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Original Article

Clinical Outcomes of XEN45 Gel Stent Implantation (*Ab Externo*, Open Conjunctival Approach) versus Trabeculectomy: A Real-World Study

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Purpose: To compare the clinical outcomes of XEN45 gel stent implantation surgery (*ab externo*, open conjunctiva) with those of trabeculectomy.

Methods: We retrospectively reviewed electronic medical record of 57 patients (62 eyes) treated with XEN implantation surgery (*ab externo*, open conjunctival approach) between April 1, 2021, and July 31, 2023, by the same surgeon. Preoperative clinical data including intraocular pressure (IOP), the number of glaucoma medications, and visual acuity were collected from 1 day to 12 months postoperatively. These data were compared and analyzed with those of 67 patients (78 eyes) received trabeculectomy between February 1, 2017, and April 30, 2022, by the same surgeon. Statistical analyses were performed with $p < 0.05$ as significant.

Results: Complete surgical success rate was 33.9% and 57.7% of the XEN and trabeculectomy groups, respectively ($p = 0.005$). The qualified success rate was 79.0% and 93.6%, respectively ($p = 0.011$). Postoperatively, the XEN group used more glaucoma medications than the trabeculectomy group (1.21 ± 1.05 vs. 0.69 ± 0.90, $p = 0.003$ at postoperative month 12). After postoperative month 1, the XEN group had a higher IOP (15.77 ± 5.07 mmHg vs. 13.17 ± 3.81 mmHg; at postoperative month 12, $p = 0.001$) and lower corneal astigmatism than the trabeculectomy group (1.32 ± 0.79 diopters vs. 1.88 ± 1.45 diopters, $p = 0.020$ at postoperative month 6). There was no significant difference in preoperative and postoperative best-corrected visual acuity (logMAR) between the groups at any of the follow-up period (favorable visual acuity subgroup; logMAR < 0.7). Postoperative complications were 0 cases of XEN group and 13 cases of trabeculectomy group (0% vs. 16.7%, $p = 0.001$). Also, XEN surgery (24 minutes 40 seconds ± 6 minutes 26 seconds) had a shorter operation time than the trabeculectomy (40 minutes 18 seconds ± 8 minutes 27 seconds, $p < 0.001$).

Conclusions: Compared to trabeculectomy, XEN surgery (*ab externo*, open conjunctiva) showed relatively lower effectiveness (surgical success rate, IOP reduction). However, it demonstrated advantages as a minimally invasive glaucoma surgery, including a surgical success rate approaching about 80%, stability in inducing corneal astigmatism, fewer postoperative complications, and shorter operation times.

Key Words: Minimal invasive glaucoma surgery, Trabeculectomy, XEN45 gel stent

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Glaucoma, the second most common cause of blindness worldwide [1], has traditionally been treated with surgical methods such as trabeculectomy and glaucoma valve implantation, if not amenable to pharmacological or procedural management. However, as important as the effective reduction of intraocular pressure (IOP) is, minimizing postoperative complications is equally crucial. Traditional surgeries have been associated with postoperative complications such as anterior chamber bleeding, anterior chamber collapse, hypotony-related retinopathy, postoperative IOP spikes, and even vision loss such as loss of light perception, with these reported to occur in 27% to 34% of trabeculectomy and 19% to 22% of glaucoma valve (primary tube) implantation [2]. While procedures such as micropulse cyclophotocoagulation can minimize complications, their achievement in lowering IOP under 30% of baseline IOP is limited to 53.3% to 60% [3], highlighting their limited role as adjunctive treatments than surgical treatments for glaucoma. The need to sufficiently lower IOP while reducing postoperative complications has led to the emergence of minimally invasive glaucoma surgeries (MIGS), which are less invasive than traditional surgeries.

Among these, XEN gel stent implantation surgery is notable for using a shunt to drain aqueous humor from the anterior chamber to the subconjunctival space, thereby lowering IOP. Made from porcine gelatin, a biocompatible material derived from collagen, the microstent is a hydrophilic tube measuring 6 mm in diameter. It is cross-linked with glutaraldehyde, which typically causes minimal inflammation in other parts of the body. The XEN45 gel stent (AbbVie Inc), with a luminal diameter of 45 µm, has demonstrated the ability to maintain a steady pressure of 7.56 mmHg at 2.5 mL/min, significantly reducing the risk of hypotony-related complications postoperatively [4]. The XEN stent implantation surgery can be traditionally performed with *ab interno*, closed conjunctival approach. However, an off-label approach with *ab externo*, open conjunctival approach has demonstrated comparable or superior clinical outcomes and surgical success rates in variable studies. Consequently, this method is increasingly being adopted among surgeons [4,5].

Recent studies suggest that the *ab externo* approach is not inferior to the *ab interno* approach [5,6], and that the open conjunctival approach may be superior to the closed conjunctival approach in terms of treatment efficacy [4]. Based on these findings, our study aims to analyze the clinical outcomes of XEN implantation surgery using the *ab externo*, open conjunctival approach. While there are previous studies on this topic [7], there is a need for additional comprehensive data through further analysis, particularly among Asian populations with a high prevalence of normal-tension glaucoma [8,9]. This study will address surgical success rates, the degree of IOP reduction, the number of glaucoma medications used, corneal astigmatism, visual acuity, spherical equivalent, need for needling revision, the presence and types of postoperative complications, and risk factors of surgical failure. Additionally, we will compare these results with data from patients who underwent traditional trabeculectomy surgery by same single surgeon.

Materials and Methods

Ethics statement

This single-center retrospective study was approved by the Institutional Review Board of Severance Hospital (No. 4-2024-0630). The requirement of informed consent was waived due to the retrospective nature of the study and the use of deidentified patient data. The study followed the principles of the Declaration of Helsinki.

