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Original Article

Efficacy of ab-interno gelatin microstent implantation in primary and refractory glaucoma

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Objective: To evaluate the outcomes of ab interno gelatin microstent implantation alone and in combination with phacoemulsification for the reduction of intraocular pressure (IOP).

Design: Retrospective cohort study.

Participants: 141 eyes of 141 patients with any glaucoma subtype, including refractory glaucoma, operated in the Centre Hospitalier de l'Université de Montréal (CHUM) from 2015-2018. Patients were included if they were over 40 years of age and had a preoperative IOP of >18 mm Hg on maximum tolerated medical therapy.

Methods: All patients received ab-interno microstent implantation (XEN-45, Allergan, Madison, NJ) with mitomycin C +/- combined phacoemulsification. The primary outcome was complete surgical success (IOP 6-18 mm Hg and <20% reduction from baseline without IOP medications or reoperations or cyclophotocoagulation); secondary outcomes included qualified success allowing for medications, percentage reduction in mean IOP and medications, and reduction in number of complications, interventions, and reoperations.

Results: Mean follow-up was 30.5 ± 10.2 months (±SD). Mean IOP was 23.3 ± 7.0 mm Hg on 3.4 ± 0.8 medications at baseline and 13.3 ± 4.7 mm Hg on 1.9 ± 1.5 medications at 24 months of follow-up ($p < 0.001$). From 24-month survival analysis estimates, complete success was achieved in 34.1% of microstent eyes versus 20.7% with combined phacoemulsification ($p = 0.02$); 79.1% versus 75.1% achieved qualified success, respectively ($p = 0.86$). Cases with combined phacoemulsification had a higher rate of failure (hazard ratio [HR] = 1.6, 95% CI 1.1−2.3, $p = 0.02$). Needling with mitomycin-C or 5-fluorouracil postoperatively occurred in 54 eyes (38.3%). Complications included transient hypotony (10.6%), transient hyphema (6.4%), macular edema (4.3%), and microstent exposure (2.8%). There were 33 eyes (23.4%) with reoperations and 14 (9.9%) requiring subsequent cyclophotocoagulation lasers.

Conclusions: Microstent implantation required topical therapy in most cases 24 months following surgery in primary and refractory glaucoma and, when combined with phacoemulsification, had a higher risk of failure.

Objectif: Évaluer les résultats de l'implantation ab interno d'une micro-endoprothèse en gélatine seule ou en association avec la phacoémulsification, en vue de réduire la pression intraoculaire (PIO).

Nature: Étude de cohorte rétrospective.

Participants: Ont été inclus 141 yeux de 141 patients (peu importe le type de glaucome, y compris le glaucome réfractaire) qui ont fait l'objet d'une chirurgie au Centre hospitalier de l'Université de Montréal (CHUM) entre 2015 et 2018. Les patients ont été admis à l'étude s'ils avaient plus de 40 ans et si leur PIO préopératoire était > 18 mm Hg sous l'effet du traitement médicamenteux maximal toléré.

Méthodes: Tous les patients ont fait l'objet de l'implantation ab interno d'une micro-endoprothèse (XEN-45, Allergan, Madison, NJ) sous couvert de mitomycine C avec ou sans phacoémulsification. Le paramètre principal était la réussite chirurgicale complète (PIO : 6-18 mm Hg et baisse < 20 % par rapport aux valeurs de départ, sans prise de médicament permettant d'abaisser la PIO ni nouvelle intervention ou cyclophotocoagulation); au nombre des paramètres secondaires, mentionnons les suivants : succès mitigé s'accompagnant de la prise de médicaments, réduction en pourcentage de la PIO moyenne et du nombre de médicaments administrés, et baisse du nombre de complications, d'interventions et de nouvelles chirurgies.

