, NA‡ |
| Combined pars plana vitrectomy | 0 | 4 (2.4%) | 1 (0.2%) | 5 (0.5%) | NA*, NA†, 0.07‡ |

Logistic regression or linear regression accounting for the correlation between fellow eyes for categorical or numerical variables, respectively. Adjusted *P*-values by Bonferroni correction for multiple comparisons.
*(LB vs. FBTA-
†LB vs. FBTA+
‡FBTA- vs. FBTA+).

Mean, standard deviation and (range) are shown for numerical variables; NA, not available; FBTA- indicates fornix-based incision without Tenon advancement; FBTA+, fornix-based incision with Tenon advancement; IOP, intraocular pressure; LB, limbus-based incision; logMAR, logarithm of the minimal angle of resolution; NVG, neovascular glaucoma; POAG, primary open angle glaucoma; SD, standard deviation; UG, uveitic glaucoma; XFG, exfoliative glaucoma.

attempted in 545 procedures and was unsuccessful in 10 (1.8%). After the exclusion of ineligible cases, 296 eyes of 262 patients, 167 eyes of 154 patients, and 535 eyes of 470 patients were included in the LB, FBTA-, and FBTA+ groups, respectively. LB, FBTA-, and FBTA+ were the most common procedures between 2004 and 2007, 2008 and 2010, and 2011 and 2017, respectively. In the period between 2004 and 2007, there were 224 (77.2%), 57 (19.7%), and 9 (3.1%) cases in the LB, FBTA-, and FBTA+ groups, respectively. Between 2008 and 2010, there were 64 (29.2%), 82 (37.4%), and 73 (33.3%) cases in the LB, FBTA-, and FBTA+ groups, respectively. Between 2011 and 2017, there were 8 (1.6%), 28 (5.7%), and 453 (92.6%) cases in the LB, FBTA-, and FBTA + groups, respectively. Baseline patient characteristics were presented in Table 1. Comparing the characteristics of the subjects according to the surgical methods of the 3 groups, there were significant differences in the medical history of diabetes mellitus, percentage of primary open angle glaucoma and neovascular glaucoma, preoperative IOP, preoperative antiglaucoma medication scores, preoperative best-corrected visual acuity, previous cataract surgery, and previous trabeculotomy.

## Bleb-Related Infections

Of the 998 eyes, 10 eyes (1.0%) developed bleb-related infections during the follow-up period. In the LB group, bleb-related infection was observed in 8 eyes (2.7%), stage I in 4 eyes and stage III in 4 eyes. A stage III infection developed in 1 eye in both the FBTA- (0.4%) and FBTA+ (0.2%) groups.

The Kaplan–Meier survival curves of the cumulative incidence of bleb-related infections are shown in Figure 2. The cumulative incidence of bleb-related infection at 5 years after trabeculectomy was $4.8 \pm 1.7\%$, $0.8 \pm 0.8\%$, and $0.3 \pm 0.3\%$ in the LB, FBTA-, and FBTA+ groups, respectively. A multivariate Cox proportional hazards model with propensity score as a covariate was used to determine the HRs of bleb-related infections. The propensity score was calculated based on baseline variables with significant differences between the groups, including diabetes mellitus, glaucoma types, baseline values of IOP, medication scores, and visual acuity, and preoperative cataract surgery and trabeculotomy. The FBTA+ group had a lower risk of developing bleb-related infections than the LB group (HR, 0.06; 95%CI, 0.01 to 0.39; $P = 0.009$). In contrast, the infection risk between the FBTA- group and the LB groups and between the FBTA+ group and the FBTA- groups were not significant (HR, 0.24, 0.32; 95%CI, 0.03 to 2.19, 0.04 to 2.42; $P = 0.62$, 0.81, respectively).

