Glaucoma Surgery Comparison: SIBS Microshunt Versus Gelatin 45 μm Microstent Versus Trabeculectomy as Primary Surgical Interventions

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• PURPOSE: Compare surgical success, risk factors, and postoperative course of the SIBS microshunt, gelatin 45 μm microstent, and trabeculectomy with mitomycin C (MMC) as a primary surgical intervention in patients with glaucoma. We present a multicenter,12-month, retrospective, nonrandomized, interventional case series.

• DESIGN: Multicenter,12-month, retrospective, nonrandomized, interventional case series.

• METHODS: Consecutive patients with glaucoma on maximally tolerated medical therapy received either primary SIBS microshunt, gelatin 45 μm microstent, or trabeculectomy with MMC as a stand-alone procedure at one of six participating centers (Canada, Italy, the Netherlands, Belgium, Singapore, Dominican Republic) from August 2015 to August 2020. Main outcome measures were proportion of eyes at 12-months with (1) no two consecutive intraocular pressures (IOPs) > 17 mm Hg or clinical hypotony (IOP < 6 mm Hg with a loss of> 2 lines of vision), without (complete) or with (qualified) glaucoma medications; and (2) ≥20% reduction from baseline IOP. Secondary outcomes included IOP thresholds of 14 and 21 mm Hg, median IOP, medications, risk factors, postoperative interventions, complications, and reoperations.

• RESULTS: Records from 577 eyes from 521 patients with SIBS microshunt (n = 235), gelatin 45 μm microstent (n = 201), or trabeculectomy (n = 141) were included. Baseline decision IOP was lower in the SIBS group, and baseline number of glaucoma medications was also lower in the SIBS and trabeculectomy groups. After 12-month follow-up, complete success occurred in 68.8% of patients with SIBS microshunt, 46.2% with gelatin 45 μm microstent, and 58.0% with trabeculectomy (P = .0002). Qualified success occurred in 89.7%, 70.1%, and 83.6% of eyes, respectively (P = .0002). In the multivariate analysis, eyes receiving a gelatin 45 μm microstent relative to SIBS microshunt (hazard ratio [HR] 2.0; 95% confidence interval [CI] 1.5-2.7), trabeculectomy relative to SIBS microshunt (HR 1.6; 95% CI 1.2-2.2), or intraoperative MMC dose less than 0.4 mg/mL (HR 1.5; 95% CI 1.1-2.0) was significantly associated with failure. Complications occurred in 33.6%, 42.8% and 56% of eyes (P = .0001); needling in 12.3%, 29.9% and 22% (P < .0001); revisions in 10.6%, 8.5% and 8.5% (P = .68); and reoperations in 5.5%, 13.9% and 7.8% (P < .001) with SIBS microshunt, gelatin 45 μm microstent, or trabeculectomy, respectively.

• CONCLUSIONS: Overall, patients with the SIBS microshunt achieved higher success rates compared to both trabeculectomy and the gelatin 45 μm microstent group, with fewer postoperative complications, interventions, and reoperations for glaucoma. (Am J Ophthalmol 2025;277: 169–183. © 2025 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.)

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INTRODUCTION

PREVIOUS ESTIMATES REPORT THE GLOBAL PREVALENCE of glaucoma to be 79.6 million people worldwide and warn the impact could grow to 111.8 million people

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by 2040, with residents of Africa and Asia disproportionality affected.[1,2] Glaucoma continues to be the leading cause of irreversible blindness globally, blinding an estimated 11.2 million people worldwide and accounting for 8% of global blindness.[1,3] The cornerstone of glaucoma treatment remains the lowering intraocular pressure (IOP)—slowing disease progression and limiting further visual field losses.[4] First line therapy consists of either topical eye drops or laser trabeculoplasty, with both interventions showcasing similar efficacy profiles.[5] When these initial therapies fail, a surgical glaucoma procedure is often undertaken. Glaucoma filtering surgeries, such as trabeculectomy or traditional tube shunt, achieve sustained IOP reduction and are cost-effective but have significant sight-threatening short and long-term side effects, such as hypotony and blebitis.[6] However, novel microinvasive glaucoma surgical techniques and devices have promised to alleviate many of these added risks with improved safety profiles.[7,8]

While several choices exist for angle-based trabecular bypass microinvasive glaucoma surgical, clinical data and expert opinion suggest a lesser IOP lowering capacity relative to subconjunctival bleb-forming surgeries.[9,10] One of the more challenging aspects of trabeculectomy is achieving the appropriate outflow resistance through creation of the scleral flap. The variability of the technique in this procedure may lead to more inconsistent outcomes, thereby reducing its predictability. Recently, in response to this challenge, two flow regulated implants (microinvasive bleb surgeries [MIBS]) have emerged that are designed to connect the anterior chamber into the subtenon's space.[11] The XEN45 gel stent (gelatin 45 μm microstent; Allergan) is composed of crosslinked gelatin and possesses a simple tubular design.[12] The Preserflo MicroShunt (SIBS microshunt; Santen) is composed of bioinert poly(styrene-block-isobutylene-block-styrene) (SIBS) material and has two radial fins designed to help seat the device within the scleral tract—mitigating peri–tubular flow and device migration.[13]

A limited number of studies have reported on the efficacy of trabeculectomy compared to either the SIBS microshunt or gelatin 45 μm microstent. A single-center, retrospective study by Theilig et al[14] comparing trabeculectomy ($n = 100$) and gelatin 45 μm microstent ($n = 100$) showcased no difference in IOP lowering and topical medications between both procedures, with a higher rate of postoperative complications in the trabeculectomy group. Schlenker et al[15] also showed no difference in surgical success between gelatin 45 μm microstent ($n = 281$) and trabeculectomy ($n = 228$), and similar rates of postoperative complications. Another retrospective study by Wagner et al[16] assessed the efficacy of trabeculectomy, gelatin 45 μm microstent, and SIBS microshunt, albeit with 35 eyes in each group. There was no notable difference in surgical success after 6 months between each procedure. Similarly, other smaller, retrospective studies also demonstrated no statistically significant difference in IOP lowering postoperatively between either the gelatin 45 μm microstent vs SIBS microshunts or SIBS microshunt vs trabeculectomy.[17,18] In contrast, a larger, multicenter, randomized controlled trial (RCT) investigated the efficacy of SIBS microshunt ($n = 132$) and trabeculectomy ($n = 395$) and reported a higher rate of surgical success in the trabeculectomy group albeit with higher rates of postoperative interventions and transient hypotony.[19,20] These results, however, must be interpreted in the context of the low dose of Mitomycin C (MMC) (0.2 mg/mL) used, as well as the significantly greater proportion of African American patients (over two times) in the microshunt group, representing a potential failure of randomization, and the greater likelihood of these patients to experience surgical failure.[21] Another RCT comparing gelatin 45 μm microstent ($n = 95$) vs trabeculectomy ($n = 44$) showed no statistically significant difference in surgical success, but lower mean IOP, numerically lower failure rate and less need for glaucoma medications in the trabeculectomy group.[22]

To the best of our knowledge, there are no large, multicenter studies reporting concurrently the efficacy of gelatin 45 μm microstent, SIBS microshunt, and trabeculectomy in glaucomatous eyes on maximally tolerated medical therapy. This study aims to summarize rates of surgical success, risk factors for failure, and adverse events observed in patients with glaucoma who received either the gelatin 45 μm microstent, SIBS microshunt, or standard trabeculectomy with MMC as a stand-alone procedure in a multicenter, retrospective study over a 12-month follow-up period.

METHODS

This study reports 1-year outcomes from an investigator-initiated, multicenter, retrospective interventional case series of consecutive patients receiving trabeculectomy or MIBS with a SIBS microshunt or with a gelatin 45 μm microstent and MMC between August 2015 and August 2020. Surgeries were performed by an international group of academic ophthalmology centers located in Canada, Italy, the Netherlands, Belgium, Singapore, Dominican Republic. This study adhered to the tenets of the Declaration of Helsinki, and institutional review board approval was obtained from Trillium Health Partners. All patients provided informed consent for surgery. Baseline preoperative characteristics collected include demographics (age, eye, sex, ethnicity, diabetes status) and ocular characteristics (best-corrected visual acuity [BCVA]; IOP at which the decision for surgery was made [decision IOP]; glaucoma medications; glaucoma diagnosis; cup-to-disc ratio; visual field mean deviation; and history of previous cataract surgery, other ocular surgery, or laser trabeculoplasty).

• **INCLUSION AND EXCLUSION CRITERIA:** Data on consecutive eyes were collected. The microshunts were im-

planted, or trabeculectomy performed in glaucomatous eyes with an IOP above target and/or progressing on maximally tolerated medical therapy. Eyes with prior incisional glaucoma surgical intervention were excluded from the analysis, and procedures combined with phacoemulsification were excluded. Eyes were also excluded if they had less than 1 month of follow-up or if they received MMC doses greater than 0.4 mg/mL.

