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Original Article

One-Year Outcomes of Ab Externo XEN45 Gel Stent Implantation with an Open Conjunctiva Approach in Patients with Open-Angle Glaucoma

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Purpose: This study aimed to evaluate the 1-year surgical outcomes of XEN45 gel stent implantation with an open conjunctiva approach in patients with open-angle glaucoma (OAG).

Methods: This retrospective cohort study included 19 eyes of 19 patients who underwent XEN45 gel stent implantation with an open conjunctival approach. Surgical success was defined by intraocular pressure (IOP) ≤18 mmHg and one of the following: IOP reduction ≥30% or reduction of two glaucoma medications with final IOP if baseline IOP ≤18 mmHg. The cumulative probability of success rate was analyzed using Kaplan-Meier survival analysis. Cox proportional hazard regression analysis was used to assess prognostic factors for surgical failure.

Results: IOP reduced from 32.37 ± 12.08 mmHg preoperatively to 15.14 ± 2.25 mmHg at 1 year (p = 0.001). The number of glaucoma medication reduced from 3.89 ± 0.32 preoperatively to 0.86 ± 1.35 at 1 year (p = 0.001). The success rates were 78.9% at 6 months and 73.7% at 1 year. Eyes with bleb horizontal extent ≥2 clock hours at 1 month postoperatively had a significantly higher success rate (log-rank test, p < 0.001). Greater bleb horizontal extent at 2 weeks and 1 month postoperatively was associated with a lower surgical failure rate (2 weeks: hazard ratio, 0.119; p = 0.024; 1 month: hazard ratio, 0.046; p = 0.007). Bleb needling and additional glaucoma surgeries were necessary in 10 (52.6%) and five eyes (26.3%), respectively.

Conclusions: XEN45 gel stent implantation with the open conjunctiva approach is effective in reducing IOP and glaucoma medication for over 1 year in patients with OAG.

Key Words: Open-angle glaucoma, Open conjunctiva approach, XEN45 gel stent

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Trabeculectomy with either mitomycin C (MMC) or 5-fluorouracil has been performed as the standard surgery for patients with uncontrolled glaucoma [1]. However, complications, including cataract formation, hyphema, hypotony, choroidal effusion, bleb leakage, bleb-related infection, and vision deterioration, may occur [2,3]. Minimally invasive glaucoma surgery (MIGS) was developed to effectively reduce the intraocular pressure (IOP) and complications of conventional glaucoma surgery [4,5]. The XEN45 gel stent (AqueSys Inc) is a 6-mm long biocompatible gelatin tube with a 45-μm lumen, and it is the first MIGS device that is designed to perform in an ab interno manner and to create an aqueous outflow into the subconjunctival space [6].

The ab interno method had a success rate of 50% to 70%, and reduced 2 to 2.5 medications [5,7]. The ab interno method is only possible in the superonasal or inferonasal quadrant, whereas the ab externo method is accessible in any superior quadrant [8]. The ab externo method also minimizes the procedure in the anterior chamber and the use of viscoelastic materials, thereby reducing complications, including leakage from corneal incision, residual viscoelastic material and increase in IOP, and damage to the crystalline lens or corneal endothelium [9]. In addition, the ab externo method with an open conjunctiva approach allows for the removal or dissection of Tenon capsule and fine adjustment of the stent position [10].

There were a few studies reported the outcomes of the open conjunctiva approach [11–13]. However, in previous studies, bleb morphology was not analyzed. There were very few participants of Asian ethnicity [11,12]. Because the numbers of fibroblasts, macrophages, mast cells, and goblet cells in the conjunctiva differ according to ethnicity, postoperative fibrosis and the success rate may be different [14]. In addition, the East Asian population, including Korean and Japanese individuals, has a high prevalence of myopia. Thus, complications associated with hypotony are more frequent after trabeculectomy with MMC [15–17].

In this study, we evaluated surgical outcomes and prognostic factors, including bleb morphology, of ab externo XEN45 gel stent implantation with an open conjunctiva approach in Korean patients with open-angle glaucoma (OAG).

Materials and Methods

Ethics statement

This study was performed in accordance with the tenets of the Declaration of Helsinki and approved by the Institutional Review Board of the Pusan National University Hospital (No. 2110-013-108). All patients provided written informed consent for the surgical procedures and for their information to be stored in the hospital database and used for the research. This retrospective cohort study is registered in the Clinical Trial Registry of Korea (No. KCT0007873).

Study design

This retrospective cohort study was conducted on 19 eyes of 19 patients with OAG who underwent ab externo XEN45 gel stent implantation with an open conjunctiva approach between May 2020 and February 2021 at the Department of Ophthalmology, Pusan National University Hospital (Busan, Korea) and were followed up for at least 12 months postoperatively. If both eyes had XEN45 gel stent implantation, the first eye that underwent surgery was included. OAG was diagnosed based on the presence of glaucomatous optic disc changes and corresponding visual field defects, as confirmed by two reliable visual field