Study population

The study enrolled patients who underwent glaucoma surgery with XEN45 gel stent implantation between April 1, 2021, and July 31, 2023, by a single surgeon (HWB). Inclusion criteria encompassed glaucoma patients with uncontrolled IOP with medications. Exclusion criteria included the following: (1) loss of follow-up before postoperative 6 months; and (2) a history of glaucoma surgery (including trabeculectomy, Ahmed valve implantation surgery, micropulse transscleral laser therapy, etc.) or trauma. In contrast, patients with a history of glaucoma surgery (including XEN stent implantation) were excluded from the patients who underwent glaucoma surgery with trabeculectomy between February 1, 2017, and April 30, 2022, by the same single surgeon for comparative analysis. This study analyzed only patients who underwent each surgery as a standalone procedure.

Preoperative assessment

A comprehensive preoperative evaluation comprised uncorrected and best-corrected visual acuity (BCVA) measurements (converted to logarithm of the minimum angle of resolution [logMAR]), subjective refraction, corneal astigmatism and central corneal thickness with autokeratometry refractor, slit-lamp examination, IOP with Goldmann applanation tonometry, and fundoscopy. Biometric assessments were performed using a swept-source optical coherence tomography–based optical biometer (IOL Master-700, Carl Zeiss Meditec), and Humphrey field analyzer was used for detecting information of monocular visual field. If there was a history of previous glaucoma surgery or ocular trauma, the subjects were excluded from the analysis.

Surgical technique

All operations were performed by the same surgeon (HWB). Surgeries were performed under topical anesthesia (proparacaine). Brimonidine tartrate was applied to minimize bleeding of the surgical eye with the patient in a supine position. Two different surgical procedures are listed below.

1) XEN stent implantation

After applying a tractional suture with 7-0 Vicryl (Ethicon Inc) to pull in the inferotemporal direction, about 6 mm fornix-based conjunctival flap was made at superonasal area of surgical eye. After three to four tiny sponges soaked with mitomycin C (MMC), concentration of 0.04% were placed in the subconjunctival space (Tenon capsule) for 3 minutes, vigorous irrigation with balanced solution was done twice. Thereafter the XEN tube was implanted via an *ab externo* approach entering the sclera 2.0 mm posterior from the limbus. And the surgeon pressured the cornea with cotton tip gently to compress the anterior chamber and ensure stable aqueous outflow through the XEN implant. Then, the peritomy was closed using water-tight 8-0 Vicryl. YAG laser or needling was considered in cases with poor postoperative IOP control to resolve tip occlusion.

2) Trabeculectomy

After applying a tractional suture at the 90° meridian with 7-0 Vicryl to pull in the counter-direction of surgical area, a fornix-based conjunctival flap and about 2.5 × 2.5-mm-sized trapezoid scleral flap was created at the 120° meridian (superotemporal area of the right eye and the superonasal area of the left eye). Following the same procedure as above using MMC and balanced solution, The 1 × 1-mm-sized corneoscleral excision was made and punch trabeculectomy with peripheral iridectomy was conducted under applying miotics. After gauging the proper flow from anterior chamber through the filter site, the scleral flap was closed with several interrupted 10-0 nylon sutures. Then, the conjunctival flap was sutured continuously with 8-0 Vicryl, placing a Ologen (round-shaped biodegradable collagen implant with a diameter of 12 mm and a height of 1 mm) above scleral flap to promote scar-free wound healing [10]. If postoperative IOP was not controlled appropriately, laser suture cut or bleb needling were considered.

Following surgery, all eyes received a standardized postoperative regimen, including topical applications of antibiotics, steroids, and additional mydriatics in eyes of trabeculectomy.

Postoperative assessment

Follow-up assessments occurred at 1 day, 1 week, and 1, 3, 6, and 12 months postoperatively, encompassing uncorrected distance visual acuity (UCVA), BCVA, IOP with Goldmann applanation tonometry, slit-lamp examinations, spherical equivalent and corneal astigmatism measured with autokeratometry. The number of glaucoma medications required after surgery, the presence, the frequency and timing of needling or additional glaucoma surgery, and the occurrence and timing of complications were recorded. These factors were used to determine the success (complete or qualified) or failure of the surgery. Postoperative glaucoma medications were recorded based on the number of eye drops used, and when oral medications were administered concurrently, they were categorized and distinguished accordingly. Also, postoperative complications were recorded separately according to their specific types.

Statistical analysis

Baseline characteristics and comorbidities were characterized using descriptive statistics. Continuous variables were presented as mean±standard deviation, whereas categorical variables were presented as frequency (percentage). Group differences were evaluated through Student *t*-test or the Mann-Whitney *U*-test, depending on Levene test for equality of variances. Treatment efficacy was assessed using paired *t*-test or Wilcoxon signed rank tests. The chi-square test or Fisher exact test were utilized for comparisons of proportions and frequencies between groups. All tests were two-tailed, with a significance level set at $p<0.05$. The statistical analyses were performed using IBM SPSS ver. 23.0 (IBM Corp).

Results

This study included a total of 62 eyes from 57 patients of the XEN group with an average age of 48.45 ± 16.22 years

Table 1. Clinical characteristics measured in preoperative evaluation

Characteristic	XEN group (n = 62)	Trabeculectomy group (n = 78)	*p*-value
Female sex	29 (46.8)	24 (30.8)	0.052
Age (yr)	48.45 ± 16.22	43.38 ± 15.08	0.058
Laterality (right)	26 (41.9)	44 (56.4)	0.089
Diagnosis			0.971
Normal-tension glaucoma	2 (3.2)	2 (2.6)	
Primary open-angle glaucoma	36 (58.1)	46 (59.0)	
Juvenile open-angle glaucoma	6	12	
Other	24 (38.7)	30 (38.5)	
Secondary glaucoma	17	28	
Uveitis-related	6	11	
Steroid-induced	4	8	
Neovascular glaucoma	2	5	
Pseudoexfoliative glaucoma	2	2	
Pigmentary	1	0	
Syndrome-related*	2	2	
Angle-closure	1	1	
Other	6	1	
BCVA (logMAR)	0.43 ± 0.57	0.29 ± 0.47	0.113
Intraocular pressure (mmHg)	26.08 ± 7.54	29.60 ± 10.01	0.019‡
Spherical equivalent (D)	–2.89 ± 3.79	–3.24 ± 3.15	0.552
Corneal astigmatism†	1.13 ± 0.70	1.16 ± 1.14	0.842
Axial length (mm)	25.63 ± 2.55	25.55 ± 1.97	0.822
Anterior chamber depth (mm)	3.71 ± 0.61	3.65 ± 0.44	0.521
Endothelial cell count (/mm^2)	2,215.62 ± 578.28	2,349.14 ± 504.16	0.158
Central corneal thickness (μm)	533.62 ± 45.98	543.02 ± 43.75	0.248
Visual field			
Mean deviation (dB)	–14.33 ± 12.30	–12.43 ± 9.11	0.313
Pattern standard deviation (dB)	6.92 ± 4.09	6.80 ± 4.13	0.872
Visual field index (%)	57.80 ± 34.82	68.66 ± 29.40	0.056