## Intraocular Pressure Control

The Kaplan–Meier survival curves for qualified success are shown in Figure 3. For criterion A, the cumulative surgical success rates at 5 years in the LB, FBTA-, and FBTA+ groups were 68.3%, 69.5%, and 70.0%, respectively. For criterion B, the success rates were 56.0%, 61.7%, and 60.5%, respectively. For criterion C, the success rates were 40.0%, 46.5%, and 42.4%, respectively. The Cox proportional hazard model showed that the surgical success rate by all criteria in the FBTA- group was not significantly different from that in the LB group. For criteria B and C, the FBTA+ group had a significantly higher surgical success rate than the LB group (Table 2).

As for the complete success, the cumulative surgical success rates at 5 years in criterion A for the LB, FBTA-, and FBTA+ groups were 37.1%, 46.6%, and 37.0%, respectively. For criterion B, the success rates of the three groups were 36.5%, 43.5%, and 35.2%, respectively, and for criterion C, the success rates were 32.9%, 39.5%, and 29.3%, respectively. There were no significant differences in the surgical success rate between the FBTA- and LB groups and between the FBTA+ and LB groups (Table 2).

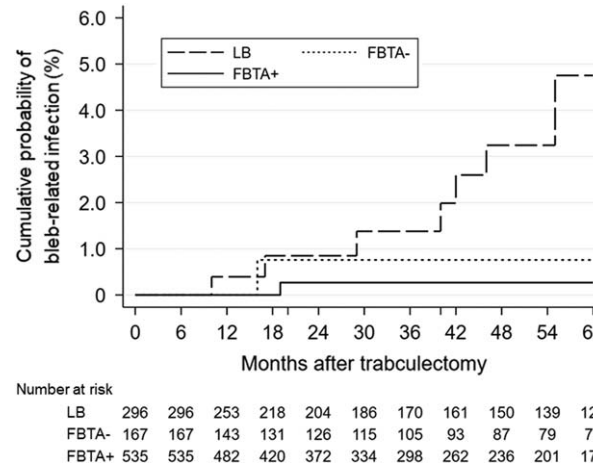


**FIGURE 2.** Kaplan–Meier curves for bleb-related infection after trabeculectomy with mitomycin C: Comparison of the 3 types of conjunctival flaps. LB indicates limbus-based conjunctival incision; FBTA, fornix-based conjunctival incision without Tenon advancement; FBTA+, fornix-based conjunctival incision with Tenon advancement.

## Complications, Bleb Morphology, and Postoperative Interventions

Table 3 shows the frequencies of early and late complications in each group. Among the early complications, choroidal detachment was significantly less in the FBTA+ group than in the LB group. There were significantly lower rates of late-onset bleb leak in the FBTA+ group than in the LB group, but there were no significant differences between the LB and FBTA- groups and between the FBTA- and FBTA+ groups. Among 20 eyes with late-onset bleb leak, 5 received no additional treatment, 8 received topical autologous serum application, 3 received suture treatment, 1 received needling, and 3 received bleb revision. One patient in the LB group and 2 in the FBTA- group underwent bleb revision. All 3 eyes with bleb-related infection received topical autologous serum application before developing an infection. Avascular blebs could be determined at 12 months postoperatively in 920 cases (92.2%). In 78 cases, because of the short follow-up period, bleb morphology was assessed at the last observation. The agreement in the first assessment of avascular blebs between the 2 physicians was almost perfect (Kappa coefficient = 0.89). The FBTA+ group had a significantly lower incidence of avascular blebs than other groups. Comparing eyes with and without bleb-related infections, there were significantly higher rates of late-onset bleb leak and avascular blebs in eyes with bleb-related infection (Table 4). Comparisons of postoperative interventions among the LB, FBTA-, and FBTA+ groups were presented in Table 5. There were significantly higher rates of postoperative cataract surgery in the FBTA+ group than in the LB and FBTA- groups.