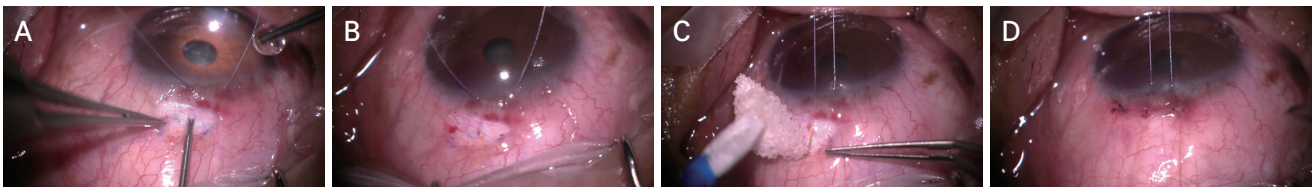

Fig. 1. Surgical technique of ab externo XEN45 gel stent (AqueSys Inc) implantation with the open conjunctiva approach. (A) After peritomy and blunt dissection between Tenon capsule and sclera, the XEN45 gel stent injector is placed bevel up in the sclera. (B) The XEN45 gel stent is placed 2.0 mm from the limbus. (C) Aqueous outflow through the stent is confirmed. (D) Tenon capsule and the conjunctiva were pulled anteriorly and closed with an interrupted suture.

tests and an open anterior chamber angle [18]. Eyes that had undergone previous ocular surgery, except uncomplicated cataract extractions, were excluded. Other exclusion criteria were eyes with coexisting neurological disease or retinal disease that could affect the visual field or alter the optic nerve.

Preoperatively, all patients underwent thorough ophthalmic examination, including best-corrected visual acuity (BCVA), slit-lamp examination, IOP measurement with Goldmann applanation tonometry, gonioscopy, dilated funduscopy, red-free retinal nerve fiber layer and optic disc stereoscopic photographs biometry using the IOL Master (Carl Zeiss Meditec), and standard automated perimetry. Automated perimetry was performed using a Humphrey Visual Field Analyzer 750i instrument (Carl Zeiss Meditec) with the Swedish interactive threshold algorithm 24-2. Central corneal thickness was measured using ultrasonic pachymetry (Pachmate, DGH Technology). Keratometry was performed using an auto kerato-refractometer (ARK-510A, Nidek Co Ltd).

At every postoperative visit, the IOP measured by Goldmann applanation tonometry, BCVA, number of glaucoma medications, complications, and need for additional glaucoma surgery were evaluated. Bleb morphology at every postoperative visit, including 1 week, 2 weeks, 1 month, and 12 months, was analyzed using the Indiana Bleb Appearance Grading Scale [19]. These standards comprise slit-lamp images for grading bleb height (H), horizontal extent (E), vascularity (V), and leakage graded using Seidel test (S). Bleb height evaluates the vertical dimension of the filtering bleb above the scleral surface and is divided into four scales: H0, flat bleb without visible elevation; H1, low bleb elevation; H2, moderate bleb elevation; and H3, high bleb as compared with the standard images. Bleb extent evaluates the horizontal dimension of the filtering bleb and is also divided into four scales based on clock hours: E0, no visible bleb extent to less than 1 clock hour; E1, extent equal to or greater than 1 clock hour but less than 2 clock hours; E2, extent equal to or greater than 2 clock hours but less than 4 clock hours; and E3, extent equal to greater than 4 clock hours. Bleb vascularity assesses the surface and deep vessel visibility of the conjunctiva over the filtering bleb and is divided into five scales: V0, avascular white (no microcysts); V1, avascular cystic (microcysts of the conjunctiva visible); V2, mild vascularity; V3, moderate vascularity; and V4, extensive vascularity (vascular engorgement). The V1 bleb is relatively transparent, whereas the V0 is white and relatively opaque. The Seidel test assessment is divided into three scales: S0, no bleb leak; S1, pinpoint transconjunctival leakage on bleb surface (at multiple pinpoints) without streaming of fluid within 5 seconds of application; and S2, streaming aqueous egress visible within 5 seconds of application of fluorescein (diffuse or localized).

Surgical technique

The XEN45 gel stent implantation with the open conjunctiva approach and MMC is shown in Fig. 1A–1D. Sur-

Table 1. Demographics and baseline clinical characteristics of patients who underwent XEN45 gel stent (AqueSys Inc) implantation

Characteristic	Value (n = 19)
Follow-up time (yr)	1.08 ± 0.08 (1.00–1.29)
Age (yr)	54.26 ± 18.85 (20.42–82.20)
Female sex	5 (26.3)
Eye laterality (right)	8 (42.1)
Diagnosis	
Primary open-angle glaucoma	15 (78.9)
Pseudoexfoliation glaucoma	4 (21.1)
Preoperative visual acuity (logMAR)	0.32 ± 0.37 (1.4–0)
Preoperative IOP (mmHg)	32.37 ± 12.08 (16–58)
No. of glaucoma medication	3.89 ± 0.32 (3–4)
History of glaucoma medication (yr)	5.16 ± 3.29 (0.24–10.40)
Previous laser trabeculoplasty	3 (15.8)
Preoperative lens status	
Phakic	13 (68.4)
Pseudophakic	6 (31.6)
Central corneal thickness (μm)	530.05 ± 17.85
Axial length (mm)	25.55 ± 2.38
Spherical equivalent (diopters)	–2.86 ± 2.51
Visual field parameter	
Visual Field Index (%)	38.79 ± 35.18
Mean deviation (dB)	–20.47 ± 11.15
Pattern standard deviation (dB)	7.47 ± 3.64

Values are presented as mean ± standard deviation (range), number of eyes (%), or mean ± standard deviation.
logMAR = logarithm of the minimum angle of resolution; IOP = intraocular pressure.