• **SURGICAL PROCEDURES:** The procedure for SIBS MicroShunt implantation has been previously described in detail.[23] An open conjunctival ab-externo approach was used. The procedure for the gelatin 45 μm microstent was previously described in detail.[24] A closed conjunctival ab-interno approach was used. Trabeculectomy was accomplished using a fornix-based conjunctival flap with partial thickness scleral flap as has been described previously.[15] All filtering surgeries were performed with intraoperative MMC. The dose used was according to the surgeon's decision.

• **POSTOPERATIVE MANAGEMENT:** After the procedure, patients were instructed to stop all glaucoma medications and start steroid drops every 2 hours for the first week, followed by a slow taper over 8 to 10 weeks. Topical moxifloxacin drops were used for a week, and a nonsteroidal anti-inflammatory drop for 1 month. Patients were seen at postoperative day 1, postoperative day 3/4, and then as needed at the surgeon's discretion. Reintroduction of glaucoma medications, needling, digital ocular compression, AC reformation, surgical revisions, and reoperations were performed as per surgeon discretion.

• **PRIMARY OUTCOME:** The primary outcome was the proportion of eyes at 1 year achieving surgical success. Complete success was defined as: (1) no two consecutive IOP readings greater than 17 mm Hg, nor clinical hypotony (IOP less than 6 mm Hg and more than 2 lines of vision loss from sequalae of hypotony), (2) at least a 20% reduction from decision IOP (at the time surgical treatment was decided to be pursued), and (3) no glaucoma medication use. Qualified success allowed for medication use. Surgical revisions, reoperation, or loss of light perception vision were considered immediate failures. Out-of-range IOP or medication use in the first month was not considered a failure, nor were in-clinic interventions, including needlings.

• **SECONDARY OUTCOMES:** Secondary efficacy outcome measures had modified upper IOP thresholds of 14 and 21 mm Hg for complete and qualified success criteria with a 20% IOP reduction from baseline. Also reported are median IOP and medication burden, time to first medication use, and BCVA in logarithm of the minimum angle of resolution (logMAR) units at last follow-up or at reoperation. In additional secondary analyses, we explored risk factors for failure, including sex, age, ethnicity, right vs left eye, lens status, previous trabeculoplasty, glaucoma type, glaucoma severity, decision IOP, preoperative vision, diabetes status, and MMC dose.

• **SAFETY OUTCOMES:** Postoperative interventions, complications (including leak or dehiscence, hyphema, vitreous hemorrhage, choroidal detachments, macular folds, prolonged inflammation, corneal decompensation, macular edema, diplopia, iris incarceration, or blocked or exposed microshunt), more serious complications (including angle closure, retinal detachment, suprachoroidal hemorrhage, malignant glaucoma, blebitis, endophthalmitis, or no light perception vision), and reoperations were recorded and similarly analyzed for risk factors.

• **STATISTICAL ANALYSIS:** All statistical analyses were run on SAS university edition software (SAS Institute Inc). Graphs were drawn with either SAS university edition software or Prism 9 (Version 9.1.2, GraphPad Software, LLC). Categorical variables were displayed as proportions, and comparisons were made using a Fisher's exact test. Continuous outcomes were described as means (standard deviation) or medians (interquartile range [IQR]), depending on normality, and then compared with either 2-sided t-tests or Wilcoxon tests as appropriate. All Snellen visual acuity measurements were converted to logMAR. Overall treatment success was calculated using survival analysis to statistically account for loss to follow-up and demonstrated with Kaplan–Meier curves. The results were stratified by the risk factors for failure listed below and again visualized using Kaplan–Meier curves for the various IOP cut-offs for complete and qualified success, with the log-rank test used to evaluate differences between strata.

Cox proportional hazard models were used to identify risk factors for surgical failure and other adverse events. Factors analyzed included type of glaucoma surgery, age, sex, eye, phakic status, previous laser trabeculoplasty, baseline BCVA, disease severity, ethnicity, elevated decision IOP, MMC dose, and diabetes diagnosis on both a univariable (crude) and multivariable (adjusted) basis. For type of glaucoma surgery and other included variables, effect modification was investigated by inspecting the appropriate Kaplan–Meier curves. In cases of significant effect modification, a Cox model was created stratified by the modifying variable. The Efron method was used to approximate data with equivalent failure intervals. There was assumed to be no competing risk factors that could have impacted data censoring. Collinearity was assessed by regression using a Condition Index threshold of >30. Martingale residuals were used to determine if the proportional hazards prerequisites were met for each variable. If this assumption was violated, it was addressed through either: (1) adding a time-variable interaction term, or (2) stratifying the model by the nonproportional variable. If the regression coefficient of the time-variable interaction term indicates it accounts for less than 1% of the change in hazard over time, the

time-variable interaction term was excluded from the final model. As some patients had both eyes enrolled or came from different surgical sites, we accounted for this intracluster dependence using a frailty model with an approach popularized by Lee et al,[25] which estimates the regression parameters in the Cox model by maximum partial likelihood estimates under an independent working assumption and employs a robust sandwich covariance matrix estimate. In short, the random effects models had a nested structure by surgical site and then patient eye. Secondary categorical or continuous outcomes were analyzed with a general linear model on both a univariable and multivariable basis. A 2-sided P value of <.05 was considered statistically significant.

RESULTS

• **STUDY POPULATION AND BASELINE CHARACTERISTICS:** This study identified 691 eyes from 623 patients who underwent bleb-forming surgery between August 2015 and August 2020. Eyes ($n = 114$) that had less than 1-month of follow-up were excluded from the analysis. The final cohort included 577 eyes from 521 patients with a 91% follow-up rate over 1 year. The follow-up rate was 92.8% for SIBS microshunt eyes, 94.5% for gelatin 45 μm microstent eyes, and 83% for patients with trabeculectomy. Table 1 summarizes the baseline characteristics of the included patients, consisting of SIBS microshunt eyes ($n = 235$), gelatin 45 μm microstent eyes ($n = 201$), and trabeculectomy eyes ($n = 141$). The median (IQR) follow-up time was 14 (12.7-17.2) months for the entire cohort, 14.0 (12.9-17.1) months for SIBS microshunt eyes, 14.4 (12.6-18.5) months for gelatin 45 μm microstent eyes, and 13.8 (12.8-16.1) months for trabeculectomy eyes.

Patients who received SIBS microshunt had significantly lower baseline IOP and received lower dose of MMC than the gel stent or trabeculectomy patients. Patients who received the gelatin 45 μm microstent were more likely to be Caucasian and to take more glaucoma medications at baseline compared to the remainder of the cohort.

• **PRIMARY OUTCOME:** Complete surgical success at 1-year (Figure 1, B) defined as no IOP above 17 mm Hg or below 6 mm Hg (also with clinical hypotony) on 2 consecutive visits and a 20% reduction from the decision IOP was significantly higher ($P = .0002$) in SIBS microshunt eyes (68.8%) compared to gelatin 45 μm microstent eyes (46.2%) and trabeculectomy eyes (58.0%). Using the same success criteria and allowing for postoperative glaucoma medication use (qualified success, Figure 1, E), success rates of gelatin 45 μm microstent eyes (70.1%) were significantly lower ($P = .0002$) than that of SIBS microshunt eyes (89.7%) and trabeculectomy eyes (83.6%). Median (IQR) with 95% confidence interval (CI) time to failure (for complete success) was significantly longer ($P < .001$) for SIBS microshunt eyes compared to gelatin 45 μm microstent and trabeculectomy eyes (5.5 [4.2-8.2] months [$n = 68$] vs 2.8 [1.4-6.9] months [$n = 107$] and 2.8 [1.4-4.9] months [$n = 57$], respectively). No failures occurred due to clinical hypotony in any group.

• **SECONDARY IOP OUTCOMES:** Using an upper IOP cut-off of 14 mm Hg, complete success (Figure 1, A) was significantly higher ($P < .0001$) in SIBS microshunt eyes (65.3%) compared to gelatin 45 μm microstent eyes (40.1%) and trabeculectomy eyes (52.1%); and qualified success (Figure 1, D) was significantly lower ($P = .0002$) in gelatin 45 μm microstent eyes (67.3%) compared to SIBS microshunt eyes (87.9%) and trabeculectomy eyes (81.1%). With an upper cut-off of 21 mm Hg, complete success (Figure 1, C) was significantly higher ($P < .0001$) in SIBS microshunt eyes (69.3%) compared to gelatin 45 μm microstent (47.6%) and trabeculectomy eyes (60.3%); and qualified success (Figure 1, F) was significantly lower ($P < .0001$) in gelatin 45 μm microstent eyes (71.7%) compared to SIBS microshunt eyes (91.1%) and trabeculectomy eyes (86.8%). Complete and qualified success rates for all IOP cut-offs are summarized in Table 2.