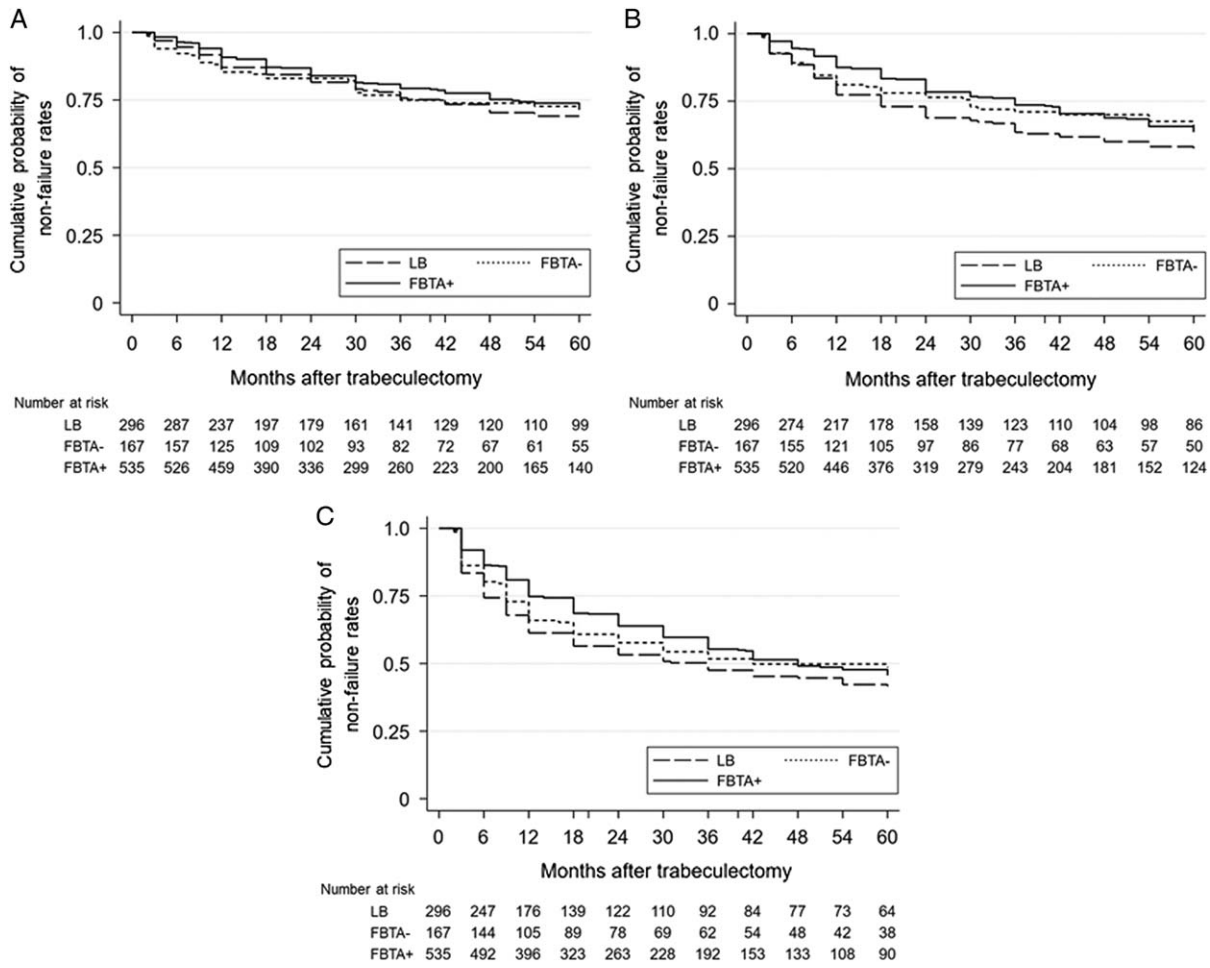


**FIGURE 3.** Kaplan–Meier survival curves of qualified surgical success: Comparison of the 3 types of conjunctival flaps. Cumulative probability of nonfailure rates based on the 3 criteria of intraocular pressure (IOP) without further glaucoma surgery. A, $5 \leq IOP \leq 18$ mm Hg and $\geq 20\%$ IOP reduction. B, $5 \leq IOP \leq 15$ mm Hg and $\geq 20\%$ IOP reduction. C, $5 \leq IOP \leq 12$ mm Hg and $\geq 20\%$ IOP reduction. LB indicates limbus-based conjunctival incision; FBTA, fornix-based conjunctival incision without Tenon advancement; FBTA+, fornix-based conjunctival incision with Tenon advancement.