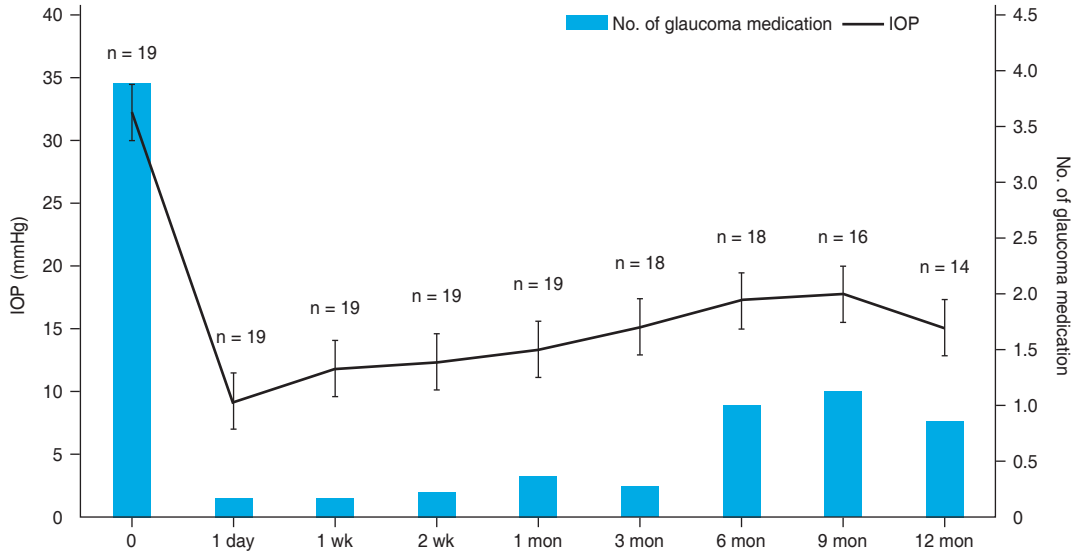

Fig. 2. Changes in the mean intraocular pressure (IOP) and mean number of glaucoma medications after XEN45 gel stent (AqueSys Inc) implantation. The IOP and the number of glaucoma medications at each time point are significantly lower than those of preoperative visit (all $p \leq 0.001$). Data are censored after an additional glaucoma surgery. The error bars are 95% confidence intervals (mean ± standard error × 1.96).

Table 2. Comparison of bleb morphology based on the Indian Bleb Appearance Grading Scale

Variable	Bleb at 1 mon (n = 19)	Bleb at 1 yr (n = 14)	*p*-value*
Bleb height			>0.999
H0 (flat bleb)	0 (0)	0 (0)	
H1 (low bleb)	2 (10.5)	1 (7.1)	
H2 (medium bleb)	17 (89.5)	13 (92.9)	
H3 (high bleb)	0 (0)	0 (0)	
Horizontal extent			0.480
E0 (<1 clock hours)	0 (0)	0 (0)	
E1 (≥1 and <2 clock hours)	3 (15.8)	3 (21.4)	
E2 (≥2 and <4 clock hours)	13 (68.4)	7 (50.0)	
E3 (≥4 clock hours)	3 (15.8)	4 (28.6)	
Vascularity			>0.999
V0 (avascular white)	0 (0)	0 (0)	
V1 (avascular cystic)	0 (0)	0 (0)	
V2 (mild vascularity)	18 (94.7)	14 (100)	
V3 (moderate vascularity)	1 (5.3)	0 (0)	
V4 (extensive vascularity)	0 (0)	0 (0)	
Seidel test			>0.999
S0 (no leak)	19 (100)	14 (100)	
S1 (multiple pinpoint leaks)	0 (0)	0 (0)	
S2 (streaming leak)	0 (0)	0 (0)	

Values are presented as number (%). Data are censored after an additional glaucoma surgery.
*Wilcoxon signed-rank test.

gery was performed by a single surgeon (JL) with the patients under local anesthesia as described by Panarelli et al. [10]. The limbal conjunctiva was incised by 2 to 3 mm to form a fornix-based conjunctival flap, and the conjunctiva and Tenon capsule were dissected toward the conjunctival sac. Surgical sponges (Eye Spear, Huizhou Foryou Medical Devices Co) soaked in MMC diluted at 0.4 mg/mL were placed between Tenon capsule and sclera for 2.5 minutes, and the area exposed to MMC was irrigated with 20 mL of balanced salt solution after removing the sponges. The XEN45 gel stent injector was placed bevel up in the sclera, 2.0 mm from the limbus, and the injector was carefully removed to avoid amputation or removal of the stent. After checking for aqueous outflow through the stent, the stent position was finely adjusted with tying forceps to locate them within 1.0 to 1.5 mm in the anterior chamber; then, the position of the stent was assessed using a Zeiss four-mirror gonioscope. Tenon capsule and conjunctiva were pulled anteriorly and closed with interrupted sutures.

Postoperatively, administration of topical eye drops, including levofloxacin (Cravit, Santen Pharm Co) four times a day and prednisolone acetate (Predbell, CKD Pharm Co) six times a day for 1 month, was commenced and tapered over 8 to 12 weeks. Bleb management was performed using digital massage or bleb needling if inadequate bleb function was identified.