• **CHARACTERISTICS ASSOCIATED WITH SURGICAL FAILURE:** For the Cox regression analysis identifying risk factors for failure (Figure 2), we used the 6 to 14 mm Hg IOP cut-off with ≥20% IOPR—as it was the strictest of the criteria and provided highest statistical power. In the adjusted multivariable analysis, procedures involving gelatin 45 μm microstent implantation (hazard ratio [HR] 2.0; 95% CI 1.5-2.7), trabeculectomy (HR 1.6; 95% CI 1.2-2.2), or less than 0.4 mg/mL intraoperative MMC concentration (HR 1.5; 95% CI 1.1-2.0) had a significantly higher risk of failure. Among these significant variables, intraoperative MMC concentration was impacted by substantial effect modification between surgery types. When stratified by surgery type, the HR for receiving less than 0.4 mg/mL intraoperative MMC was significant for SIBS microshunt eyes (HR 2.0; 95% CI 1.3-3.1) and nonsignificant for gelatin 45 μm microstent (HR 1.5; 95% CI 0.9-2.4) and trabeculectomy (HR 0.7; 95% CI 0.3-1.5) eyes. Previous trabeculoplasty, baseline BCVA > 0.4 logMAR, baseline IOP ≥ 21 mm Hg, age <70, diabetes, advanced disease, pseudophakia, gender, glaucoma type, and ethnicity all had insufficient evidence to support prognostic utility. No variables were impacted by collinearity.

• **IOP, MEDICATION USE, AND BCVA:** Figure 3 illustrates significant differences in median (IQR) IOP and medication at different follow-up points. Eyes receiving the gelatin 45 μm microstent had significantly higher median IOP at the 3-, 6- and 12-month follow-up compared to SIBS microshunt eyes ($P < .001$) and trabeculectomy eyes ($P < .01$). At 1-year, the median IOP was 12 (10-15) mm

TABLE 1. Baseline Characteristics

Demographic	SIBS, $N = 209$ (Eyes, $n = 235$)	Gelatin Microstent, $N = 187$ (Eyes, $n = 201$)	Trab, $N = 125$ (Eyes, $n = 141$)	*P* Value
Age, median (IQR), y	63 (54-73)	67 (56-77)	66 (58-74)	.01
>70 y, *n* (%)	67 (28.5%)	78 (38.8%)	56 (39.7%)	.03
Left eye, *n* (%)	117 (49.8%)	102 (50.8%)	76 (53.9%)	.74
Female, *n* (%)	93 (39.6%)	88 (43.8%)	68 (48.2%)	.25
Diabetes, *n* (%)	32 (13.6%)	44 (21.9%)	29 (20.6%)	.06
Ethnicity, *n* (%)				
White	136 (57.9%)	138 (68.7%)	77 (54.6%)	.02
Non-white	99 (42.1%)	63 (31.3%)	64 (45.4%)	
Vision				
Preop VA (logMAR), median (IQR)	0.18 (0.1-0.3)	0.18 (0.1-0.4)	0.18 (0.1-0.4)	.23
Preop BCVA ≥0.4 logMAR, *n* (%)	201 (85.5%)	159 (79.1%)	110 (78%)	.11
Glaucoma type and severity				
Decision IOP, median (IQR)[a]	20 (16.5-25)	22 (18-26)	22 (17-29)	.01
Medication classes, median (IQR)	3 (3-4)	4 (3-4)	3 (3-4)	.01
Cup-to-disk ratio, median (IQR)	0.85 (0.75-0.9)	0.85 (0.75-0.9)	0.9 (0.8-0.9)	.41
Preop MD, median (IQR), dB	−12.2 (−20.8 to −5.3)	−12.4 (−20.7 to −5.3)	−13.4 (−20.9 to −6.9)	.55
Disease type				
POAG, *n* (%)	164 (69.8%)	135 (67.2%)	87 (61.7%)	.27
PXG, *n* (%)	11 (4.7%)	24 (11.9%)	16 (11.3%)	.01
Other OAG, *n* (%)	45 (19.1%)	33 (16.4%)	27 (19.1%)	.60
ACG, *n* (%)	1 (0.4%)	4 (2%)	2 (1.4%)	.32
NTG, *n* (%)	12 (5.1%)	3 (1.5%)	9 (6.4%)	.05
OHT, *n* (%)	2 (0.9%)	2 (1%)	0	.51
Disease severity, *n* (%)[b]				
Mild	48 (20.4%)	48 (23.9%)	24 (17%)	.30
Moderate	54 (23%)	41 (20.4%)	37 (26.2%)	.45
Advanced	133 (56.6%)	112 (55.7%)	80 (56.7%)	.98
Previous ocular laser/surgery, *n* (%)				
Trabeculotomy/microbypass, *n* (%)	19 (8.1%)	22 (10.9%)	9 (6.4%)	.31
Laser trabeculoplasty, *n* (%)	100 (42.6%)	102 (50.8%)	57 (40.4%)	.11
Previous cataract surgery, *n* (%)	109 (46.4%)	101 (50.3%)	62 (43.9%)	.49
MMC concentration, *n* (%)				
0.2 mg/mL	100 (42.6%)	45 (22.4%)	33 (23.4%)	.01
0.4 mg/mL	135 (57.5%)	156 (77.6%)	108 (76.6%)	.01

ACG = angle closure glaucoma; BCVA = best-corrected visual acuity; IOP = intraocular pressure; IQR = interquartile range; logMAR = logarithm of the minimum angle of resolution; MD = mean deviation; MMC = mitomycin C; NTG = normal tension glaucoma; OAG = open-angle glaucoma; OHT = ocular hypertension; POAG = primary open-angle glaucoma; PXG = pseudoexfoliation glaucoma; SIBS = poly(styrene-block-isobutylene-block-styrene; Trab = trabeculectomy; VA = visual acuity.

[a]IOP measured at the visit when the decision was made to proceed with surgery.

[b]Based on visual field mean deviation: mild = 0 dB to >−6 dB; moderate = −6 dB to >−12 dB; and advanced = −12 dB or worse.

Hg and the median medication use was 0 (0-1) for SIBS microshunt eyes; 14 (11-17) mm Hg and 0 (0-2) for gelatin 45 μm microstent procedures; and 13 (10-16) mm Hg and 0 (0-1) for trabeculectomy eyes, respectively (Figure 3). There was no significant difference between groups in median medication use at the 12-month follow-up point.

An individualized representation of patient IOP changes from the decision for surgical intervention to the first reported visit 1-year postoperatively is shown in Figure 4. At 1 year, a significantly greater proportion of SIBS microshunt eyes ($n = 169$, 72%) and trabeculectomy eyes ($n = 93$, 64%) were glaucoma medication free compared to gelatin 45 μm microstent eyes ($n = 104$, 50%). Of the SIBS microshunt eyes that achieved qualified success, at 1-year, 63 (27%) were on fewer medications than at the time the decision was made for surgery—19 (8%) were on the same, and 6 (3%) were on more. Of the gelatin 45 μm microstent eyes that achieved qualified success, 64 (31%) were on