**TABLE 2.** Comparison of Surgical Success Between 3 Types of Conjunctival Flaps

| | Criterion A | | | Criterion B | | | Criterion C | | |
|---|---|---|---|---|---|---|---|---|---|
| | $5 \leq IOP \leq 18$ mm Hg and $\geq 20\%$ Reduction | | | $5 \leq IOP \leq 15$ mm Hg and $\geq 20\%$ Reduction | | | $5 \leq IOP \leq 12$ mm Hg and $\geq 20\%$ Reduction | | |
| | HR | 95%CI | *P* | HR | 95%CI | *P* | HR | 95%CI | *P* |
| Qualified success | | | | | | | | | |
| Reference: LB | | | | | | | | | |
| FBTA- | 0.91 | 0.61–1.38 | 1.0 | 0.73 | 0.51–1.04 | 0.23 | 0.79 | 0.59–1.06 | 0.35 |
| FBTA+ | 0.78 | 0.57–1.07 | 0.36 | 0.65 | 0.49–0.86 | 0.009 | 0.72 | 0.58–0.90 | 0.012 |
| Complete success | | | | | | | | | |
| Reference: LB | | | | | | | | | |
| FBTA- | 0.82 | 0.61–1.11 | 0.59 | 0.83 | 0.62–1.11 | 0.60 | 0.88 | 0.68–1.15 | 1.0 |
| FBTA+ | 0.86 | 0.69–1.07 | 0.50 | 0.86 | 0.69–1.06 | 0.48 | 0.86 | 0.71–1.06 | 0.47 |

Multivariate Cox proportional hazards model with cluster robust standard errors accounting for the correlation between fellow eyes and adjusting for baseline variables with significant differences between groups. *P*-values are adjusted by Bonferroni correction for multiple comparisons.

FBTA- indicates fornix-based incision without Tenon advancement; FBTA+, fornix-based incision with Tenon advancement; HR, hazard ratio; CI, confidence interval; LB, limbus-based incision.

## DISCUSSION

We showed that the FBTA+ group had a significantly lower risk of bleb-related infections during the 5 postoperative years than the LB group. Moreover, the FBTA+ group did not have a higher risk of surgical failure than the other groups did. Overall, the Tenon advancement technique for the FB conjunctival flap appears to be more effective in preventing bleb-related infections without compromising bleb survival than the LB technique. Although the incidence of infection was not significantly different between the FBTA+ and FBTA- groups, avascular bleb formation (which was significantly associated with bleb-related infection) was significantly lower in FBTA+ treated eyes than in FBTA- treated eyes, suggesting the potential benefit of the Tenon advancement technique.

Several retrospective and prospective studies with large sample sizes have addressed the incidence of late-onset bleb-related infections. Solus et al[25] reported the estimated cumulative incidence of bleb-related infections at 4 years was 1.2% in the LB flaps and 0.3% in the FB flaps. Another retrospective study with 1959 eyes by Kim et al[13] found no significant difference in the incidence of bleb-related infections between the LB and FB flaps. In a prospective study by Yamamoto et al,[12] the Collaborative Bleb-Related Infection Incidence and Treatment Study, showed that the 5-year cumulative incidence of bleb-related infections in eyes with LB flaps was not significantly different from those with FB flaps (2.3% vs. 1.9%). In contrast, Rai et al[26] reported a lower risk of infection in eyes with FB flaps, while Luebke et al[27] reported a lower risk of infection in eyes with LB flaps., In these studies, there were no major differences in surgical procedure between the LB flap and FB flap groups except for the conjunctival incision sites.[12,13,25–27] Therefore, there is no consensus as to whether LB or FB flaps are associated with a higher risk of bleb-related infection. Moreover, no previous study has reported the effects of handling Tenon's tissue on the incidence of bleb-related infections. In this study, the incidence of bleb-related infections was significantly lower in eyes with FB flaps, especially when the Tenon advancement technique was used.