Definition of surgical success and complications

Surgical success was defined as IOP ≤18 mmHg and one of the following: IOP reduction ≥30% or reduction of two glaucoma medications with final IOP ≤ baseline IOP if baseline IOP was ≤18 mmHg [20,21]. If the difference between the two IOP values was greater than 2 mmHg, a third IOP was measured, the mean of which was used in the analysis [22]. Surgical failure was defined as follows: (1) not meeting the above criteria at two consecutive visits after 1 month postoperatively; (2) loss of light perception; and (3) need for additional glaucoma surgery defined as trabeculectomy or tube shunt surgery [20]. Bleb needling and hypotony without maculopathy were not considered surgical failures [20]. Hypotony was defined as an IOP of ≤5 mmHg in two consecutive tests after 6 weeks postoperatively, while persistent hypotony was defined as two consecutive IOP ≤5 mmHg after postoperative 3 months [23]. Bleb leak within 1 month was defined as an early wound leak [24], and postoperative decrease in visual acuity was defined as a decrease in Snellen visual acuity ≥2 lines [23].

Statistical analysis

IBM SPSS ver. 26.0 (IBM Corp) was used for all the statistical analyses. The normality of the numerical data distribution was checked using Kolmogorov-Smirnov test. Wilcoxon signed-rank test was used to compare preopera-

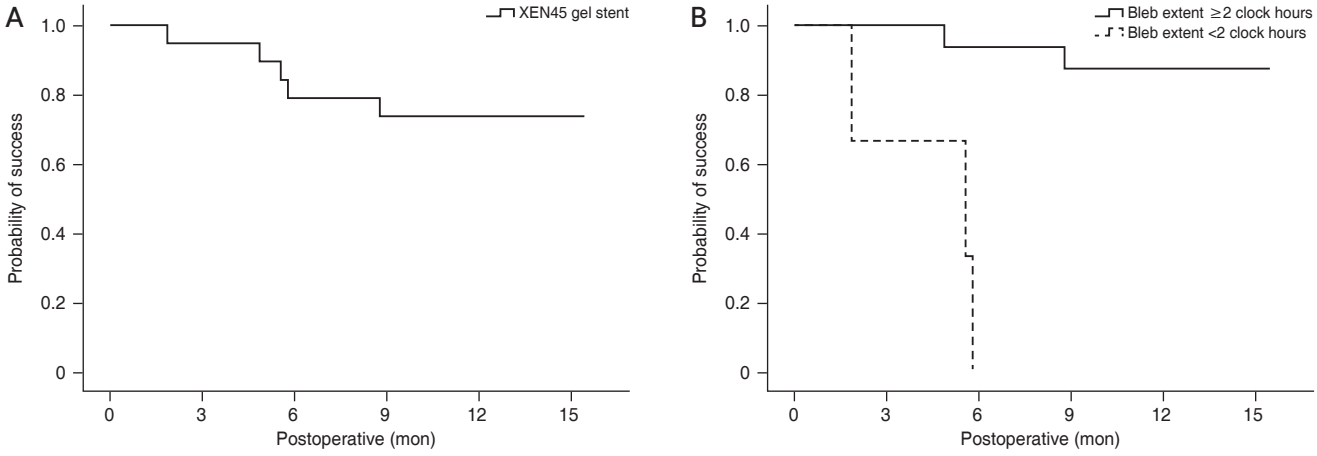

Fig. 3. Cumulative probabilities of surgical success after XEN45 gel stent (AqueSys Inc) implantation. (A) The mean success rates are 78.9% at 6 months and 73.7% at 1 year. (B) Eyes with bleb horizontal extent ≥2 clock hours at 1 month postoperatively had significantly higher success rate than eyes with bleb horizontal extent <2 clock hours (Mantel-Cox log-rank test, $p < 0.001$). Surgical success is defined as intraocular pressure ≤18 mmHg and one of the following: intraocular pressure (IOP) reduction ≥30% or reduction of two glaucoma medications with final IOP ≤ baseline IOP if baseline IOP ≤18 mmHg.

tive and postoperative variables. Snellen visual acuity was converted to the logarithm of the minimal angle of resolution (logMAR) equivalents for data analysis. Kaplan-Meier survival analyses were used to evaluate the success rate according to these criteria. The prognostic factors for surgical failure were evaluated using Cox proportional hazard regression analysis with forward stepwise method. The following factors were included in the univariable analysis: sex, age, glaucoma type, preoperative lens status, number of preoperative glaucoma medications, previous laser tra-

Table 3. Results of univariable and multivariable analyses for identifying prognostic factors for surgical failure

