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Intraocular Pressure Outcomes and Risk Factors for Failure in the Collaborative Bleb-Related Infection Incidence and Treatment Study

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Purpose: To evaluate the efficacy and safety of trabeculectomy for patients with glaucoma who were enrolled in the Collaborative Bleb-related Infection Incidence and Treatment Study (CBIITS).

Design: Multicenter, prospective, cohort study.

Participants: A total of 829 eyes in 829 patients with glaucoma who had undergone trabeculectomy alone or trabeculectomy combined with phacoemulsification at 34 clinical centers were examined in this study.

Main Outcome Measures: Intraocular pressures (IOPs, in millimeters of mercury), risk factors for surgical failure, and surgical complications.

Methods: The enrollment period was 2 years, and follow-up was conducted every 6 months for up to 5 years. Outcomes were measured at 6-month intervals. Four levels of success were defined by achievement of the following IOP: (A) $4 < \text{IOP} < 22$, (B) $4 < \text{IOP} < 19$, (C) $4 < \text{IOP} < 16$, and (D) $4 < \text{IOP} < 13$. The primary outcome was the qualified success rate according to the defined criteria. The secondary outcomes included IOP, risk factors for surgical failure, and surgical complications.

Results: Mean IOP and preoperative antiglaucoma medications were significantly decreased from 24.9±9.0 to 12.6±5.2 mmHg ($P < 0.0001$) and from 2.8±1.0 to 1.2±1.3 mmHg ($P < 0.0001$), respectively, 5 years after surgery. For criteria A, B, C, and D, the qualified success rates were 90.1%, 88.9%, 77.6%, and 57.7% at 1 year, respectively, and 71.9%, 66.7%, 50.1%, and 29.9% at 5 years, respectively. The third or subsequent trabeculectomy was less effective than the first and second trabeculectomies. Preoperative lens status and preoperative higher IOP were risk factors for trabeculectomy failure. The needling procedure and cataract surgery were associated with the risk of failure. The rates of postoperative hyphema, shallow anterior chamber, bleb leak, and choroidal detachment were 2.7%, 3.1%, 1.9%, and 7.2%, respectively, in our series.

Conclusions: Trabeculectomy with mitomycin C is an effective and safe procedure for reducing IOP in the CBIITS. The number of previous glaucoma surgeries, preoperative lens status and IOP, the needling procedure, and cataract surgery after trabeculectomy influenced the success rate, as determined by the target IOP. *Ophthalmology 2015;■:1–11 © 2015 by the American Academy of Ophthalmology.*

To improve the success rate of intraocular pressure (IOP) management and decrease the rate of surgical complications, surgical procedures for glaucoma, such as the use of glaucoma drainage devices (e.g., Baerveldt tube [Abbott Medical Optics, Abbott Park, IL], Express [Boston Scientific, Marlborough, MA], iStent [Glaukos, Laguna Hills, CA]), have been proposed as viable alternatives to trabeculectomy.[1–3] So far, trabeculectomy is the most common surgical procedure for controlling IOP in patients with glaucoma. The antimetabolite mitomycin C (MMC) was introduced as an adjunctive therapy for trabeculectomy and augmented the control of IOP.[4] However, the application of MMC at the time of trabeculectomy increased the incidence of bleb-related infection and hypotony maculopathy.[5,6]

The Japan Glaucoma Society initiated a prospective study to investigate the incidence and severity of bleb-related infection (Collaborative Bleb-Related Infection Incidence and Treatment Study [CBIITS]).[7,8] The 5-year cumulative incidence of bleb-related infection was 2.2%± 0.5% in eyes treated with MMC-augmented trabeculectomy or trabeculectomy combined with phacoemulsification and intraocular lens implantation. Bleb leakage and younger age were the main risk factors for infections.[7,8]

The amount of filtered aqueous flow under the conjunctiva might affect the prevalence of bleb-related infection. The limited aqueous flow in eyes with high IOP and those with high aqueous flow in the bleb with low IOP might result in the difference in the prevalence of bleb-related infections. Interpreting the report by the CBIITS group

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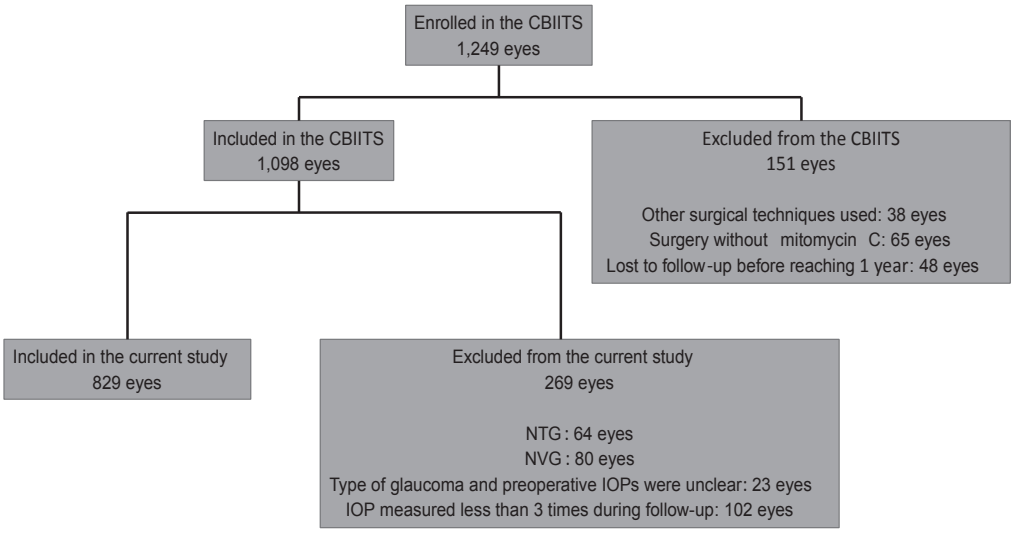