Résultats: La durée moyenne du suivi a été de 30,5 ± 10,2 mois (± é.-t.). La PIO moyenne se chiffrait à 23,3 ± 7,0 mm Hg malgré la prise de 3,4 ± 0,8 médicaments au départ et à 13,3 ± 4,7 mm Hg malgré la prise de 1,9 ± 1,5 médicament lors du suivi à 24 mois ($p < 0,001$). Selon l'analyse de survie à 24 mois, on estime que 34,1 % des yeux qui ont reçu une micro-endoprothèse ont bénéficié d'une réussite complète, comparativement à 20,7 % pour le groupe avec phacoémulsification ($p = 0,02$); le succès a été mitigé dans 79,1 % des yeux qui ont reçu une micro-endoprothèse, comparativement à 75,1 % dans le groupe avec phacoémulsification ($p = 0,86$). Le taux d'échec a été plus élevé dans le groupe avec phacoémulsification (rapport de risque [RR] = 1,6; intervalle de confiance [IC] à 95 %: 1,1−2,3; $p = 0,02$). On a dû recourir à un aiguilletage de mitomycine C ou de 5-fluorouracil en période postopératoire dans 54 yeux (38,3 %). L'hypotonie transitoire (10,6 %), l'hyphéma transitoire (6,4 %), l'œdème maculaire (4,3 %) et l'extrusion de la micro-endoprothèse (2,8 %) comptaient au nombre des complications. On a dû opérer à nouveau 33 yeux (23,4 %), et 14 yeux (9,9 %) ont dû par la suite faire l'objet d'une cyclophotocoagulation au laser.

Conclusions: Dans la plupart des cas, l'implantation d'une micro-endoprothèse a dû être complétée d'un traitement topique dans les 24 mois suivant la chirurgie visant le traitement d'un glaucome primaire et réfractaire. Qui plus est, l'ajout d'une phacoémulsification s'accompagnait d'un risque plus élevé d'échec.

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Glaucoma is one of the leading causes of irreversible blindness in the world.[1] Reduction of intraocular pressure (IOP) is the only effective treatment to prevent disease progression and can be achieved through topical medications and laser and surgical therapies.[2] Trabeculectomy has been the standard of care for advanced glaucoma that progresses despite maximal medically tolerated therapy.[3] While effective at lowering IOP,[4] it is a surgery with notable complications, including choroidal effusions,[5] blebitis,[6] endophthalmitis,[7] and labile pressures in the early postoperative period.[8] An alternative approach is microinvasive glaucoma surgery (MIGS), novel surgical treatments to lower IOP for patients with mild to moderate glaucoma with a high safety profile.[9,10]

One example is the gelatin microstent (XEN-45, Allergan, Madison, NJ), a 6 mm biocompatible tube made of gelatin with a 45 μm lumen.[11] It decreases IOP by draining aqueous humour from the anterior chamber (AC) directly into the subconjunctival space and can be implanted via an ab interno approach with no dissection of the conjunctiva.[12] Previous studies suggest that it can effectively reduce IOP with a good safety profile in the first postoperative years.[13–15] Few studies have directly compared outcomes of combined phacoemulsification and microstent implantation with the microstent alone. Phacoemulsification has a lowering effect on IOP,[16] but combined phacoemulsification with bleb-based procedures such as trabeculectomy may have poorer long-term IOP reduction compared with trabeculectomy alone.[17] The gelatin microstent is a bleb-forming MIGS device, and the effect of combined phacoemulsification is not fully understood. This is the first study to evaluate the surgical outcomes of ab interno gelatin microstent implantation with and without phacoemulsification in Quebec.

Methods

This is a single-centre retrospective cohort study of consecutive patients who underwent gelatin microstent implantation with or without phacoemulsification from December 2015 to December 2018 by 3 experienced surgeons (H.S., Y.A., and F.L.) using a technique described in detail.[18] This study was approved by the Institutional Review Board of the University of Montreal Hospital Centre (CHUM), conforming to the principles of the Declaration of Helsinki.

The gelatin microstent was placed via an ab interno approach with subconjunctival injection of 0.2 mL of 0.2 mg/mL mitomycin C (MMC). Implantations occurred as standalone procedures (microstent) or in combination with phacoemulsification (phaco-microstent).

The procedure started with a temporal clear corneal main incision and a side-port incision. The AC was filled with viscoelastic, and the needle tip of the injector was inserted through the main incision across the AC and into the trabecular meshwork, advancing the needle through the trabecular meshwork, sclera, and Tenon's capsule into the superonasal quadrant. Once in the subconjunctival space, the gelatin microstent was deployed, the injector was removed, and the AC was flushed with balanced salt solution to remove viscoelastic and irrigate the stent, forming a subconjunctival bleb. In cases combined with phacoemulsification, cataract extraction and intraocular lens insertion were performed first, followed by implantation of the microstent.