Prognostic factor	Univariable analysis		Multivariate model 1		Multivariate model 2	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Sex						
Male	Reference		-	-	-	-
Female	0.593 (0.066–5.321)	0.641				
Age (yr)	0.985 (0.938–1.033)	0.530	-	-	-	-
Glaucoma type			-	-	-	-
Primary open-angle glaucoma	Reference					
Pseudoexfoliation glaucoma	2.734 (0.451–16.562)	0.274				
Preoperative lens status			-	-	-	-
Phakic	Reference					
Pseudophakic	0.867 (0.145–5.197)	0.876				
No. of preoperative glaucoma medication	24.396 (0–3,482,425.465)	0.598	-	-	-	-
Previous laser trabeculoplasty	1.157 (0.129–10.371)	0.896	-	-	-	-
Axial length (mm)	1.119 (0.806–1.554)	0.502	-	-	-	-
Preoperative visual acuity (logMAR)	3.051 (0.460–20.250)	0.248	-	-	-	-
Preoperative mean deviation (dB)	1.003 (0.927–1.085)	0.941	-	-	-	-
Preoperative IOP (mmHg)	1.008 (0.941–1.079)	0.829	-	-	-	-
Postoperative IOP (mmHg)			-	-	-	-
At 1 day	1.053 (0.916–1.210)	0.467				
At 1 wk	1.009 (0.734–1.387)	0.956				
At 2 wk	1.015 (0.728–1.415)	0.932				
At 1 mon	1.423 (0.996–2.033)	0.053				
Bleb height			-	-	-	-
At 1 wk	0.715 (0.080–6.428)	0.765				
At 2 wk	0.715 (0.080–6.428)	0.765				
At 1 mon	0.405 (0.045–3.647)	0.422				
Bleb horizontal extent						
At 1 wk	0.336 (0.062–1.819)	0.205	-	-	-	-
At 2 wk	0.119 (0.019–0.760)	0.024	0.119 (0.019–0.760)	0.024	-	-
At 1 mon	0.046 (0.005–0.439)	0.007	-	-	0.046 (0.005–0.439)	0.007

Cox proportional hazards regression analyses were used for analyses. Multivariate model 1 adjusted for postoperative IOP at 1 month and bleb horizontal extent at 2 weeks. Multivariate model 2 adjusted for postoperative IOP at 1 month and bleb horizontal extent at 1 month.
HR = hazard ratio; CI = confidence interval; logMAR = logarithm of the minimum angle of resolution; IOP = intraocular pressure.

beculoplasty, axial length, preoperative BCVA (logMAR), preoperative visual field mean deviation, preoperative IOP, postoperative IOP at 1 day, 1 week, 2 weeks and 1 month, and bleb height and horizontal extent at 1 week, 2 weeks, and 1 month. Variables with a $p < 0.20$ in univariable analysis were included in multivariable analysis. A $p < 0.05$ was considered statistically significant.

Results

A total of 19 eyes from 19 patients underwent ab externo XEN45 gel stent implantation using an open conjunctiva approach, with 15 patients (78.9%) diagnosed with primary OAG (POAG) and four patients (21.1%) with pseudoexfoliation glaucoma (PXG). Mean age was 54.26 ± 18.85 years and follow-up time was 1.08 ± 0.08 years. Six eyes (31.6%) were pseudophakic at the time of the surgery. Preoperative IOP was 32.37 ± 12.08 mmHg with a mean number of 3.89 ± 0.32 glaucoma medications. Three eyes underwent previous laser trabeculoplasty. Patient demographic and baseline clinical characteristics are presented in Table 1.

After censoring for additional glaucoma surgery, 14 eyes were eligible for 12-month data analysis. The IOP and the number of glaucoma medications significantly reduced from 32.37 ± 12.08 mmHg preoperatively to 15.14 ± 2.25 mmHg and from 3.89 ± 0.32 preoperatively to 0.86 ± 1.35 at 1 year, respectively (both $p = 0.001$) (Fig. 2). All postoperative values were significantly lower than the preoperative values at all visits (all $p \leq 0.001$) (Fig. 2).

The postoperative bleb morphology at 1 month and at 1 year are presented in Table 2. There was no significant difference in bleb height, horizontal extent, vascularity, and leakage graded using Seidel test between the two visits (all $p \geq 0.480$). The most common bleb morphology was H2, E2, V2, and S0. No avascular bleb was observed.

The cumulative success rates were 78.9% at 6 months and 73.7% at 1 year. The eyes with bleb extent ≥2 clock hours at 1 month postoperatively had a significantly higher success rate than those with bleb extent <2 clock hours (log-rank test, $p < 0.001$) (Fig. 3A, 3B). In univariable analysis, bleb horizontal extent at 2 weeks and 1 month were significantly associated with surgical outcomes. In the multivariable analysis, greater bleb horizontal extent at 2 weeks and 1 month postoperatively was significantly associated with a lower surgical failure rate (2 weeks: hazard ratio, 0.119; $p = 0.024$; 1 month: hazard ratio, 0.046; $p = 0.007$) (Table 3).

The bleb morphology and success rates according to glaucoma type were also analyzed. Bleb in the POAG group was higher than that in the PXG group at postoperative 1 week, 2 weeks, and 1 month, respectively (all $p \leq 0.035$). Bleb horizontal extent was greater in the POAG group than in the PXG group at postoperative 1 week and 2 weeks, respectively (all $p = 0.061$). There were not significant bleb morphology scales at postoperative 1 year (all $p \geq 0.143$) (Supplementary Table 1). The mean success rate at 6 month was 50.0 % in the PXG group and 86.7% in the POAG group, and the mean success rate at 1 year was 50.0 % and 80.0 %, respectively (Mantel-Cox log-rank test, $p = 0.254$).