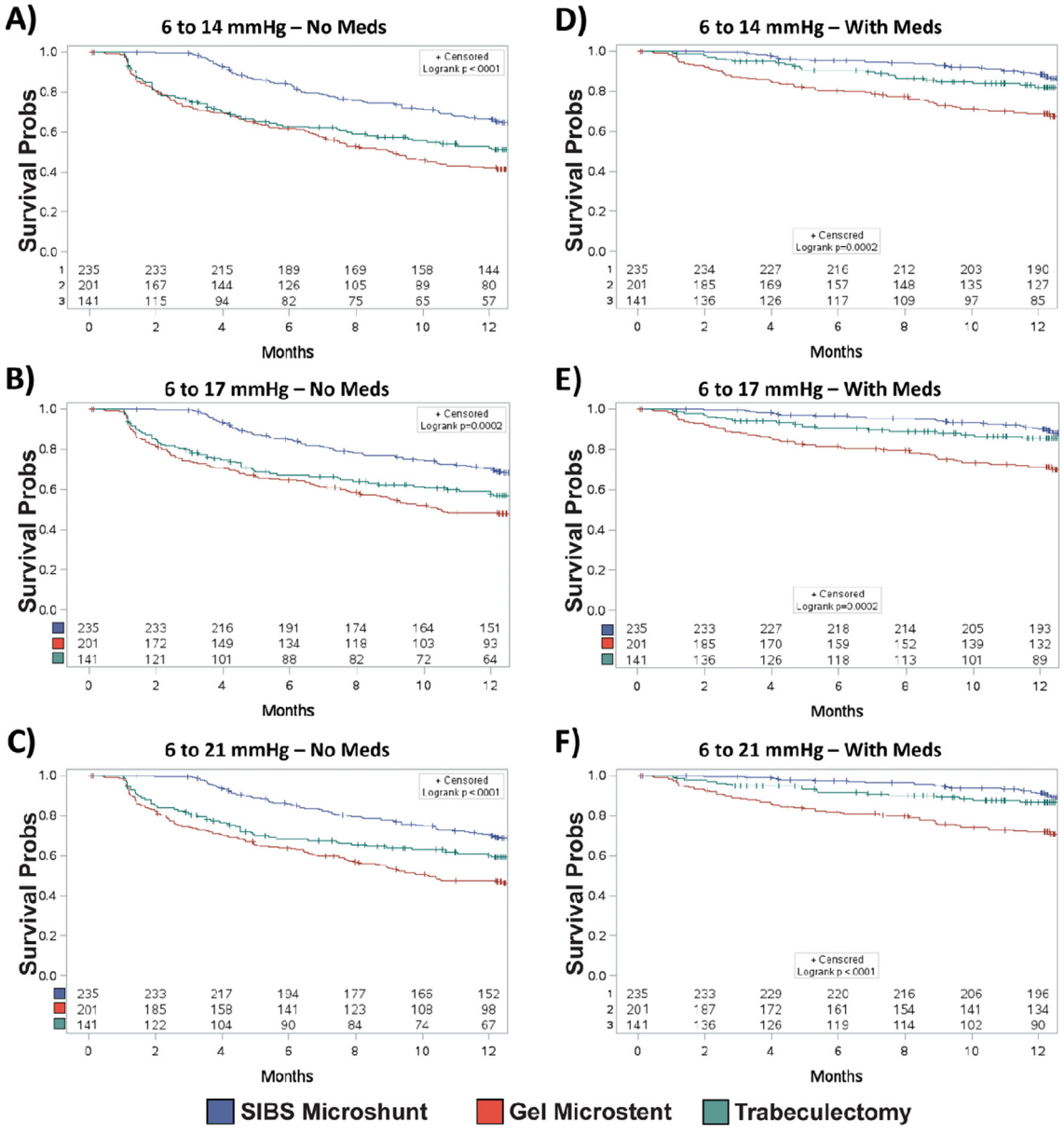

FIGURE 1. Kaplan–Meier survival curves for complete and qualified success through 12 months. (A-C) Kaplan–Meier survival curves for complete success defined as patients being medication free, achieving a ≥20% IOPR, and within one of the following IOP ranges: (A) 6-14 mm Hg, (B) 6-17 mm Hg, (C) 6-21 mm Hg. (D-F) Qualified success was defined as patients requiring medications to achieve a ≥20% IOPR and one of the following IOP ranges: (D) 6-14 mm Hg, (E) 6-17 mm Hg, (F) 6-21 mm Hg.

fewer medications, 27 (13%) were on the same, and 2 (1%) were on more. For trabeculectomy eyes, 31 (21%) were on fewer medications, 13 (9%) were on the same, and 4 (3%) were on more medications after 1-year follow-up.

BCVA at 12 months was significantly better ($P = .0016$) in SIBS microshunt eyes compared to the gelatin 45 μm microstent and trabeculectomy eyes (median [IQR] logMAR 0.18 [0.1-0.3] vs 0.3 [0.1-0.5] and 0.3 [0.1-0.5], respectively). The proportion of eyes losing greater than 2 lines of vision at last follow-up or reoperation was significantly lower ($P < .0001$) in SIBS microshunt eyes ($n = 35$, 15%) compared to gelatin 45 μm microstent ($n = 51$, 25%) or trabeculectomy eyes ($n = 42$, 30%).

• **COMPLICATIONS:** Transient hypotony (IOP < 6 mm Hg at any time) occurred significantly more often ($P < .0001$) in trabeculectomy eyes ($n = 81$, 57.4%) compared to SIBS microshunt ($n = 86$, 36.6%) or gelatin 45 μm microstent eyes ($n = 69$, 34.3%). Two hundred forty-four patients (46.8%) had a postoperative complication (Table 3).

TABLE 2. Success Rates With 20% IOPR

Complete	SIBS, $N = 209$ (Eyes, $n = 235$)	Gelatin Microstent, $N = 187$ (Eyes, $n = 201$)	Trab, $N = 125$ (Eyes, $n = 141$)	Log-Rank P Value
6-14	65.3%	40.1%	52.1%	<.0001
6-17	68.8%	46.2%	58.0%	.0002
6-21	69.3%	47.6%	60.3%	<.0001
Qualified				
6-14	87.9%	67.3%	81.1%	.0002
6-17	89.7%	70.1%	83.6%	.0002
6-21	91.1%	71.7%	86.8%	<.0001

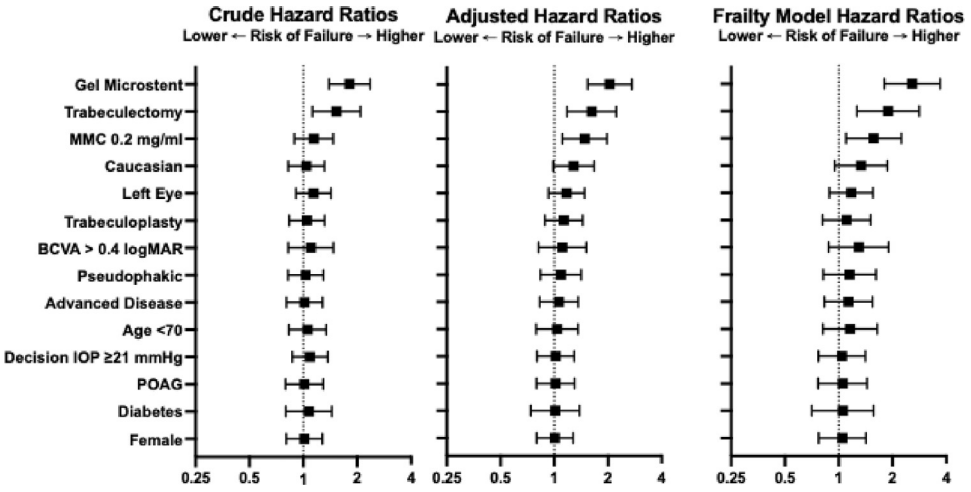

FIGURE 2. Crude and adjusted hazard ratios for surgical failure at 12-month follow-up. Shown are crude (Left), adjusted (Middle), and frailty model (Right) hazard ratios for the indicated risk factors, with 95% confidence intervals.

Eyes with SIBS microshunt had significantly fewer postoperative complications compared to gelatin 45 μm microstent or trabeculectomy (SIBS microshunt: 26.8% vs gelatin 45 μm microstent: 38.8% and trabeculectomy: 53.9%; $P < .001$). Serious complications occurred significantly more frequently ($P < .05$) in gelatin 45 μm microstent ($n = 10$, 5%) and trabeculectomy ($n = 6$, 4.3%) eyes compared to SIBS microshunt eyes ($n = 2$, 0.9%).

• **POSTOPERATIVE INTERVENTIONS:** Overall, 180 eyes (31%) received postoperative interventions (Table 4). Eyes receiving the SIBS microshunt were significantly less likely to experience postoperative interventions compared to gelatin 45 μm microstent or trabeculectomy (SIBS microshunt: 19.6% vs gelatin 45 μm microstent: 44.3% and trabeculectomy: 31.9%; $P < .001$). Needling rates were significantly lower ($P < .0001$) in SIBS microshunt eyes ($n = 29$, 12.3%) relative to both gelatin 45 μm microstent ($n = 60$, 29.9%) and trabeculectomy eyes ($n = 31$, 22%).

• **CHARACTERISTICS ASSOCIATED WITH RECEIVING NEEDLING:** Eyes receiving the gelatin 45 μm microstent (HR 2.3; 95% CI 1.4-3.6), trabeculectomy (HR 2.1; 95% CI 1.2-3.6), or having a baseline IOP ≥21 mm Hg (HR 3.91.6; 95% CI 1.1-2.3) were significantly associated with an increased risk of needling in the multivariable analysis. The median (IQR) time to needling was 3.5 (1.3-7.7) months for SIBS microshunt eyes, which was significantly longer ($P = .0002$) than for gelatin 45 μm microstent eyes (2.5 [1.3-5.9] months) and trabeculectomy eyes (2.1 [1.0-8.6] months). The median (IQR) IOP and medication use at the time of needling was 20 (18-27) mm Hg and 0 (0-2) classes for SIBS microshunt eyes, 22 (19-30) mm Hg and 0 (0-2) classes for gelatin 45 μm microstent eyes, and 23 (17-32) mm Hg and 0 (0-2) classes.