Values are presented as mean ± standard deviation, number (%), or number only.
BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution; D = diopters.
*Syndrome-related diagnosis involves iridocorneal endothelial syndrome, Sturge-Weber syndrome, and Posner-Schlossman syndrome; †Calculated as "K2 – K1" measured with autokeratometry; ‡Statistically significant.

and 78 eyes of 67 patients of trabeculectomy group with 43.38 ± 15.08 years ($p = 0.058$). Other 28 eyes of XEN group and 12 eyes of trabeculectomy group were excluded because of previous glaucoma surgery history such as trabeculectomy, XEN, iStent or Ahmed valve implantation, cyclodestructive surgery, deep sclerectomy with collagen implant. Also, five eyes of each group were excluded due to follow-up loss less than postoperative month 6.

Intraocular pressure

The preoperative IOP was found to be 26.08 ± 7.54 mmHg in the XEN group and 29.60 ± 10.01 mmHg in the trabeculectomy group ($p = 0.019$). There were no statistically significant differences in other clinical characteristics between the two groups in preoperative evaluation. Detailed numerical data of preoperative clinical characteristics can be found in Table 1. At postoperative 1 year, the IOP was found to be 15.77 ± 5.07 mmHg in the XEN group and 13.17 ± 3.81 mmHg in the trabeculectomy group ($p = 0.001$). The reduction in IOP between preoperative evaluation and at the last follow-up of over 6 months was –9.98 ± 9.09 mmHg in the XEN group and –16.69 ± 10.85 mmHg in the trabeculectomy group ($p < 0.001$). The changes in IOP before and after surgery can be seen in Fig. 1A.

Surgical success rate

In this study, the range of IOP defining surgical success was set between 6 and 21 mmHg postoperatively. Additionally, analyses were conducted with the upper IOP limits set at 18 and 15 mmHg to further detail the trends in surgical success rates. In all three scenarios, surgical failure was defined as follows: if the IOP exceeded 21 mmHg on two consecutive follow-up visits after postoperative 1 month, or if additional glaucoma surgeries or conjunctival incisional procedures (excluding needling, laser suture cuts, and YAG laser for tip occlusion) were performed. Furthermore, surgical failure was also defined if the last

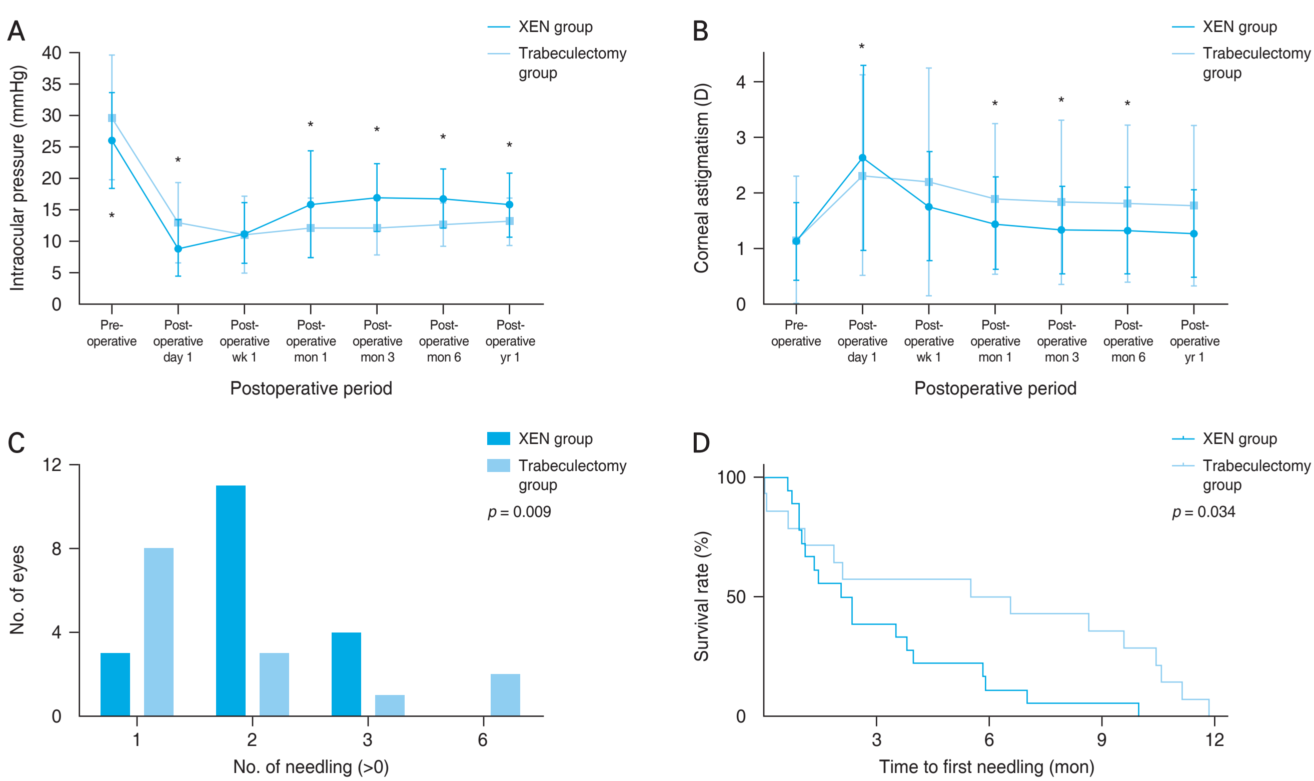

Fig. 1. Postoperative clinical outcomes of the XEN and trabeculectomy groups. (A) Intraocular pressure trends at preoperative evaluation and from postoperative day 1 to year 1. (B) Corneal astigmatism trends at preoperative evaluation and from postoperative day 1 to year 1. (C) Distribution of the total number of postoperative needling. (D) Kaplan-Meier survival curve about first needling within postoperative year 1. D = diopters. *Statistically significant.