The frequency and type of postoperative complications, subsequent interventions, and additional glaucoma surger-

Table 4. Postoperative complications, subsequent interventions, and additional glaucoma surgery (n = 19)

Variable	No. (%)
Postoperative complication	
Early wound leakage	1 (5.3)
Shallow anterior chamber	0 (0)
Choroidal effusion and/or detachment	1 (5.3)
Transient hypotony (at POD 1)	5 (26.3)
Persistent hypotony	0 (0)
Hyphema	0 (0)
Decreased visual acuity at final visit	1 (5.3)
Conjunctival erosion and/or stent exposure	0 (0)
Stent malposition	0 (0)
Fibrin plugging	0 (0)
Iris plugging	0 (0)
Blebitis and/or Endophthalmitis	0 (0)
Subsequent intervention	
Bleb needling	10 (52.6)
1	8 (42.1)
≥2	2 (10.5)
Cataract extraction	1 (5.3)
Additional glaucoma surgery	
Trabeculectomy	4 (21.1)
Tube shunt surgery	1 (5.3)

A decrease in visual acuity was defined as a "decrease in Snellen visual acuity ≥2 lines."
POD = postoperative day.

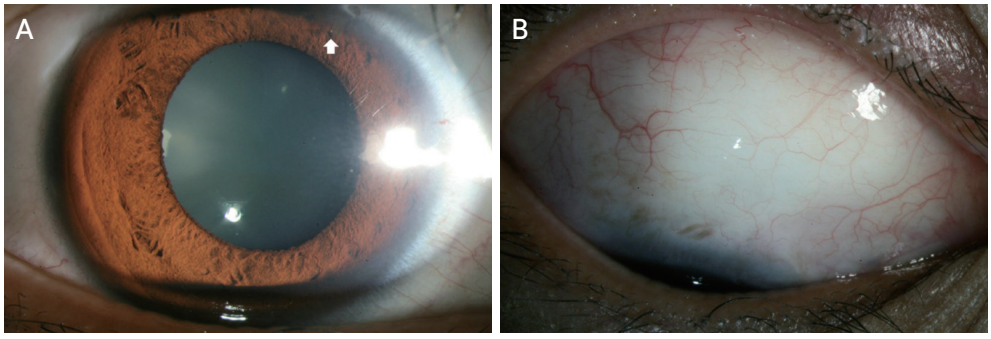

Fig. 4. Slit-lamp photograph of bleb after XEN45 gel stent (AqueSys Inc) implantation. A 28-year-old man with primary open-angle glaucoma received XEN45 gel stent implantation with open conjunctival approach at superonasal quadrant of right eye. (A) The arrow indicates the visible XEN45 gel stent in the anterior chamber. (B) The bleb has a medium height, 4-clock hour extent, and mild vascularity. Intraocular pressure was 15 mmHg without glaucoma medication at postoperatively 1 year.

ies during the follow-up period are presented in Table 4. Early wound leakage occurred in one eye (5.3%) 1 month after surgery and resolved at 2 months without intervention. Choroidal detachment occurred in one eye (5.3%) and extended posteriorly to the equator without involvement of the macula, which resolved spontaneously. Transient hypotony developed in five eyes (26.3%) at postoperative 1 day and resolved spontaneously at postoperative 1 week. One eye (5.3%) had decreased visual acuity ≥2 Snellen lines at the final visit, which was associated with the development of central retinal vein occlusion with macular edema. Postoperative bleb needling was performed in 10 eyes (52.6%). Cataract extraction was performed in one eye (5.3%). Additional glaucoma surgery was required in five eyes (26.3%), of which four eyes underwent trabeculectomy and one eye underwent tube shunt surgery. No bleb-related infection, stent exposure, or malposition occurred during the follow-up period.

A 28-year-old man with POAG underwent ab externo XEN45 gel stent implantation with an open conjunctiva approach in the superonasal quadrant of the right eye. The length and position of the XEN45 gel stent were 1 mm in the anterior chamber (Fig. 4A). One year after surgery, the bleb photograph showed a bleb of medium height, 4-clock hour extent, and mild vascularity. The IOP was 15 mmHg without glaucoma medication (Fig. 4B).

Discussion

The XEN45 gel stent implantation with an open conjunctiva approach effectively reduced IOP and glaucoma medication for over 1 year after surgery in patients with OAG. Multivariate Cox regression analysis showed that greater bleb horizontal extent at 1 month postoperatively was associated with a lower failure rate.

The success rate of XEN45 gel stent implantation with an open conjunctiva approach was 78.9% at 6 months and 73.7% at 12 months, showing superior results compared to those of the ab interno method [5–7,12]. The success rate of the ab interno method in patients with OAG ranged from 49.4% to 67.2% based on the criterion of IOP reduction ≥20% or IOP <18 mmHg with or without medication at 6 months [5,6]. Karimi et al. [7] reported that the success rate of the ab interno method in OAG was 61.5% according to the criteria of IOP ≤21 mmHg and IOP reduction ≥20% with or without medication at 12 months.

In contrast to the ab interno approach, dissection of Tenon capsule in the open conjunctiva approach may reduce the contact between the distal end of the XEN45 gel stent and Tenon capsule, and subsequently improve surgical outcome [12]. In this study, a greater bleb horizontal extent at 2 weeks and 1 month postoperatively was associated with a lower surgical failure rate, and the bleb horizontal extent was more than 2 clock hours at 1 month and 12 months postoperatively in the majority of the eyes.