Postoperative follow-up occurred at 1 day, 1 week, 1 month, and then every 6 months afterward. IOP was determined at baseline and at each postoperative visit using Goldmann applanation tonometry. Patients were started on topical steroids (prednisolone acetate 1%, every 2 hours and tapered qid, tid, bid, and qd weekly) and topical antibiotics (moxifloxacin). IOP-lowering medications were discontinued after surgery and restarted if IOP increased above target. Needlings and subconjunctival antifibrotics (MMC and 5-fluorouracil [5-FU]) were administered in the postoperative period if the surgeon noted increased vascularity or fibrosis with or without increased IOP.

Data collection

Charts were reviewed by 2 independent reviewers, and deidentified data were inputted into a database. Patients were included if they were over 40 years of age with any glaucoma subtype, a preoperative IOP of >18 mm Hg on maximum tolerated medical therapy, and underwent ab interno gelatin microstent implantation with MMC. Exclusion criteria were less than 1 year of follow-up and combined corneal-retinal surgery. If a patient underwent a second microstent implantation in the fellow eye, only the first eye was included.

The primary outcome was complete surgical success, defined as maintaining IOP of 6−18 mm Hg and ≥20% reduction from baseline on no IOP-lowering medications and no vision-threatening complications or subsequent glaucoma surgery or cyclophotocoagulation (CPC).[19] If the IOP was outside the target range, including hypotony, for more than 2 consecutive visits despite in-clinic maneuvers, the surgery was considered failed. Qualified surgical success included the same IOP threshold allowing for IOP-lowering medications. Preoperative risk factors for complete surgical success were assessed. Complication, intervention, and reoperation rates also were calculated and compared between microstent and phaco-microstent eyes. Complications were deemed transient if they resolved within 2 months with medical therapy and did not cause vision loss. Glaucoma severity was defined using visual field mean deviation values (mild: −6 to 0 dB; moderate: −12 to −6 dB; advanced: less than −12 dB).

Statistical analysis

Visual acuities of count fingers, hand motion, light perception (LP), and no LP were approximated as follows:

Table 1—Baseline characteristics of patients prior to microstent implantation

Characteristic	Microstent (n = 83)	Phaco + microstent (n = 58)
Demographics		
Age, y		
Median (IQR)	66.4 (59.4–74.5)	68.2 (61.1–74.4)
≤75, n (%)	63 (75.9%)	44 (75.9%)
>75, n (%)	20 (24.1%)	14 (24.1%)
Left eye, n (%)	46 (55.4%)	29 (50.0%)
Female, n (%)	41 (49.4%)	27 (46.6%)
Vision		
Preoperative visual acuity, median (IQR), logMAR	0.1 (0.0–0.3)	0.2 (0.1–0.3)
Lens status		
Phakic	29 (34.9%)	58 (100.0%)
Preoperative IOP		
Median (IQR), mm Hg	22.0 (18–30)	21.0 (18–26)
>21, n (%)	43 (51.8%)	28 (48.3%)
>30, n (%)	12 (14.5%)	7 (12.1%)
Preoperative medication classes		
Median (IQR)	3.0 (3.0–4.0)	4.0 (3.0–4.0)
Glaucoma type and severity		
Disease type, n (%)		
Primary open angle	51 (61.4%)	34 (58.6%)
Pseudoexfoliative	3 (3.6%)	0 (0.0%)
Primary angle closure	5 (6.0%)	4 (6.9%)
Combined mechanism	8 (9.6%)	5 (8.6%)
Pigment dispersion*	1 (1.2%)	6 (10.3%)
Uveitic	4 (4.8%)	2 (3.4%)
Angle recession	2 (2.4%)	0 (0.0%)
Normal tension	4 (4.8%)	7 (12.1%)
Neovascular	1 (1.2%)	0 (0.0%)
Other	4 (4.8%)	0 (0.0%)
Cup-to-disc ratio, median (IQR)	0.8 (0.7–0.9)	0.8 (0.7–0.9)
Preoperative mean deviation, median (IQR)	−10.0 (−4.3 to −16.7)	−6.8 (−1.4 to −16.0)
Disease severity, n (%)		
Mild	26 (31.3%)	27 (46.6%)
Moderate*	25 (30.1%)	9 (15.5%)
Advanced	32 (38.6%)	22 (37.9%)
Medical comorbidities		
Diabetes	11 (13.3%)	8 (13.8%)
Hypertension	11 (13.3%)	15 (25.9%)
Previous ocular laser/surgery		
Previous laser peripheral iridotomy, n (%)	10 (12.0%)	10 (17.2%)
Previous laser trabeculoplasty, n (%)*	35 (42.2%)	13 (22.4%)
Previous CPC micropulse, n (%)	7 (8.4%)	3 (5.2%)
Previous CPC G-Probe, n (%)*	7 (8.4%)	0 (0.0%)
Previous angle surgery, n (%)*	9 (10.8%)	1 (1.7%)
Previous trabeculectomy, n (%)	1 (1.2%)	0 (0.0%)
Previous tube shunt, n (%)	6.0 (7.2%)	1.0 (1.7%)
Surgeon learning stage		
Early (1–10 cases)	16.0 (19.3%)	8.0 (13.8%)
Middle (11–20 cases)	15.0 (18.1%)	11.0 (19.0%)
Late middle (21–30 cases)	13.0 (15.7%)	14.0 (24.1%)
Late (31+ cases)	39.0 (47.0%)	25.0 (43.1%)