IOP at follow-up of over 6 months exceeded the upper limit (21, 18, or 15 mmHg) of each respective scenario. Cases not falling into the above-defined failures were categorized based on how IOP was managed: if IOP was controlled without medication, it was defined as complete success; if IOP was controlled with medication, it was defined as qualified success (Table 2).

For an IOP success range between 6 and 21 mmHg, the qualified success rate was 79.0% (49 eyes) in the XEN group, 93.6% (73 eyes) in the trabeculectomy group ($p = 0.011$) and the complete success rate was 33.9% (21 eyes) and 57.7% (45 eyes), respectively ($p = 0.005$). The surgical failure rate was 21.0% (13 eyes) and 6.4% (5 eyes), respectively.

For an IOP success range between 6 and 18 mmHg, the qualified success rate was 69.4% (43 eyes) in the XEN group, 91.0% (71 eyes) in the trabeculectomy group ($p = 0.001$). Also, the complete success rate was noted as 30.6% (19 eyes) and 57.7% (45 eyes), respectively ($p = 0.001$). Failure rate was 30.6% (19 eyes) in the XEN group and 9.0% (7 eyes) in the trabeculectomy group.

As the success IOP range was narrowed (6 mmHg ≤ IOP ≤ 15 mmHg), the analyzed success rates also decreased significantly. The qualified success rate was 45.2%

Table 2. Surgical success rate

Variable	XEN group (n = 62)	Trabeculectomy group (n = 78)	*p*-value
Success IOP range			
6–21 mmHg			
Qualified success	49 (79.0)	73 (93.6)	0.011*
Complete success	21 (33.9)	45 (57.7)	0.005*
Failure	13 (21.0)	5 (6.4)	-
6–18 mmHg			
Qualified success	43 (69.4)	71 (91.0)	0.001*
Complete success	19 (30.6)	45 (57.7)	0.001*
Failure	19 (30.6)	7 (9.0)	-
6–15 mmHg			
Qualified success	28 (45.2)	53 (67.9)	0.007*
Complete success	13 (21.0)	39 (50.0)	<0.001*
Failure	34 (54.8)	25 (32.1)	-
Subtype (6 mmHg ≤ IOP ≤ 21 mmHg)			
Normal-tension glaucoma (n = 4)	2	2	-
Qualified success	2 (100)	0 (0)	
Complete success	0 (0)	2 (100)	
Failure	0 (0)	0 (0)	
Primary open-angle glaucoma (n = 82)	36	46	
Qualified success	30 (83.3)	44 (95.7)	0.062†
Complete success	13 (36.1)	25 (54.3)	0.100
Failure	6 (16.7)	2 (4.3)	-
Other	24	30	
Qualified success	17 (70.8)	27 (90.0)	0.072†
Complete success	8 (33.3)	18 (60.0)	0.051†
Failure	7 (29.2)	3 (10.0)	-

Values are presented as mean ± standard deviation, number (%), or number only.
IOP = intraocular pressure.
*Statistically significant; †Nearly statistically significant.

(28 eyes) in the XEN group and 67.9% (53 eyes) in the trabeculectomy group (p = 0.007), and the complete success rate was 21.0% (13 eyes) and 50.0% (39 eyes), respectively (p < 0.001).

The success rates according to types of glaucoma showed a nearly statistically significant advantage for trabeculectomy in the group of primary open-angle glaucoma and others (Table 2). The failure rate of trabeculectomy did not exceed what has been reported [11]. The survival curves for surgical failure did not show significant differences between the surgical groups in all three cases.

Visual acuity, corneal astigmatism, and spherical equivalent

Preoperatively, the decimal UCVA was 0.33 ± 0.32 in the

Table 3. Visual outcomes in the XEN- and trabeculectomy-treated groups

Outcome	XEN group (n = 62)	Trabeculectomy group (n = 78)	*p*-value
BCVA (logMAR)			
At preoperative period	0.43 ± 0.57	0.29 ± 0.47	0.113
No. of eyes	62	78	
At postoperative day 1	0.72 ± 0.71	0.48 ± 0.53	0.028*
No. of eyes	62	78	
At postoperative wk 1	0.68 ± 0.68	0.49 ± 0.50	0.078
No. of eyes	62	78	
At postoperative mon 1	0.63 ± 0.69	0.42 ± 0.47	0.040*
No. of eyes	62	78	
At postoperative mon 3	0.58 ± 0.70	0.35 ± 0.49	0.032*
No. of eyes	62	78	
At postoperative mon 6	0.57 ± 0.72	0.30 ± 0.50	0.013*
No. of eyes	62	77	
At postoperative yr 1	0.52 ± 0.71	0.30 ± 0.50	0.059†
No. of eyes	56	70	
Corneal astigmatism (D)‡			
At preoperative period	1.13 ± 0.70	1.16 ± 1.14	0.842
No. of eyes	62	78	
At postoperative day 1	2.63 ± 1.66	2.31 ± 1.81	0.334
No. of eyes	55	58	
At postoperative wk 1	1.75 ± 1.00	2.19 ± 2.05	0.120
No. of eyes	61	67	
At postoperative mon 1	1.44 ± 0.85	1.89 ± 1.36	0.023*
No. of eyes	60	69	
At postoperative mon 3	1.33 ± 0.79	1.83 ± 1.48	0.015*
No. of eyes	59	71	
At postoperative mon 6	1.32 ± 0.79	1.81 ± 1.41	0.022*
No. of eyes	52	62	
At postoperative yr 1	1.27 ± 0.79	1.77 ± 1.44	0.060†
No. of eyes	26	47	

Values are presented as mean ± standard deviation or number only.
BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution; D = diopters.
*Statistically significant; †Nearly statistically significant; ‡Corneal astigmatism measured by autokeratometry (calculated as K2 – K1).