Our results are in agreement with those of a previous study that compared the surgical outcomes of open and closed conjunctiva techniques in XEN45 gel stent implantation [11]. Do et al. [12] reported that the open conjunctiva technique has a higher success rate than the closed conjunctiva technique, with success rates according to the criterion of IOP ≤21 mmHg and IOP reduction ≥20% with or without medication at 12 months of 53% and 71% for the

closed conjunctiva and open conjunctiva methods, respectively. Based on the results of the present and earlier studies, an open conjunctiva approach with extensive dissection of Tenon capsule may be associated with a wider bleb, which may contribute to better surgical success.

PXG could be particularly challenging to manage [25,26]. Previous studies have reported that PXG had poorer long-term outcomes and different bleb morphology after glaucoma filtration surgery [27–29]. The bleb morphology and success rates according to glaucoma type were analyzed in this study. The PXG group showed lower bleb at postoperative 1 week, 2 weeks, and 1 month compared to the POAG group. These results are consistent with the results of the previous study by Kim et al. [29]. Kim et al. [29] analyzed the correlation among XEN45 gel stent tip location and bleb morphology with clinical profiles. They suggested that the uviform type (tip location) mostly created no or low wall and no or low bleb, which was associated with PXG [29]. The mean success rate was not significantly different between the two groups in this study. The mean success rate at 6 month was 50.0% in the PXG group and 86.7% in the POAG group, and the mean success rate at 1 year was 50.0% and 80.0%, respectively (Mantel-Cox log-rank test, $p = 0.254$). Glaucoma type itself was not a significant prognostic factor in this study (hazard ratio, 2.734; confidence interval, 0.451–16.562; $p = 0.274$). However, we should be cautious in the interpretation of the results from subgroup analysis according to glaucoma type because this study had a small sample size.

Complications, including improper stent location or migration (0.11%–14.02%) and stent exposure (0.54%–2.3%) after the ab interno method, have been reported [5,7,30]. However, in this study, complications related to stent exposure and malposition did not occur, which is similar to the results of a previous study [12]. Do et al. [12] reported that conjunctival erosion and stent exposure occurred in 4.9% of the cases with the closed conjunctiva technique and in 0% with the open conjunctiva approach technique; moreover, iris plugging occurred in 13.1% and 1.3% of the cases, respectively. The study hypothesized that it would be difficult to finely adjust the stent that was already implanted through the closed approach, and it would be challenging to precisely and constantly locate the stent in the subconjunctival and subtenon space. Subconjunctival-injected MMC could not be washed using the closed approach, whereas conjunctival erosion and stent exposure could be reduced because sufficient irrigation was performed after removing the sponges soaked with MMC in the open conjunctival approach [5].

Glaucoma surgery increases cataract incidence and progression, which may be the leading cause of vision loss after trabeculectomy [31,32]. In the tube versus trabeculectomy study, cataract progression (13 of 45 eyes) was most frequently attributed to vision loss after 1 year of follow-up [33]. However, in the present study, only one eye underwent cataract extraction after XEN45 gel stent implantation, which is consistent with the results of earlier XEN45 gel stent studies (2.6%–3.3%) [5,11]. Cataract formation and progression may occur due to lens trauma, inflammation, hypotony, lens-corneal touch, or the use of intraoperative MMC [1]. The XEN45 gel stent implantation with an open conjunctiva approach can be performed without corneal incision or viscoelastic use, which may minimize lens trauma and inflammation in the anterior chamber [9]. In addition, sufficient irrigation after removing MMC sponges may reduce the effect on cataract formation and progression.

Even though we opened the conjunctiva upon implantation of the stent, early wound leakage and bleb leakage occurred in only one eye, which resolved spontaneously. These results are consistent with the results of earlier studies (0.93%–9.2%) and less than those after trabeculectomy (7.1%–17%) [4,5,7,30,34]. In the present study, the conjunctiva was incised less than in trabeculectomy (6–8 mm) [1] and sufficient irrigation was performed after removing the MMC sponges. In addition, the conjunctiva with Tenon capsule was pulled anteriorly and closed with an interrupted suture, which may have served as a protective layer above the distal end of the tip. These may have contributed to reducing the frequency of early wound leakage and bleb leakage in this study.

Persistent hypotony has been the main cause of treatment failure after trabeculectomy [33]. In the East Asian population, hypotony rates have been reported with a greater incidence of 10% to 33% after trabeculectomy with MMC [15]. It has been suggested that an eye with thin sclera is more susceptible to postoperative hypotony; thus, the high prevalence of myopia with thin sclera in the Korean population may be related to this [15,16,35]. Although the mean axial length of the eyes included in this study was 25.55 mm, persistent hypotony did not occur after surgery, suggesting that XEN45 gel stent implantation may be

more effective in preventing postoperative hypotony than trabeculectomy in myopic eyes.

The bleb needling rate (52.6%) was similar to those reported in the earlier studies, which reported that the bleb needling rate ranged from 32% to 53% after XEN45 gel stent implantation [4,5,7,12,30]. In the present study, multivariable analysis showed that not the IOP at 1 month, but the greater bleb horizontal extent at 1 month, was associated with a lower surgical failure rate. The resistance of the bleb wall may greatly affect IOP because aqueous humor through the XEN45 gel stent flows to a limited space [7]. Based on the results of the present study, although the target IOP is reached 1 month postoperatively, close monitoring of bleb morphology with active bleb management, including digital massage and injection of an antimetabolite or steroid, should be considered, which may reduce the rate of bleb needling.