• **POSTOPERATIVE SURGICAL REVISIONS:** Overall, 54 (9.5%) eyes received a postoperative revision in the operating room. There were no significant differences in rates of postoperative revision between SIBS microshunt, gelatin

TABLE 3. Patients With Postoperative Complications

	Total, $N = 521$ ($n = 577$ Eyes)			*P* Value
	SIBS, $N = 209$ (Eyes, $n = 235$)	Gelatin Microstent, $N = 187$ (Eyes, $n = 201$)	Trab, $N = 125$ (Eyes, $n = 141$)	
Any complication	63 (26.8%)	78 (38.8%)	76 (53.9%)	.0001
Hyphema	22 (9.4%)	29 (14.4%)	13 (9.2%)	
Choroidal detachment	13 (5.5%)	17 (8.5%)	17 (12.1%)	
Tube touching iris	8 (3.4%)	6 (3%)	0	
Shallow AC	9 (3.8%)	10 (5%)	12 (8.5%)	
Leak/dehiscence	7 (3%)	4 (2%)	41 (29.1%)	
Binocular diplopia	3 (1.3%)	0	0	
Epithelial defect	4 (1.7%)	0	0	
Dellen	4 (1.7%)	1 (0.5%)	1 (0.7%)	
Blocked lumen/ostomy	2 (0.9%)	6 (3%)	2 (1.4%)	
Corneal edema	3 (1.3%)	0	1 (0.7%)	
Macular edema	2 (0.9%)	4 (2%)	1 (0.7%)	
Monocular diplopia	1 (0.4%)	0	0	
Iritis	1 (0.4%)	1 (0.5%)	1 (0.7%)	
Ptosis	1 (0.4%)	1 (0.5%)	0	
Iridocorneal touch	1 (0.4%)	0	2 (1.4%)	
Vitreous hemorrhage	1 (0.4%)	2 (1%)	0	
Serious complications	2 (0.9%)	10 (5%)	6 (4.3%)	.021
Hypotony maculopathy	1 (0.4%)	5 (2.5%)	2 (1.4%)	
No light perception	1 (0.4%)	0	0	
Malignant glaucoma	0	5 (2.5%)	2 (1.4%)	
Blebitis	0	0	1 (0.7%)	
Endophthalmitis	0	0	1 (0.7%)	
Other complications[a]	22 (9.4%)	41 (20.4%)	31 (22%)	.0006

AC = anterior chamber.
[a]PEE, blepharitis, blurred vision, chalazion, ERM, photopsia, floaters, pain, photophobia, PCO, ocular surface disease.

TABLE 4. Eyes With Postoperative Interventions

Intervention	SIBS, $N = 209$ (Eyes, $n = 235$)	Gelatin Microstent, $N = 187$ (Eyes, $n = 201$)	Trab, $N = 125$ (Eyes, $n = 141$)	*P* Value
Any intervention (exc. other)	46 (19.6%)	89 (44.3%)	45 (31.9%)	<.0001
AC reformation	16 (6.8%)	24 (11.9%)	15 (10.6%)	
AC tap	3 (1.3%)	16 (8%)	9 (6.4%)	
Suture removal/lysis	0	0	64 (45.4%)	
Laser tube occlusion	0	4 (2%)	0	
TpA into tube	0	2 (1%)	0	
Choroidal drainage	0	1 (0.5%)	0	
Needling	29 (12.3%)	60 (29.9%)	31 (22%)	<.0001
MMC injection	13 (5.5%)	10 (5%)	6 (4.3%)	
OVD injection	10 (4.2%)	0	1 (0.7%)	
5-FU injection	5 (2.1%)	28 (13.9%)	19 (13.5%)	
Other *(sub-conj. Avastin injection, subtenon's Kenalog injection, YAG capsulotomy)*	1 (0.4%)	1 (0.5%)	3 (2.1%)	

5-FU = 5-fluorouracil; 95% CI = ninety-five percent confidence interval; AC = anterior chamber; IOP = intraocular pressure; MMC = mitomycin C; OR = odds ratio; OVD = ophthalmic viscoelastic device; SIBS = poly(styrene-block-isobutylene-block-styrene; TpA = tissue-type plasminogen activator; Trab = trabeculectomy.

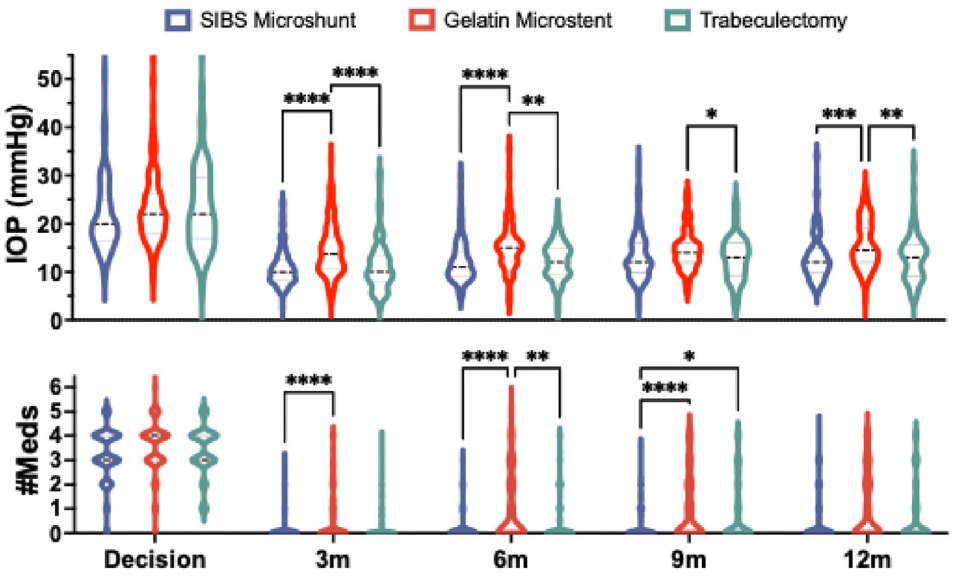

FIGURE 3. Violin plots with median and interquartile ranges of intraocular pressure and medication classes at the time the decision was made to undergo surgery and at the indicated follow-up visit. The depicted data were censored for patients with reoperations ($n = 14$). POM = postoperative month; POY = postoperative year. Width of the violin plots represents the proportion of patients at a given *y*-value within the indicated group at each follow-up visit.

45 μm microstent, or trabeculectomy eyes. In the SIBS microshunt group, 25 eyes (10.6%) experienced a revision at a mean (IQR) of 5.5 (2.1-9.7) months postoperatively. In the gelatin 45 μm microstent group, 17 eyes (8.5%) experienced a revision at a mean (IQR) of 2.1 (0.4-11.2) months postoperatively. In the trabeculectomy group, 12 eyes (8.5%) experienced a revision at a mean (IQR) of 1.2 (0.4-3.6) months postoperatively (Table 5).

• **REOPERATIONS FOR GLAUCOMA:** Fifty-two (9.1%) eyes received a reoperation for glaucoma. Eyes with a SIBS microshunt and trabeculectomy were significantly less likely to require a reoperation for glaucoma compared to eyes receiving gelatin 45 μm microstent (5.5% and 7.8%; vs 13.9%, $P < .001$).

DISCUSSION

This multicenter retrospective, interventional cohort study of consecutive patients is the largest to date comparing surgical outcomes in patients with open-angle glaucoma after SIBS microshunt implantation, gelatin 45 μm microstent implantation, or standard trabeculectomy. All procedures resulted in a significant reduction in IOP and medication use postoperatively; however, we observed differences between the three types of bleb-forming surgeries. The SIBS microshunt group achieved the highest success rates compared to the trabeculectomy or the gelatin 45 µm microstent groups. This superiority was also demonstrated across all IOP cut-offs for both complete and qualified success. Postoperative IOP was similar for SIBS microshunt and trabeculectomy. Eyes receiving the gelatin 45 µm microstent had lower success rate and significantly higher median IOP after 1-year follow-up compared to eyes receiving SIBS microshunt or trabeculectomy. However, no significant difference in medication requirements was observed at 1 year amongst the 3 procedures. Complications, postoperative interventions (including needling), and reoperations for glaucoma all occurred significantly more frequency after gelatin 45 µm microstent or trabeculectomy compared to the SIBS microshunt.