XEN group and 0.44 ± 0.38 in the trabeculectomy group ($p = 0.112$), while the BCVA (logMAR) was 0.43 ± 0.57 and 0.29 ± 0.47, respectively ($p = 0.113$). At 6 months postoperatively, the BCVA (logMAR) was better in the trabeculectomy group than the XEN group statistically significantly (0.57 ± 0.72 vs. 0.30 ± 0.50, $p = 0.013$) and at postoperative 1 year, trabeculectomy group showed a trend of superior outcomes, though not statistically significant. (0.52 ± 0.71 vs. 0.30 ± 0.50, $p = 0.059$) (Table 3).

Preoperative corneal astigmatism was 1.13 ± 0.70 diopters (D) in the XEN group and 1.16 ± 1.14 D in the trabeculectomy group ($p = 0.842$). Postoperatively, trabeculectomy consistently showed higher corneal astigmatism compared to XEN from 1 month onward. At 6 months postoperatively, corneal astigmatism was 1.32 ± 0.79 and 1.81 ± 1.41 D, respectively ($p = 0.022$). At postoperative year 1, it was 1.27 ± 0.79 and 1.77 ± 1.44 D, respectively ($p = 0.060$) (Fig. 1B).

No significant differences in spherical equivalent were observed between the two groups during the preoperative period (–2.89 ± 3.79 vs. –3.24 ± 3.15, $p = 0.552$) and all postoperative follow-up periods (at postoperative 1 year, –3.84 ± 3.62 vs. –3.07 ± 3.17; $p = 0.315$) (Table 4).

In the subgroup of patients with "favorable visual acuity" (logMAR < 0.7), which included 75.8% (47 of 62 eyes) in the XEN group and 85.9% (67 of 78 eyes) in the trabeculectomy group, preoperative BCVA (logMAR) was 0.14 ± 0.16 and 0.13 ± 0.18, respectively ($p = 0.755$). Throughout all postoperative follow-up periods, there were no significant differences in BCVA between two groups. In this subgroup, the XEN group consistently showed lower corneal astigmatism than the trabeculectomy group from 1 week postoperatively and beyond (Table 5).

Postoperative needling, additional procedures, and complications

Within postoperative 1 year, the rate of needling was 29% (18 out of 62 eyes) in the XEN group and 17.9% (14 out of 78 eyes) in the trabeculectomy group (chi-square analysis, $p = 0.121$). The first postoperative needling was performed at 91.39 ± 78.52 days in the XEN group and 171.43 ± 138.19 days in the trabeculectomy group, indicating a trend toward earlier intervention in the XEN group ($p = 0.067$). The distribution of the total number of needling procedures per group is shown in Fig. 1C. And the Kaplan-Meier survival curves for postoperative needling showed a significant difference between the two surgical groups as shown in Fig. 1D ($p = 0.034$).

Additionally, in the XEN group, YAG laser treatment for tip occlusion was performed in two eyes (3.2%), whereas in the trabeculectomy group, laser suture cuts were

Table 4. Spherical equivalent in the XEN- and trabeculectomy-treated groups

Spherical equivalent	XEN group (n = 62)	Trabeculectomy group (n = 78)	*p*-value
At preoperative period	–2.89 ± 3.79	–3.24 ± 3.15	0.552
No. of eyes	62	78	
At postoperative day 1	–3.46 ± 2.88	–4.09 ± 2.90	0.285
No. of eyes	48	51	
At postoperative wk 1	–3.06 ± 3.64	–3.41 ± 3.55	0.590
No. of eyes	60	63	
At postoperative mon 1	–3.34 ± 3.73	–3.69 ± 3.49	0.592
No. of eyes	60	66	
At postoperative mon 3	–2.98 ± 3.55	–3.39 ± 3.50	0.520
No. of eyes	56	72	
At postoperative mon 6	–3.27 ± 3.79	–3.72 ± 3.53	0.514
No. of eyes	51	60	
At postoperative yr 1	–3.84 ± 3.62	–3.07 ± 3.17	0.315
No. of eyes	62	78	

Values are presented as mean ± standard deviation, unless otherwise indicated.

performed in four eyes (5.1%) at postoperative days 4 and 6, and in two eyes at 3 weeks.

Postoperative complications occurred in 0 out of 62 eyes (0%) in the XEN group, and in 13 out of 78 eyes (16.7%) in the trabeculectomy group (p = 0.001). Among the 13 complications in the trabeculectomy group, hyphema- and hypotony-related problems were the most common, occurring in five eyes each (Fig. 2). The average time to onset of complications after trabeculectomy surgery was 20.85 ± 32.88 days.

Preoperative and postoperative medications

The number of glaucoma medications (eyedrops) used preoperatively was 2.71 ± 0.49 in the XEN group and 2.83 ± 0.38 in the trabeculectomy group (Fisher exact test,

Table 5. Visual outcomes in the XEN- and trabeculectomy-treated groups (analyzed with favorable visual acuity)