Figure 1. Flowchart showing the number of patients who were enrolled and analyzed in this study. CBIITS = Collaborative Bleb-Related Infection Incidence and Treatment Study; IOP = intraocular pressure; NTG = normal-tension glaucoma; NVG = neovascular glaucoma.

probably depends on the surgical IOP results of the CBIITS. Evaluation of the IOP results of the CBIITS revealed the outcome of trabeculectomy augmented by MMC, which represents the benchmark in Asia, especially in Japan, because all the board members of the Japan Glaucoma Society belong to the 34 institutes that participated in this study when the CBIITS started.

We reviewed the effect of trabeculectomy on IOP and surgical success rate, and explored the factors that affect the surgical success rate and incidence of surgical complications using the CBIITS data.

Methods

The CBIITS was planned in 2004, and principal investigators were recruited voluntarily from the board members of the Japan Glaucoma Society. All the 34 clinical centers directed by board members of the Japan Glaucoma Society participated and enrolled subjects. Institutional review board approval was obtained at each institution, and all patients gave written informed consent after a thorough explanation of the study. The enrollment criteria were as follows: any type of filtering surgery, including those concomitantly performed with cataract or other intraocular surgeries, and the first operated eye after study inclusion (in patients in whom both eyes were treated). There were no other concomitant surgeries, excluding cataract surgery, in the CBIITS.

The indications for surgery, selection of the operative procedure, operative technique, and postoperative medication or additional glaucoma treatment were at the discretion of local investigators. Consecutive eligible subjects were recruited at each clinical center. The follow-up period was set to a minimum of 1 year and a maximum of 5 years. The patients were recommended to visit the clinical center at 6-month intervals for up to 5 years. Additional visits to the clinical center or other ophthalmology clinics were at the discretion of the local investigators.

A total of 829 eyes in 829 patients with glaucoma were included in the present study. As previously reported, the CBIITS examined 1249 eyes in 1249 enrolled patients. The CBIITS finally included and analyzed 1098 eyes from among the 1098 patients who were treated by trabeculectomy with MMC or trabeculectomy plus cataract surgery.[7] In this study, a total of 269 eyes from among the 1098 subjects were excluded for the following reasons: The type of glaucoma and preoperative IOPs were unclear in 23 eyes, and IOP was measured <3 times during follow-up in 102 eyes. Moreover, we excluded subjects with neovascular glaucoma in 80 eyes and normal-tension glaucoma in 64 eyes. Neovascular glaucoma is a subtype of refractory glaucoma in which IOP control is more difficult to achieve than other subtypes of glaucoma.[9,10] The IOP of normal-tension glaucoma is always <21 mmHg, and the postoperative target IOP is lower than other glaucoma subtypes. Achieving clinical success with trabeculectomy for neovascular glaucoma and normal-tension glaucoma is more elusive than for other glaucoma subtypes. Therefore, we excluded subjects with neovascular glaucoma and normal-tension glaucoma from the study (Fig 1).

The IOP was measured by Goldmann applanation tonometry. From the medical records, we documented the average of 3 preoperative IOP measurements that were closest to the time of surgery and the IOP measurements closest to 6, 12, 18, 24, 32, 36, 42, 48, 54, and 60 months after surgery. Ten outcomes were measured at 6-month intervals.

We attempted to follow the outcome criteria proposed in the guidelines by the World Glaucoma Association. Four levels of success, defined by achievement of IOP (values in millimeters of mercury) were (A) $4 < IOP < 22$, (B) $4 < IOP < 19$, (C) $4 < IOP < 16$, and (D) $4 < IOP < 13$. Surgical success was stratified according to IOP control. When the IOP was above the upper limit or below the lower limit for 2 consecutive measurements, the surgery was considered to have failed at the first time point when IOP had exceeded the defined limit. In addition to the defined IOP criteria, we also examined the failure to achieve a 20% reduction in IOP to calculate the surgical success rate.

The primary outcome was the qualified success rate according to the defined criteria. Needling, resuturing the conjunctiva, subconjunctival injection of antimetabolite, and cataract surgery did not represent surgical failure. Reoperation for increased IOP and loss of perception of light were classified as failures. The secondary outcomes included the IOP, risk factors for bleb failure, and surgical complications after surgery.