The cohort evaluated is multicenter and representative of a diverse patient population, and its composition approximates that of previously published cohorts.[14,17,19,26] There were some measured differences between the groups, which are worth noting. Patients were younger and received a lower concentration of MMC in the SIBS group vs other interventions. Young age and lower concentration of MMC have been associated with increased surgical failure.[6,27] Despite this, SIBS eyes had the lowest risk of failure amongst the groups. There was a significantly higher proportion of white patients in the gelatin 45 μm microstent group, with white ethnicity being associated with a lower risk of failure in previous studies.[28] However, this association was not observed in our study. Patients in the gelatin 45 μm microstent group were on significantly higher number of glaucoma

TABLE 5. Eyes With Postoperative Revisions and Reoperations

Procedure	SIBS, $N = 209$ (Eyes, $n = 235$)	Gelatin Microstent, $N = 187$ (Eyes, $n = 201$)	Trab, $N = 125$ (Eyes, $n = 141$)	*P* Value
Any revision	25 (10.6%)	17 (8.5%)	12 (8.5%)	.68
Ab externo bleb revision	24 (10.2%)	13 (6.5%)	11 (7.8%)	
Second bleb revision	1 (0.4%)	1 (0.5%)	5 (3.5%)	
Device repositioning	5 (2.1%)	5 (2.5%)	0	
Flap revision	N/A	N/A	5 (3.5%)	
Device exchange	9 (4.3%)	0	N/A	
Any reoperation	13 (5.5%)	28 (13.9%)	11 (7.8%)	.007
SIBS microshunt	0	2 (1%)	1 (0.7%)	
Tube shunts	10 (4.4%)	21 (10.5%)	8 (5.7%)	
Baerveldt implant	6 (2.6%)	11 (5.5%)	2 (1.4%)	
Ahmed glaucoma valve	2 (0.9%)	10 (5%)	6 (4.3%)	
Paul glaucoma valve	2 (0.9%)	0	0	
ECP/CPC	3 (1.3%)	4 (2%)	2 (1.4%)	
Trabeculectomy	0	1 (0.5%)	0	

95% CI = ninety-five percent confidence interval; CPC = cyclophotocoagulation; ECP = endocyclophotocoagulation; IOP = intraocular pressure; OR = odds ratio; SIBS = poly(styrene-block-isobutylene-block-styrene; Trab = trabeculectomy.

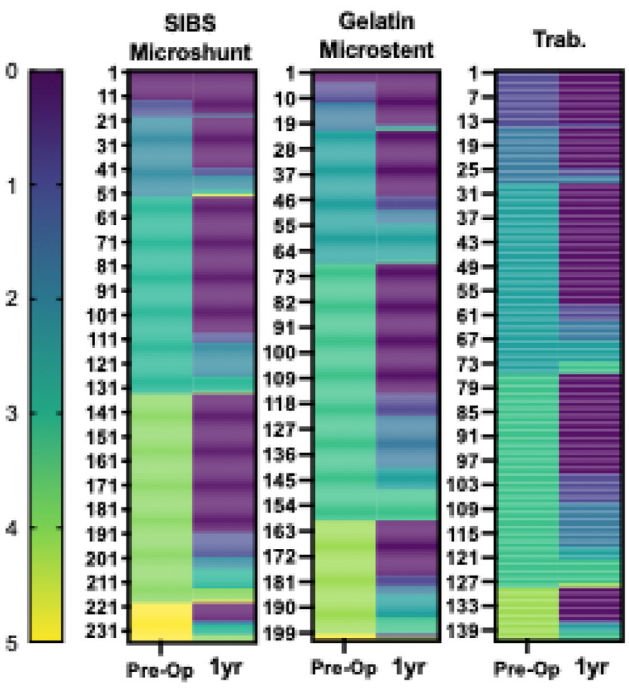

FIGURE 4. Heatmap representing the number of patients' eyes on 0 to 5 glaucoma medication classes at the time of surgical decision and at postoperative year 1.

medications (4 classes vs 3 classes) at baseline compared to other groups, which is known to be associated with increased risk of bleb failure.[29,30] This could be a confounder leading to the higher failure seen in the gelatin 45 μm microstent group. Importantly, there were no statistically significant differences in disease severity, gender, or diabetes status across all three groups. To control for potential confounders as best as possible, we reported adjusted HR, which did not materially change the relative success amongst the 3 study procedures.

The Cox proportional hazards model evaluated other risk factors for surgical failure. Three significant risk factors were identified. Receiving <0.4 mg/mL intraoperative MMC doses was associated with 1.5× the hazard relative to higher doses, which aligns with previous studies on SIBS microshunt.[31,32] When exploring the interaction between type of surgery and MMC dosage, we found that the effect of MMC was driven predominantly by the SIBS microshunt. For the gelatin 45 μm microstent, the MMC dose appeared less impactful on surgical success, though a larger sample size may have found a statistically significant positive impact. In the trabeculectomy group, the MMC dose seemed to have less influence on surgical outcomes. We postulate that single lumen micron implants draining to posterior thicker Tenons space may require a higher MMC dose compared with trabeculectomy and anterior filtration.[31] Several considerations are made when determining the appropriate dose of MMC, including surgeon's preference, patient age, Tenon anatomy, patient ethnicity, and bleb morphology, amongst others. A mega-analysis published by De Francesco et al, including 450 eyes, compared MMC concentration of 0.2 mg/mL and0.4 mg/mL in SIBS microshunt implantation. It found that patients receiving MMC 0.4 mg/mL were almost half as likely to experience surgical failure compared to the patients who received a lower dose. In addition, the MMC 0.4 mg/mL group also had higher success rates, lower

IOP, lower needling and surgical revision rates, and was not associated with increased complications.[33] These findings are consistent with the present study and reinforce the value of using higher MMC concentrations in MIBS procedures in reducing surgical failure. For trabeculectomy, MMC dosing impact is less certain and inconsistent in terms of success.

The presented results are similar to some previous studies, which suggest an increased efficacy of SIBS microshunt relative to the gelatin 45 μm microstent or trabeculectomy. Although it should be noted direct comparisons are often difficult to make as nonrandomized studies have different baseline patient characteristics, surgical techniques, site differences, varying success criteria, measured and unmeasured confounders, and different follow-up intervals. A small study by Scheres et al[17] comparing SIBS vs gelatin 45 μm microstent in 41 eyes used a similar IOP threshold and medication use success criterion without requiring a 20% reduction in IOP and included procedures combined with phacoemulsification. In their study, complete success in the SIBS microshunt group was 58% (lower than our reported 68.8%) compared to 49% in the gelatin 45 μm microstent group (comparable to our reported 46.2%). In contrast, a study by Wagner et al[16] comparing all three interventions in 105 eyes with a similar surgical success criterion (without a 20% reduction in IOP) showcased no statistically detectable differences between three groups, however, the short follow-up duration of 6 months and small sample size of 35 eyes in each group may have been insufficient to resolve any statistically significant differences between groups. They report surgical success rates for SIBS microshunt of 74.2% (higher than our reported 68.8%), for gelatin 45 μm microstent of 51.4% (higher than our reported rate of 46.2%), and for trabeculectomy of 73.5% (higher than our reported 58%).

In terms of the results compared to trabeculectomy, a recent prospective, randomized, noninferiority clinical trial comparing SIBS microshunt to trabeculectomy contradicts our results.[19] Their original definition of surgical success was *a* $\geq$20% reduction in IOP from baseline at 1 year, without increasing the number of glaucoma medications. In a post hoc analysis using criteria (6-17 mm Hg and 20% IOP reduction with no medications or reoperations) similar to our study, trabeculectomy had a higher surgical success (66.7% vs 53.9%; a 12.7% difference [95% CI: 3.0-22.5]) compared to the SIBS microshunt at 1-year follow-up. This discrepancy may stem from differences in methodology. Their study employed prespecified criteria for the reintroduction of glaucoma medications postoperatively. Furthermore, a low concentration of MMC (0.2 mg/mL) was used, which may be more impactful for MIBS procedures than trabeculectomy and has already proven to decrease the success rates of SIBS microshunt implantation.[33] In addition, most investigators had no previous experience with SIBS microshunt implantation technique and postsurgical management compared to trabeculectomy, which the authors acknowledged could explain the differential success rates favoring trabeculectomy reported compared to other published studies. Additionally, a potential randomization failure may have occurred as the SIBS microshunt group had a significantly higher proportion of African/Black patients, which is a patient population associated with a higher risk of bleb fibrosis and failure. In contrast, our surgical group collectively had extensive experience with the surgical and postsurgical management of SIBS microshunt. Taken together, these factors may explain the differences in surgical success observed between our study and that of Baker et al Further study is warranted.