Visual outcome	XEN group (n = 47, 75.8%)	Trabeculectomy group (n = 67, 85.9%)	*p*-value
BCVA (logMAR)			
At preoperative period	0.14 ± 0.16	0.13 ± 0.18	0.755
No. of eyes	47	67	
At postoperative day 1	0.41 ± 0.39	0.35 ± 0.35	0.451
No. of eyes	47	67	
At postoperative wk 1	0.36 ± 0.37	0.37 ± 0.34	0.963
No. of eyes	47	67	
At postoperative mon 1	0.31 ± 0.37	0.29 ± 0.23	0.705
No. of eyes	47	67	
At postoperative mon 3	0.26 ± 0.38	0.29 ± 0.21	0.266
No. of eyes	47	67	
At postoperative mon 6	0.23 ± 0.49	0.19 ± 0.23	0.449
No. of eyes	47	67	
At postoperative yr 1	0.24 ± 0.43	0.15 ± 0.17	0.228
No. of eyes	44	59	
Corneal astigmatism*			
At preoperative period	1.11 ± 0.62	1.16 ± 1.18	0.782
No. of eyes	47	67	
At postoperative day 1	2.49 ± 1.91	2.34 ± 1.90	0.657
No. of eyes	43	50	
At postoperative wk 1	1.67 ± 0.81	2.28 ± 1.71	0.020†
No. of eyes	47	57	
At postoperative mon 1	1.47 ± 0.88	1.90 ± 1.38	0.058
No. of eyes	45	59	
At postoperative mon 3	1.19 ± 0.60	1.91 ± 1.53	0.002†
No. of eyes	44	60	
At postoperative mon 6	1.32 ± 0.79	1.88 ± 1.45	0.020†
No. of eyes	38	53	
At postoperative yr 1	1.45 ± 0.77	1.80 ± 1.45	0.196
No. of eyes	26	42	

Values are presented as mean ± standard deviation, unless otherwise indicated. Favorable visual acuity was defined as logMAR < 0.7.
BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution; D = diopters.
*Corneal astigmatism measured by autokeratometry (calculated as "K2 – K1"); †Statistically significant.

p = 0.002), indicating a trend toward higher usage in the trabeculectomy group. However, from 1 month postoperatively, medication usage was 0.52 ± 0.99 in the XEN group and 0.17 ± 0.55 in the trabeculectomy group (p = 0.014 at postoperative 1 month), and 1.21 ± 1.05 in the XEN group and 0.69 ± 0.90 in the trabeculectomy group (p = 0.003 at postoperative 1 year), showing significantly lower usage in the trabeculectomy group.

The reduction in the number of medications from preoperative to 1 year postoperative was 1.49 ± 1.12 in the XEN group (from 2.71 ± 0.49 to 1.21 ± 1.05, p < 0.001) and 2.13 ± 0.99 in the trabeculectomy group (from 2.83 ± 0.38 to 0.69 ± 0.90, p < 0.001). Additionally, for those using oral medications for IOP reduction, a nominal variable analysis showed consistently lower usage in the trabeculectomy group from 1 month postoperatively (Fisher exact test, p = 0.080) and up to 1 year (p = 0.018). The distribution of these nominal variables is shown in Fig. 3A, 3B.

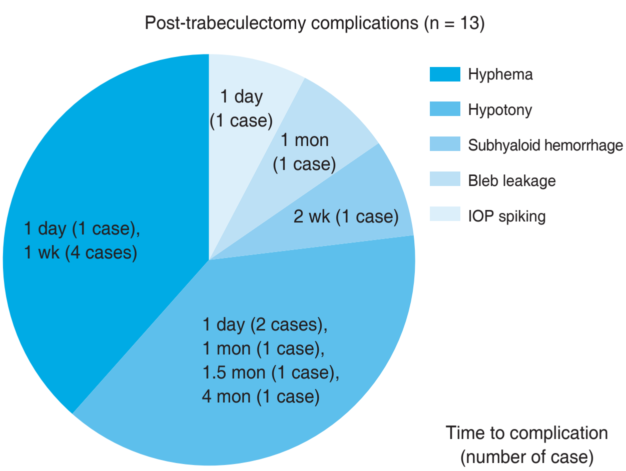

Fig. 2. Distribution of the 13 complications after trabeculectomy surgery. Data are presented as the time to occurrence of postoperative complications (number of case). IOP = intraocular pressure.

Operation time

The operation time was significantly shorter for XEN surgery (24 minutes 40 seconds ± 6 minutes 26 seconds) compared to trabeculectomy (40 minutes 18 seconds ± 8 minutes 27 seconds, p < 0.001).

Discussion

Preoperatively, the mean IOP in the XEN group was significantly lower than in the trabeculectomy group.(26.08 ± 7.54 mmHg vs. 29.60 ± 10.01 mmHg, p = 0.019) However, at the last follow-up after postoperative 6 months, both groups showed an effective reduction in IOP of over about 10 mmHg compared to preoperative levels (–9.98 ± 9.09 mmHg vs. –16.69 ± 10.85 mmHg, p < 0.001). This is comparable to the level of IOP reduction observed in other studies such as Schlenker et al. [12]. At 1 year postoperatively, the IOP was lower in the trabeculectomy group compared to the XEN group (15.77 ± 5.07 mmHg vs. 13.17 ± 3.81 mmHg, p = 0.001). This may indicate a selection bias, where patients with higher IOP were more likely to undergo the more invasive trabeculectomy surgery, while those with relatively lower IOP and suitable for MIGS opted for the XEN surgery.

Additionally, to exclude the effect of different preoperative IOP between the two surgical groups, 60 out of the 78 patients in the trabeculectomy group were selected (IOP matched). In this comparison, the last IOP measured 6 months after surgery was found to be also significantly