Several factors have been associated with the development of bleb-related infections. Among these, younger age, presence of bleb leakage,[12,25] and the use of antiproliferative agents[4,28–30] are representative risk factors. The use of MMCs increased the incidence of avascular bleb formation and bleb-related infections.[8,9,29] Higher concentration and longer application time of MMC may more strongly suppress proliferation of the Tenon's fibroblasts and vascular ingrowth, possibly leading to greater success of trabeculectomy[31,32] at the expense of increased risk of avascular bleb formation, leak, and infection. Therefore, different concentrations or application times of MMC may result in different incidences of bleb-related infection secondary to avascular, leaking blebs.

Several retrospective studies with large sample sizes have reported various MMC concentrations and exposure times. In these studies, the concentration of MMC ranged from 0.2 to 0.5 mg/ml and the exposure time ranged from 0.25 to 5 minutes; there were no differences found between the LB flap and FB flap groups.[12,13,25–27] The dose and application time of MMC used in the present study were within the ranges used in these reports. In this study of 3 different surgical procedures, MMC was consistently used at the same concentration (0.4 mg/ml) and similar exposure times (5 minutes in most of the cases); there were no major changes in MMC dosage or detailed application procedures for about 15 years examined in this study.

In terms of the bleb morphology, thin bleb walls and avascular blebs have been reported as risk factors for bleb-related infections and late-onset bleb leaks.[3,8,9,33] Our study also showed that eyes with bleb-related infections had a significantly higher rate of avascular bleb formation and late-onset bleb leakage than eyes without bleb-related infections. Of note, the FBTA+ eyes had significantly fewer avascular blebs than the FBTA- eyes, although each group had only one eye with a bleb-related infection. A benefit of FBTA+ is a supposed reduced risk of bleb-related infections, even though the incidence of infection was not significantly different between FBTA+ and FBTA- treated eyes in this study. Given that the suppression of avascular bleb formation is associated with a lower risk of late-onset bleb leak and bleb-related infections, the difference in the incidence of bleb-related infections between eyes with FBTA+ and FBTA- may become evident in longer follow-up periods.

**TABLE 3.** Comparison of Surgical Complications and Bleb Morphology Between 3 types of Conjunctival Flaps

| | LB (n = 296) | FBTA- (n = 167) | FBTA+ (n = 535) | *P* |
|---|---|---|---|---|
| Early postoperative complications* | | | | |
| Bleb leak | 11 (3.7%) | 12 (7.2%) | 43 (8.0%) | 0.36‡, 0.08§, 1.0‖ |
| Hyphema | 18 (6.1%) | 12 (7.2%) | 21 (3.9%) | 1.0‡, 0.53§, 0.27‖ |
| Shallow anterior chamber | 24 (8.1%) | 8 (4.8%) | 38 (7.1%) | 0.5‡, 1.0§, 0.89‖ |
| Choroidal detachment | 75 (25.3%) | 30 (18.0%) | 72 (13.5%) | 0.23‡, <0.001§, 0.48‖ |
| Late postoperative complication* | | | | |
| Bleb leak | 14 (4.7%) | 3 (1.8%) | 3 (0.6%) | 0.38‡, <0.001§, 0.46‖ |
| Choroidal detachment | 2 (0.7%) | 5 (3.0%) | 5 (0.9%) | 0.22‡, 1.0§, 0.19‖ |
| Hypotony maculopathy | 0 | 2 (1.2%) | 2 (0.4%) | NA‡, NA§, 0.73‖ |
| Bleb morphology | | | | |
| Avascular bleb† | 191 (64.5%) | 78 (44.7%) | 144 (26.9%) | 0.001‡, <0.001§, <0.001‖ |