A RCT comparing the gelatin 45 μm microstent to trabeculectomy found no statistically significant difference in success rates ($\geq$20% IOP reduction from baseline without medication increase) between the two groups (gelatin 45 μm microstent 62.1% vs trabeculectomy 68.2%, $P = .487$).[22] While trabeculectomy demonstrated a numerically lower failure rate and a lower mean IOP, the gelatin 45 µm microstent was associated with more favorable safety outcomes, including improved visual recovery and a lower incidence of hypotony. In contrast, our study found that the trabeculectomy group had statistically significantly higher success rates at all IOP cut-offs for both complete and qualified success, possibly because we had more stringent success criteria.

The lumen of the gelatin 45 μm microstent is significantly smaller than that of the 70 μm SIBS microshunt and thus higher resistance and lower pressure drop, comparatively at normal ranges of aqueous production.[34,35] This may limit its IOP-lowering potential compared to either the SIBS microshunt or trabeculectomy. More recently, the gelatin 63 μm microstent—a larger lumen device—has been commercialized, which may offer improved efficacy in lowering IOP. Indeed, Hussein et al[24] compared the gelatin 63 μm microstent with the 45 μm version and found higher success rates (59.5% vs 28.6%, $P = .009$) and significantly lower mean IOP (12.7 ± 4.8 vs 15.5 ± 5.1 mm Hg, $P = .001$) in the gelatin 63 μm group. However, our study did not compare the gelatin 63 μm microstent with other bleb procedures. A comparative trial using the gelatin 63 μm microstent instead of the 45 μm variant could yield different results, likely improving surgical success of the gelatin microstent. Additionally, surgeons have begun adopting new techniques for microstent placement, such as primary needling and opening the conjunctiva, which could lead to more predictable outcomes with better results than those observed in our analysis.[32,36]

Postoperative complications were significantly lower in the SIBS microshunt group compared to both the gelatin 45 μm microstent and trabeculectomy groups. These reported complication rates are in line with those reported by Baker et al[19] in their prospective study comparing SIBS microshunt vs trabeculectomy and those of Scheres et al[17] in a retrospective study comparing SIBS and gelatin 45 μm microstents. Similarly, in the RCT by Sheybani et al[22] com-

paring gelatin 45 μm microstent vs trabeculectomy, postoperative complications were more common in the trabeculectomy group, and the rates of hypotony (23.2% vs 50%) were twice as high in the trabeculectomy group compared to the gelatin 45 μm microstent. Our study also found the highest complication rates in the trabeculectomy group, including transient hypotony (trabeculectomy eyes 57.4% vs SIBS microshunt 36.6% vs gelatin 45 μm microstent 34.3%, $P < .0001$), bleb leaks, and wound dehiscence—29.1% in trabeculectomy compared to 3% in SIBS and 2% in gelatin 45 μm microstent eyes. The higher complication rates observed in the gelatin 45 μm microstent and trabeculectomy groups in our study may have been affected by the use of a higher concentration of MMC in those eyes compared to the SIBS microshunt group. As reported in previous studies, higher doses of MMC are associated with an increased risk of complications in glaucoma filtering surgery.[37,38]

Rates of postoperative interventions were significantly lower in the SIBS microshunt group compared to others (Table 3). Overall, our rate of postoperative interventions in the SIBS group (19.6%) were much lower than a recent prospective, randomized study comparing SIBS microshunt vs trabeculectomy with a 40.8% rate of intervention.[19] However, unlike our study, that study counted instances of the reintroduction of glaucoma medications postoperatively within the overall intervention count—when these instances are excluded the rate is brought in line with what is reported by our study. The most frequently performed intervention in the present study was needling, with similar rates reported in the literature previously for SIBS microshunt,[39] gelatin 45 μm microstent,[22,40] and trabeculectomy study groups.[41,42] Rates of needling in the SIBS group were significantly lower than gelatin 45 μm microstent or trabeculectomy eyes, and are corroborated by needling rates reported for trabeculectomies ranging from 8% to 30%[15,19,22] and for gelatin 45 μm microstent ranging from 23% to 43%.[15,22,40,42] Anterior chamber reformation and anterior chamber tap were relatively rare within the SIBS microshunt group—occurring in less than 7% of patients—and occurred at a significantly lower rate compared to gelatin 45 μm microstent or trabeculectomy eyes.

Overall, the rates of operating room revisions in our study were approximately 10% and did not differ significantly between study groups. The most common revision was *ab-externo* bleb revision across all groups. The rate of reoperation for glaucoma was found to be significantly lower in the SIBS microshunt and trabeculectomy groups. Previous literature supports a higher rate of reoperation for glaucoma after gelatin 45 μm microstent compared to the SIBS microshunt and trabeculectomy; Scheres et al[17] reported a 27% rate after gelatin 45 μm microstent compared to a 17% rate after SIBS microshunt, and Schlenker et al[15] reported a 10.3% rate after gelatin 45 μm microstent compared to 6% after trabeculectomy. However, variability in the definitions of "revision" and "reoperation" employed across studies presents a challenge to making direct interstudy comparisons.

Limitations of this study include its retrospective nature and the potential for selection bias—despite mitigation efforts through the collection of data from consecutive eyes. Many retrospective studies suffer from significant loss to follow-up, which may be differential and lead to biased conclusions. A relative strength of the present study was the low number of patients lost to follow-up, and most importantly, the rates were similar across study groups. Baseline characteristics were overall similar, although there were some differences, and of course, in any nonrandomized design, there are also unmeasured confounders which cannot be accounted for. However, the most striking potential confounders actually were hypothesized to negatively impact the efficacy of the SIBS microshunt group relative to the other groups, making the higher efficacy found for the SIBS microshunt more striking. Our multivariable analysis did not find significant confounding, as a further test of robustness. Finally, as IOP is an imperfect measure of glaucoma control,[42] structural and/or functional testing would ideally be utilized to better capture differential glaucoma progression rates after surgery as ultimately the most meaningful clinical outcome. However, defining surgical success in glaucoma studies will remain an ongoing challenge.[43] The absence of health economic calculations, such as quality-adjusted life years, prevents a direct and objective comparison of cost-effectiveness between all three groups.

Despite these limitations, we performed an inclusive and robust statistical analysis of the results of 3 bleb procedures, with similar baseline characteristics, a thorough analysis of confounders, and a multicenter large sample size with excellent follow-up rates. Unlike other comparative studies, we did not include combined procedure with cataract surgery, which can be another complicated factor. This study provides important new information on differences between bleb-forming surgeries, which may be generalizable.

In conclusion, all three interventions we studied lowered IOP and medication use significantly. We found higher clinical efficacy of SIBS microshunt vs gelatin 45 μm microstent and trabeculectomy in achieving complete and qualified surgical success. SIBS microshunt also demonstrated a more favorable safety profile with fewer postoperative complications, interventions, and reoperations for glaucoma, which may lead to improved patient outcomes and lower healthcare cost utilization. Further randomized prospective trials would help to further evaluate these findings.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

James J. Armstrong: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ticiana De Francesco:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Henny J. Beckers:** Writing – review & editing, Visualization, Data curation. **Ingeborg Stalmans:** Writing – review & editing, Methodology, Data curation. **Antonio M. Fea:** Writing – review & editing, Methodology, Data curation. **Chelvin C.A. Sng:** Writing – review & editing, Methodology, Data curation. **Juan F. Batlle Sr:** Writing – review & editing, Methodology, Data curation. **Matthew B. Schlenker:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Iqbal Ike K. Ahmed:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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REFERENCES

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol*. 2006;90(3):262–267.
2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11):2081–2090.
3. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. *Br J Ophthalmol*. 2012;96:614–618.
4. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E. Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Arch Ophthalmol*. 2003;121(1):48–56.
5. Samples JR, Singh K, Lin SC, et al. Laser trabeculoplasty for open-angle glaucoma: a report by the American academy of ophthalmology. *Ophthalmology*. 2011;118:2296–2302.
6. Jampel HD, Musch DC, Gillespie BW, Lichter PR, Wright MM, Guire KE. Collaborative Initial Glaucoma Treatment Study Group. Perioperative complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol*.. 2005;140:16–22.
7. Shah M. Micro-invasive glaucoma surgery – an interventional glaucoma revolution. *Eye and Vision*. 2019;6:1–5.
8. Saheb H, Ike I, Ahmed K. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol*. 2012;23:96–104.
9. Durr GM, Marolo P, Fea A, Ahmed IIK. Controversies in the use of MIGS. In: Sng CCA, Barton K, eds. *Minimally Invasive*