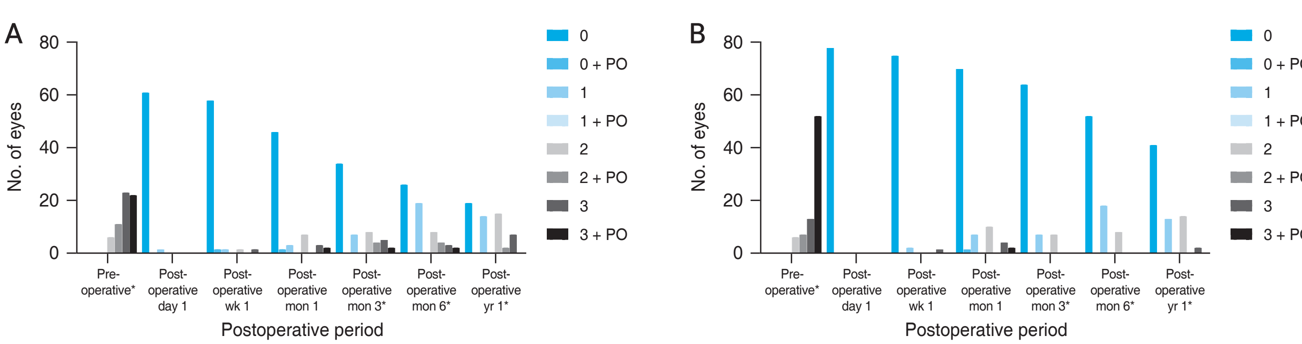

Fig. 3. Changes in the number of eyedrops used and whether usage of oral medications for intraocular pressure reduction at preoperative and postoperative follow-up periods. Data are represented using color matching according to a categorized scale. (A) XEN group (62 eyes). (B) Trabeculectomy group (78 eyes). PO = per oral medication (acetazolamide). *Statistically significant.

lower in the trabeculectomy group compared to the XEN group (preoperative IOP [XEN group vs. trabeculectomy group]: 26.08 ± 7.54 mmHg vs. 26.60 ± 7.00 mmHg, $p = 0.694$; last IOP [XEN group vs. trabeculectomy group]: 16.10 ± 5.04 mmHg vs. 13.47 ± 3.63 mmHg, $p = 0.001$).

The surgical success rates (both complete and qualified) were higher in the trabeculectomy group compared to the XEN group across all IOP thresholds of 21, 18, and 15 mmHg. The success rate of the XEN surgery in this study similar or slightly exceeded that of other studies employing similar surgical success/failure criteria for the open conjunctiva XEN surgery (encompassing both *ab externo* and *ab interno*; Do et al. [4], qualified success 71% and complete success 56%) or *ab externo* approach XEN surgery (including open and closed conjunctival; Ruda et al. [5], 74%).

The XEN surgery having a relatively narrow outflow pathway, achieved nearly an 80% success rate when using an IOP threshold of 21 mmHg (79.0% vs. 93.6%, $p = 0.011$) The survival curves for surgical failure for the two surgeries are shown in Fig. 4A–4C (no significant statistically different curve in all three graphs according to different surgical success criteria).

In the analysis of all patients, after postoperative 6 months, the trabeculectomy group showed a trend of higher corneal astigmatism (1.32 ± 0.79 vs. 1.81 ± 1.41, $p = 0.022$ at postoperative 6 months; 1.27 ± 0.79 vs. 1.77 ± 1.44, $p = 0.060$ at postoperative 1 year) and even better BCVA (logMAR) compared to the XEN group (0.57 ± 0.72 vs. 0.30 ± 0.50, $p = 0.013$ at 6 months; 0.52 ± 0.71 vs. 0.30 ± 0.50, $p = 0.059$ at 1 year) as shown in Table 4. As previously reported in other studies, surgically induced astigmatism was not neutral in both surgical groups [13]. However, the better postoperative BCVA (logMAR) in the trabeculectomy group compared to the XEN group did not align with preoperative BCVA (logMAR), higher postoperative corneal astigmatism trends and typical expectations.

Given the potential for selection bias, it can be assumed that patients selected for the less invasive XEN surgery had relatively lower IOP, or those with advanced glaucoma, where the postoperative prognosis might be worse. Advanced glaucoma often results in poorer postoperative BCVA [14]; hence, we excluded extreme cases for additional analysis.