*Onset at ≤1 month or >1 month after surgery for early or late complications, respectively.
†Evaluated at 1 year postoperatively or at the final follow-up visit.
Logistic regression accounting for the correlation between fellow eyes. *P*-values are adjusted by Bonferroni correction for multiple comparisons.
‡(LB vs. FBTA-
§LB vs. FBTA+
‖FBTA- vs. FBTA+).
FBTA- indicates fornix-based incision without Tenon advancement; FBTA+, fornix-based incision with Tenon advancement; LB, limbus-based incision; NA, not available.

**TABLE 4.** Association of Bleb-related Infection with Late-onset Bleb Leak or Avascular Bleb

| | Without Bleb-related Infection (n = 988) | With Bleb-related Infection (n = 10) | Odds Ratio | *P*‡ |
|---|---|---|---|---|
| Late-onset bleb leak* | 17 (1.7%) | 3 (30.0%) | 24.5 | < 0.001 |
| Avascular bleb† | 405 (41.0%) | 8 (80.0%) | 5.8 | 0.027 |

*Onset > 1 month after surgery.
†Evaluated at 1 year postoperatively or at the final follow-up visit.
‡Logistic regression accounting for the correlation between fellow eyes.

Several studies have adopted success criteria for glaucoma surgeries according to the guidelines of the World Glaucoma Association.[34] Among them, Sugimoto and colleagues reported surgical success rates of trabeculectomy in a large-scale multicenter study with a Japanese population stratified by different IOP criteria. The qualified success rates defined as ≥20% IOP reduction from baseline and IOP criteria of A, B, and C in our study were 65.0%, 49.5%, and 29.3% at 5 years, respectively.[35] These results were comparable to the surgical success rate in our study.

As reported by Solus et al[25] and Kuroda et al,[36] some reports compared LB and FB groups for surgical success and reported no significant difference. Yokota et al[37] reported in a prospective study a significantly higher surgical failure rate in the FB group than in the LB group of patients with open angle glaucoma. Proliferation of fibroblasts in the Tenon's capsule has a significant role in postoperative scarring at the filtration site,[38,39] and tenonectomy was reported to significantly reduce surgical failure rates in trabeculectomy for pediatric glaucoma.[40] Accordingly, the presence of Tenon tissue over the filtration site by repositioning the Tenon capsule may facilitate scarring of the bleb, and, therefore, may increase the frequency of bleb needling. However, the FBTA+ group had noninferior surgical success rates than the FBTA- or LB groups. Furthermore, there was no significant difference in the number of needling between the groups. Thus, our study showed that the Tenon advancement technique may not necessarily increase the possibility of surgical failure owing to reduced filtration.

Our study has several limitations. First, this study was conducted in a single center exclusively for Japanese patients. Husain et al[41] pointed out a trend of poorer success and higher complication rates for trabeculectomy in the East Asian population (including those of Japanese descent) compared with that in other races; this is possibly due to various factors including more aggressive scarring and a higher prevalence of normal tension glaucoma and myopia. Therefore, the results of this study may not be applicable to other ethnicities.

Given that the 3 surgical methods concerning the conjunctival incision and handling of the Tenon tissue were not adopted randomly but used continuously for certain periods of time, the follow-up periods were restricted to 5 years after trabeculectomy to match the follow-up periods among the 3 groups. The surgical techniques were gradually switched from LBTA- to FBTA-, and then again to FBTA +, but the timing varied between different surgeons. The selection of 1 of the 3 surgical techniques in each case did not depend on the surgeon's experience or knowledge, the surgical outcome of the fellow eye, or preoperative or intraoperative assessment of the eye; therefore, the selection bias regarding the surgical techniques should not have had a major impact on the study outcomes.