There were some limitations to the present study, such as its retrospective nature, which induced a selection bias. This study had a small sample size because it was performed at a single center. However, a single surgeon performed all the surgeries using a standardized method. For future studies, randomized controlled prospective clinical trials are needed to assess the surgical outcomes of XEN45 gel stent implantation with an open conjunctiva approach in the management of OAG. All patients in the study population were Korean; therefore, the influence of the open conjunctiva approach on XEN45 gel stent implantation may be different in other populations. A future study would require a control group of eyes with the ab interno method or trabeculectomy to determine the actual beneficial effect of the open conjunctival approach in cases of OAG. Bleb horizontal extent was a significant factor in the present study; thus, analysis of intrableb structure by anterior-segment optical coherence tomography (AS-OCT) may be needed in future studies [36]. The macroscopic characterization of the filtering bleb analysis by slit-lamp examination conducted in this study is closely related to the function of the filtering bleb. However, there is a disadvantage that the intrableb structure, which is related to the long-term surgical success or failure, was assessed in this study [29,36,37]. Kim et al. [29] reported that the intraconjunctival and intratenon type classified by the XEN45 gel tip location on day 1 became high sparse bleb wall as assessed with AS-OCT or avascular bleb as assessed with slit-lamp examination were more associated with lower mean IOP at 6 months postoperatively. Lenzhofer et al. [37] also suggested that the intratenon or subtenon location of the XEN45 gel tip assessed by AS-OCT was associated with surgical success. Both studies represented that a deeper XEN45 gel stent position in the conjunctiva showed better IOP control. An earlier diagnosis of nonfunctionality might have a benefit for managing the bleb after XEN45 gel stent implantation, since bleb needling is one of the most frequently performed procedure after the surgery and can affect bleb appearance [29,36].

The clinical implications of this study for evaluating the safety and efficacy of XEN45 gel stent implantation are as follows. The open conjunctiva approach allows for direct anatomical confirmation of stent placement and prevents complications associated with stent location, which are frequent complications of the ab interno method. In addition, it allows for dissection of Tenon capsule from the sclera, subsequently creating a wide bleb. Wider bleb horizontal extent was associated with a lower rate of surgical failure.

In conclusion, XEN45 gel stent implantation with the open conjunctiva approach is considered a safe and effective method for reducing IOP, glaucoma medications, and complications, with favorable surgical outcomes in eyes with OAG.

Supplementary Materials

Supplementary Table 1. Comparison of bleb morphology between primary open angle glaucoma and pseudoexfoliation glaucoma based on the Indian Bleb Appearance Grading Scale (n = 19)

Supplementary materials are available from https://doi.org/10.334/kjo.2023.0044.

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Supplementary Table 1. Comparison of bleb morphology between POAG and PXG based on the Indian Bleb Appearance Grading Scale (n = 19)

Variable	1 wk			2 wk			1 mon			1 yr		
	PXG (n = 4)	POAG (n = 15)	*p*-value	PXG (n = 4)	POAG (n = 15)	*p*-value	PXG (n = 4)	POAG (n = 15)	*p*-value	PXG (n = 2)	POAG (n = 12)	*p*-value
Height			0.004			0.004			0.035			0.143
H0 (flat bleb)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
H1 (low bleb)	3 (75.0)	0 (0)		3 (75.0)	0 (0)		2 (50.0)	0 (0)		1 (50.0)		
H2 (medium bleb)	1 (25.0)	15 (100)		1 (25.0)	15 (100)		2 (50.0)	15 (100)		1 (50.0)	12 (100)	
H3 (high bleb)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
Horizontal extent			0.061			0.061			0.192			0.231
E0 (<1 clock hours)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
E1 (≥1 and <2 clock hours)	2 (50.0)	0 (0)		2 (50.0)	0 (0)		2 (50.0)	1 (6.7)		1 (50.0)	2 (16.7)	
E2 (≥2 and <4 clock hours)	2 (50.0)	12 (80.0)		2 (50.0)	12 (80.0)		2 (50.0)	11 (73.3)		0 (0.0)	7 (58.3)	
E3 (≥4 clock hours)	0 (0)	3 (20.0)		0 (0)	3 (20.0)		0 (0)	3 (20.0)		1 (50.0)	3 (25.0)	
Vascularity			>0.999			0.530			>0.999			>0.999
V0 (avascular white)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
V1 (avascular cystic)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
V2 (mild vascularity)	4 (100)	12 (80.0)		3 (75.0)	0 (0)		4 (100)	14 (93.3)		2 (100)	12 (100)	
V3 (moderate vascularity)	0 (0)	3 (20.0)		1 (25.0)	12 (80.0)		0 (0)	1 (6.7)		0 (0)	0 (0)	
V4 (extensive vascularity)	0 (0)	0 (0)		0 (0)	3 (20.0)					0 (0)	0 (0)	
Seidel test			>0.999			>0.999			>0.999			>0.999
S0 (no leak)	4 (100)	15 (100)		4 (100)	15 (100)		4 (100)	15 (100)		2 (100)	12 (100)	
S1 (multiple pinpoint leaks)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
S2 (streaming leak)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	

Values are presented as number of eyes (%). Data are censored after an additional glaucoma surgery.
POAG = primary open-angle glaucoma; PXG = pseudoexfoliation glaucoma.