Glaucoma Surgery Springer Singapore; 2021:133–145. doi:10.1007/978-981-15-5632-6_10.
10. Abegao Pinto L, Sunaric Mégevand G, Stalmans I, et al. European Glaucoma Society – a guide on surgical innovation for glaucoma. *Br J Ophthalmol*. 2023;107(suppl 1):1–114 PMID: 38128960. doi:10.1136/bjophthalmol-2023-egsguidelines.
11. Do AT, Parikh H, Panarelli JF. Subconjunctival microinvasive glaucoma surgeries: an update on the Xen gel stent and the PreserFlo MicroShunt. *Curr Opin Ophthalmol*. 2020;31:132–138.
12. Chaudhary A, Salinas L, Guidotti J, Mermoud A, Mansouri K. XEN Gel Implant: a new surgical approach in glaucoma. *Expert Rev Med Devices*. 2018;15:47–59.
13. Pinchuk L, Riss I, Batlle JF, et al. The development of a micro-shunt made from poly(styrene-block-isobutylene-block-styrene) to treat glaucoma. *J Biomed Mater Res B: Appl Biomater*. 2017;105:211–221.
14. Theilig T, Rehak M, Busch C, Bormman C, Schargus M, Unterlauft JD. Comparing the efficacy of trabeculectomy and XEN gel microstent implantation for the treatment of primary open-angle glaucoma: a retrospective monocentric comparative cohort study. *Sci Rep*. 2020;10:1–11.
15. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Efficacy, safety, and risk factors for failure of standalone Ab Interno Gelatin microstent implantation versus standalone trabeculectomy. *Ophthalmology*. 2017;124:1579–1588.
16. Wagner FM, Schuster AK, Munder A, et al. Comparison of subconjunctival microinvasive glaucoma surgery and trabeculectomy. *Acta Ophthalmol*. 2022;100(5):e1120–e1126. doi:10.1111/aos.15042.
17. Scheres LMJ, Kujovic-Aleksov S, Ramdas WD, et al. XEN® Gel Stent compared to PRESERFLO™ MicroShunt implantation for primary open-angle glaucoma: two-year results. *Acta Ophthalmol*. 2021;99:e433–e440.
18. Pillunat KR, Herber R, Haase MA, Jamke M, Jasper CS, Pillunat LE. PRESERFLO™ MicroShunt versus trabeculectomy: first results on efficacy and safety. *Acta Ophthalmol*. 2022;100(3):e779–e790.
19. Baker ND, Barnebey HS, Moster MR, et al. INN005 Study Group. Ab-Externo MicroShunt versus Trabeculectomy in Primary Open-Angle Glaucoma: One-Year Results from a 2-Year Randomized, Multicenter Study. *Ophthalmology*. 2021;128(12):1710–1721.
20. Panarelli JF, Moster MR, Garcia-Feijoo J, et al. Ab-Externo MicroShunt versus trabeculectomy in primary open-angle glaucoma: two-year results from a randomized, multicenter study. *Ophthalmology*. 2024;131:266–276.
21. Nguyen AH, Fatehi N, Romero P, et al. Observational outcomes of initial trabeculectomy with mitomycin C in patients of African descent vs patients of European descent: five-year results. *JAMA Ophthalmol*. 2018;136:1106–1113.
22. Sheybani A, Vera V, Grover DS, et al. Gel stent versus trabeculectomy: the randomized, multicenter, gold-standard pathway study (GPS) of effectiveness and safety at 12 months. *Am J Ophthalmol*. 2023;252:306–325.
23. Schlenker MB, Durr GM, Michaelov E, Ahmed IIK. Intermediate outcomes of a novel standalone ab externo SIBS microshunt with mitomycin C. *Am J Ophthalmol*. 2020;215:141–153.
24. Hussein IM, De Francesco T, Ahmed IIK. Intermediate outcomes of the novel 63-μm gelatin microstent versus the conventional 45-μm gelatin microstent. *Ophthalmol Glaucoma*. 2023;6:580–591.
25. Lee EW, Wei LJ, Amato DA, Leurgans S. *Cox-type regression analysis for large numbers of small groups of correlated failure time observations. Surviv Anal State Art*. 1992:237e247.
26. Wagner FM, Schuster AK, Munder A, et al. Comparison of subconjunctival microinvasive glaucoma surgery and trabeculectomy. *Acta Ophthalmol*. 2021:1–7. doi:10.1111/aos.15042.
27. AGIS InvestigatorsThe Advanced Glaucoma Intervention Study (AGIS): 11. Risk factors for failure of trabeculectomy and argon laser trabeculoplasty. *Am J Ophthalmol*. 2002;134:481–498.
28. Landers J, Martin K, Sarkies N, Bourne R, Watson P. A twenty-year follow-up study of trabeculectomy: risk factors and outcomes. *Ophthalmology*. 2012;119:694–702.
29. Boimer C, Birt CM. Preservative exposure and surgical outcomes in glaucoma patients: the PESO study. *J Glaucoma*. 2013;22:730–735.
30. Kitazawa Y, Suemori-Matsushita H, Yamamoto T, Kawase K. Low-dose and high-dose mitomycin trabeculectomy as an initial surgery in primary open-angle glaucoma. *Ophthalmology*. 1993;100:1624–1628.
31. De Francesco T, Armstrong JJ, Hussein IM, Costa VP, Ahmed IIK. Mitomycin C 0.2 mg/ml vs. mitomycin C 0.4mg/ml during the implantation of an ab externo SIBS microshunt: a mega-analysis. *Ophthalmol Glaucoma*. 2024;7:454–465.
32. Kerr NM, Lim S, Simos M, Ward T. Primary needling of the ab interno gelatin microstent reduces postoperative needling and follow-up requirements. *Ophthalmol Glaucoma*. 2021;4(6):581–588 Epub 2021 Mar 8. PMID: 33705977. doi:10.1016/j.ogla.2021.02.004.
33. Lee JJ, Park KH, Youn DH. The effect of low-and high-dose adjunctive mitomycin C in trabeculectomy. *Korean J Ophthalmol*. 1996;10(1):42e47.
34. Pinchuk L, Riss I, Batlle JF, et al. The development of a micro-shunt made from poly(styrene-block-isobutylene-block-styrene) to treat glaucoma. *J Biomed Mater Res B: Appl Biomater*. 2017;105(1):211–221 Epub 2015 Sep 18. PMID: 26380916; PMCID: PMC5215625. doi:10.1002/jbm.b.33525.
35. Sheybani A, Reitsamer H, Ahmed II. Fluid dynamics of a novel micro-fistula implant for the surgical treatment of glaucoma. *Invest Ophthalmol Vis Sci*. 2015;56(8):4789–4795 PMID: 26218906. doi:10.1167/iovs.15-16625.
36. Do A, McGlumphy E, Shukla A, et al. Comparison of clinical outcomes with open versus closed conjunctiva implantation of the XEN45 gel stent. *Ophthalmol Glaucoma*. 2021;4(4):343–349. doi:10.1016/j.ogla.2020.12.003. Epub 2020 Dec 13. Erratum in: Ophthalmol Glaucoma. 2021 Nov-Dec;4(6):649. doi: 10.1016/j.ogla.2021.09.009. PMID: 33321200; PMCID: PMC8197767
37. Kitazawa Y, Suemori-Matsushita H, Yamamoto T, Kawase K. Low-dose and high-dose mitomycin trabeculectomy as an initial surgery in primary open-angle glaucoma. *Ophthalmology*. 1993;100(11):1624–1628.
38. Chen CW, Huang HT, Bair JS, Lee CC. Trabeculectomy with simultaneous topical application of mitomycin-C in refractory glaucoma. *J Ocul Pharmacol*. 1990;6(3):175e182.
39. Schlenker MB, Armstrong JJ, De Francesco T, Ahmed IIK. All consecutive ab externo SIBS microshunt implantations

with mitomycin C: one-year outcomes and risk factors for failure. *Am J Ophthalmol.* 2023;255:125–140 Epub 2023 Jun 22. PMID: 37352909. doi:10.1016/j.ajo.2023.06.009.
40. Reitsamer H, Sng C, Vera V, Lenzhofer M, Barton K, Stalmans IApex Study Group. Two-year results of a multicenter study of the ab interno gelatin implant in medically uncontrolled primary open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol.* 2019;257:983–996.
41. King AJ, Rotchford AP, Alwitry A, Moodie J. Frequency of bleb manipulations after trabeculectomy surgery. *Br J Ophthalmol.* 2007;91:873–877.
42. Grover DS, Flynn WJ, Bashford KP, et al. Performance and safety of a new Ab interno gelatin stent in refractory glaucoma at 12 months. *Am J Ophthalmol.* 2017;183:25–36.
43. Schlenker MB, Matt K, Vinay, et al. How Mean Intraocular Pressures Are Failing Patients. *Ophthalmol Glaucoma.* 2021;4(6):553–557.