Moreover, considerable differences between the groups existed in the demographic data due to the nonrandomized study design. Given the low incidence of bleb infections, we used the propensity scores as a covariate to adjust for the influence of the imbalance in demographic data without losing statistical power in the Cox proportional hazards models, although the inherent bias may still remain. Using this statistical method, this study was able to successfully identify the reduced risk of bleb-related infections in the FBTA+ group compared with the LB group. In contrast, the FBTA- group did not have significantly lower risk of infection than the LB group partly due to the small sample size. The estimated power of 54% to detect a hazard ratio of 0.24 in the comparison between the 2 groups would have been 90% if the sample size of the FBTA- group were the same as the FBTA+ group. Much larger sample size would be needed to detect statistical significance in the incidence of bleb infections between the

**TABLE 5.** Comparisons of Postoperative Interventions Between 3 types of Conjunctival Flaps

| | LB (n = 296) | FBTA- (n = 167) | FBTA+ (n = 535) | *P* |
|---|---|---|---|---|
| Needling* | 80 (27.0%) | 32 (19.2%) | 115 (21.5%) | 0.17‡, 0.23§, 1.0‖ |
| Filtration surgeries† | 27 (9.1%) | 14 (8.4%) | 40 (7.5%) | 1.0‡, 1.0§, 1.0‖ |
| Trabeculotomy | 5 (1.7%) | 2 (1.2%) | 19 (3.6%) | 1.0‡, 0.41§, 0.42‖ |
| Cyclophotocoagulation | 4 (1.4%) | 0 | 2 (0.4%) | NA‡, 0.41§, NA‖ |
| Cataract surgery | 59 (19.9%) | 30 (18.0%) | 156 (29.2%) | 1.0‡, 0.02§, 0.02‖ |
| Pars plana vitrectomy | 6 (2.0%) | 9 (5.4%) | 13 (2.4%) | 0.18‡, 1.0§, 0.15‖ |
| Corneal transplantation | 6 (2.0%) | 0 | 5 (0.9%) | NA‡, 0.69§, NA‖ |

*Performed > 1 month after surgery.
†Including surgical bleb revision, trabeculectomy, or tube-shunt surgery.
Logistic regression accounting for the correlation between fellow eyes. *P*-values are adjusted by Bonferroni correction for multiple comparisons.
‡(LB vs. FBTA-
§LB vs. FBTA+
‖FBTA- vs. FBTA+).
FBTA- indicates fornix-based incision without Tenon advancement; FBTA+, fornix-based incision with Tenon advancement; LB, limbus-based incision.

FBTA- and FBTA+ groups. Future studies involving many study sites are needed to increase the sample size.

As the incidence of bleb-related infection was low, both eyes were included if eligible to make the most of available data, and statistical analysis was used, accounting for the correlation between fellow eyes as was the case in previous reports on bleb-related infections where data from both eyes were analyzed.[13,25] Despite this, complete elimination of the possible influence of correlation between paired eyes on the results may not be possible.

Although the Tenon advancement technique was modified according to the thickness of the Tenon's capsule, older patients with thinner conjunctiva and/or less Tenon's capsule may be more likely to develop avascular blebs. The distribution of age did not differ between the LB, FBTA-, and FBTA+ groups; therefore, age should not have had a significant influence on the differences in avascular bleb formation between groups. Postoperative management, including laser suture lysis, bleb needling, and the addition of IOP-lowering medications, was at the discretion of each surgeon, which may have affected the results. However, the relatively large number of cases and surgeons participating in this study would have reduced the influence.

In conclusion, FB trabeculectomy with the Tenon advancement technique appeared to have a lower risk of developing bleb-related infections than LB trabeculectomy. This surgical method may be effective in preventing avascular bleb formation and bleb-related infections without compromising surgical success. Further studies are warranted to prove the effects and safety of our surgical technique during long-term follow-up and to optimize the surgical procedures, including MMC dosage, for better surgical outcomes.

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