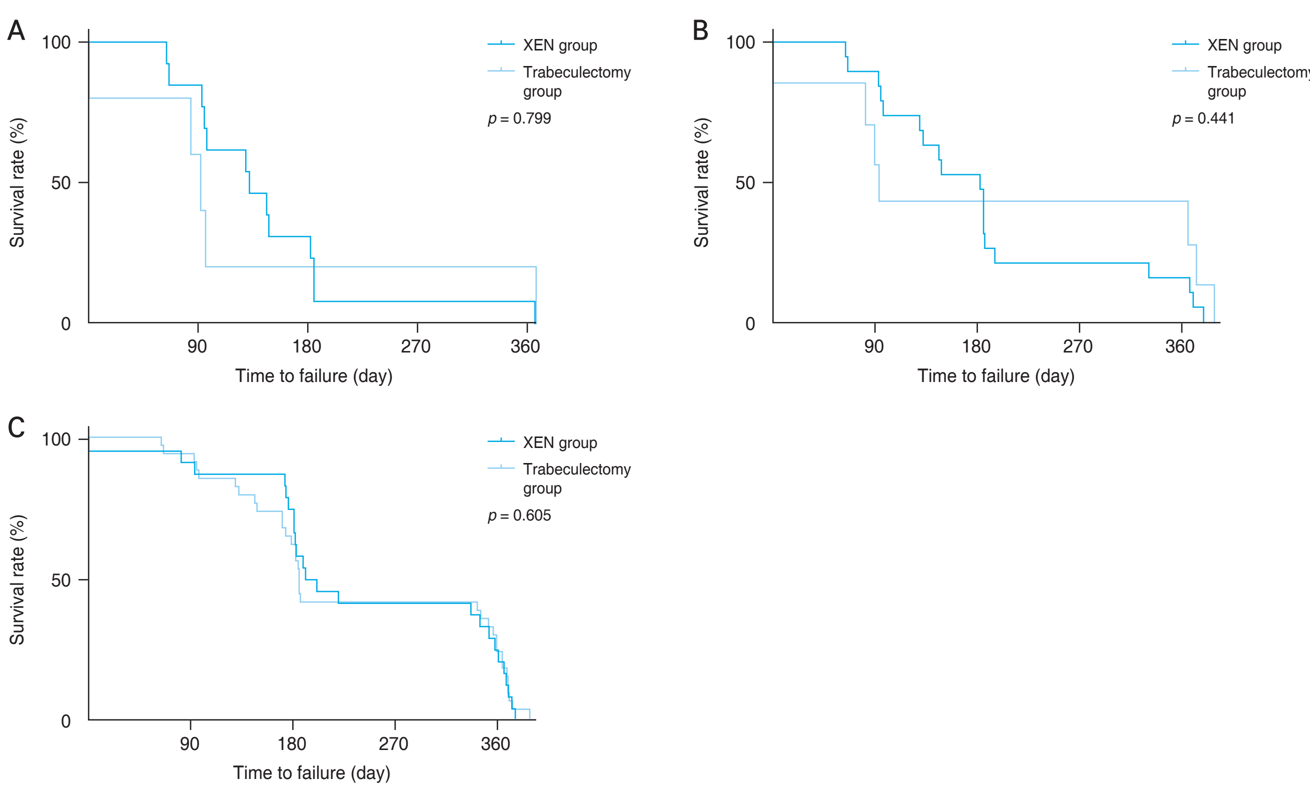

Fig. 4. Kaplan-Meier survival curve about surgical failure of the XEN and trabeculectomy groups postoperatively according to three different surgical success intraocular pressure (IOP) range: (A) 6–21 mmHg, (B) 6–18 mmHg, and (C) 6–15 mmHg.

Patients with BCVA (logMAR) <0.7 were classified as the "favorable visual acuity group," comprising 47 eyes (75.8%) in the XEN group and 67 eyes (85.9%) in the trabeculectomy group. The preoperative BCVA (logMAR) was 0.14 ± 0.16 and 0.13 ± 0.18 ($p = 0.755$), respectively. The unfavorable visual acuity patients had preoperative IOP of 30.20 ± 8.06 and 26.36 ± 8.12 mmHg, for the XEN and trabeculectomy groups, respectively ($p = 0.245$), and preoperative BCVA (logMAR) of 1.33 ± 0.42 and 1.22 ± 0.62, respectively ($p = 0.631$). In the "favorable visual acuity group" analysis, postoperatively from 1 week onwards, the XEN group consistently exhibited significantly lower corneal astigmatism, while visual acuity did not show significant differences between the groups. Detailed numbers and trends are presented in Table 5.

Additionally, the preoperative visual field-visual field index was 57.80% ± 34.82% in the XEN group and 68.66% ± 29.40% in the trabeculectomy group ($p = 0.056$). This result, nearly statistically significant, suggested that the XEN group had a higher severity of glaucoma before surgery, potentially contributing to the lower postoperative BCVA.

XEN surgery demonstrated excellent safety as a minimally invasive procedure with no significant postoperative complications (0 of 62 eyes), whereas the trabeculectomy group had 13 eyes of 78 eyes (16.7%) with complications. The trabeculectomy complications included five cases of hyphema, five cases of hypotony, one case of subhyaloid hemorrhage, one case of bleb leakage, and one case of IOP spiking. IOP spiking was up to 33 mmHg at postoperative day 1 from preoperative 22 mmHg and resolved with immediate bleb revision on the same date. Post-trabeculectomy complications were infrequent, and all cases were temporary.

The number of medications used before and after surgery mirrored the IOP trends. The trabeculectomy group used more medications preoperatively (2.71 ± 0.49 vs. 2.83 ± 0.38, $p = 0.002$) due to higher IOP and fewer medications postoperatively due to lower IOP, compared to the XEN group (1.21 ± 1.05 vs. 0.69 ± 0.90, $p = 0.003$ at postoperative 1 year)

Considering the learning curve of XEN surgery, a comparison between the first 31 eyes and the latter 31 eyes in this study showed no significant differences that were seen in other studies [15]. Preoperative IOP of first and latter 31 eyes of XEN group was 26.29 ± 7.82 and 25.87 ± 7.38 mmHg, respectively ($p = 0.820$). The surgical success rates were 53.1% and 46.9%, respectively ($p = 0.534$), and the last IOP within 1 year postoperatively was 16.19 ± 6.10 and 16.00 ± 3.80 mmHg, respectively ($p = 0.881$).

The analysis in this study revealed a significant difference in operation time, with XEN implantation surgery taking 24 minutes and 40 seconds ± 6 minutes and 26 seconds, compared to 40 minutes and 18 seconds ± 8 minutes and 27 seconds for trabeculectomy ($p < 0.001$). Given that almost all glaucoma surgeries are performed under local anesthesia, except in some exceptional cases, the shorter operation time for XEN implantation surgery can reduce the physical burden on patients. Additionally, considering the nature of glaucoma surgery and the possibility of needling in the future, the shorter time of XEN implantation surgery as an initial surgery can help alleviate the psychological burden and fear of future procedures on patients, highlighting a major advantage of MIGS.

The main limitation of this study is its retrospective design, which cannot eliminate selection bias entirely. Nonetheless, a key strength of this study is the ability to conduct a 1:1 comparison, rather than other papers, between XEN implantation surgery using *ab externo*, open conjunctival approach and trabeculectomy using a fornix-based approach, both performed by the same single surgeon with identical techniques such as conjunctival opening and application of MMC. The only difference between the two surgeries is whether XEN stent alone is inserted or scleral flap is created in junction with punch trabeculectomy and iridectomy. Additionally, Ologen was only utilized in trabeculectomy and could not be used in XEN surgeries due to supply issues. It should be considered that the scar-free wound healing effect of Ologen might have influenced the success rate of the surgeries. Also, due to only 26 cases of XEN surgery patients being evaluated for corneal astigmatism at the postoperative 1-year mark, additional information is needed. Additionally, a detailed analysis with age-matched groups and factors related to surgical failure could provide comprehensive insights for patient selection and prognosis prediction in XEN implantation surgery and trabeculectomy.

In conclusion, compared to trabeculectomy, the XEN45 stent implantation (*ab externo*, open conjunctival approach) demonstrated relatively lower effectiveness (complete and qualified success rates, and IOP reduction). However, it exhibited advantages as a MIGS, including stability in inducing corneal astigmatism, a significantly lower incidence of identifiable postoperative complications and shorter operation time with lower physical, psychological burdens on patients. Considering the characteristics and clinical outcomes of XEN surgery, it may be preferred over more invasive traditional surgeries for patients who require relatively less IOP reduction or for those with end-stage glaucoma.

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