IQR, interquartile range; IOP, intraocular pressure; CPC, cyclophotocoagulation.
*$p < 0.05$ microstent versus phaco + microstent group.

count fingers = 20/800; hand motion = 1/800; LP = 1/1600; no LP = 1/3200.[19] A mixed linear model was used to perform a 2-way repeated-measures analysis of variance to assess differences in IOP, medications, and visual acuity (VA) over time, comparing eyes with and without phacoemulsification, with a Bonferroni adjustment for multiple comparisons. Kaplan–Meier survival analyses were performed to assess postoperative surgical success. Univariate Cox regression analyses were used to determine preoperative risk factors for failure. To calculate differences in baseline characteristics and complications between groups, χ^2 and Fischer's exact tests were used. A p value of ≤0.05 was deemed statistically significant. All statistical analyses were conducted using SPSS version 22 (IBM, Armonk, NY).

Results

We included 141 consecutive eyes of 141 patients in the analysis. There were 58 cases (41.1%) combined with phacoemulsification. The mean ± SD follow-up for all eyes was 30.5 ± 10.2 months. Baseline characteristics are summarized in Table 1.

The majority of characteristics were equal between groups. The median (interquartile range [IQR]) age of all patients was 68.2 years (range, 61.1–74.4 years), and 48.2% of patients were female. There were 29 phakic eyes (34.9%) in the microstent group. The most common glaucoma subtype was primary open angle (POAG; n = 85, 60.3%) followed by primary angle closure (n = 13, 9.2%), and normal tension (n = 11, 7.8%). Median (IQR) visual acuity was 0.2 logMAR (range, 0.1–0.3 logMAR).

Patients had a median preoperative IOP of 22.0 mm Hg (range, 18.0–28.0 mm Hg; microstent: 22.0 mm Hg [range, 18.0–30.0 mm Hg]; phaco-microstent: 21.0 mm Hg [range, 18.0–26.0 mm Hg]) and were on 4.0 medications (range, 3.0–4.0 medications). There were more patients with moderate glaucoma in the microstent group (n = 25, 30.1% versus n = 9, 15.5%; χ^2 [1, N = 141] = 3.97; $p = 0.046$).

There were 8 patients (5.7%) with previous glaucoma surgery and 17 (12.1%) with previous CPC (micropulse n = 10, 7.1%; G-Probe n = 7, 5.0%; G-Probe Delivery Device, IRIDEX Corp, Mountain View, Calif.). There was no significant difference in previous glaucoma surgery between groups (χ^2 [1, N = 141] = 2.87; $p > 0.05$). However, there were more patients with previous laser trabeculoplasty (42.2% versus 22.4%), angle surgery (10.8% versus 1.7%), and G-Probe CPC (8.4% versus 0.0%) in the microstent group ($p < 0.05$).

Intraocular pressure, medication use, and visual outcomes

Mean IOP and medication use are demonstrated in Figure 1. In all eyes, mean IOP was 23.3 ± 7.0 mm Hg at baseline, 14.3 ± 5.1 mm Hg at 12 months, and 13.3 ± 4.7 mm Hg at 24 months ($p < 0.001$). This represented a 38.6% and 42.7% reduction in IOP from baseline, respectively. Mean medication use in all eyes was 3.4 ± 0.8 classes at baseline, 1.7 ± 1.5 classes at 1 year, and 1.9 ± 1.5 classes at 2 years ($p < 0.001$), a mean reduction in medication use by 1.7 and 1.5 classes, respectively ($p < 0.001$). More

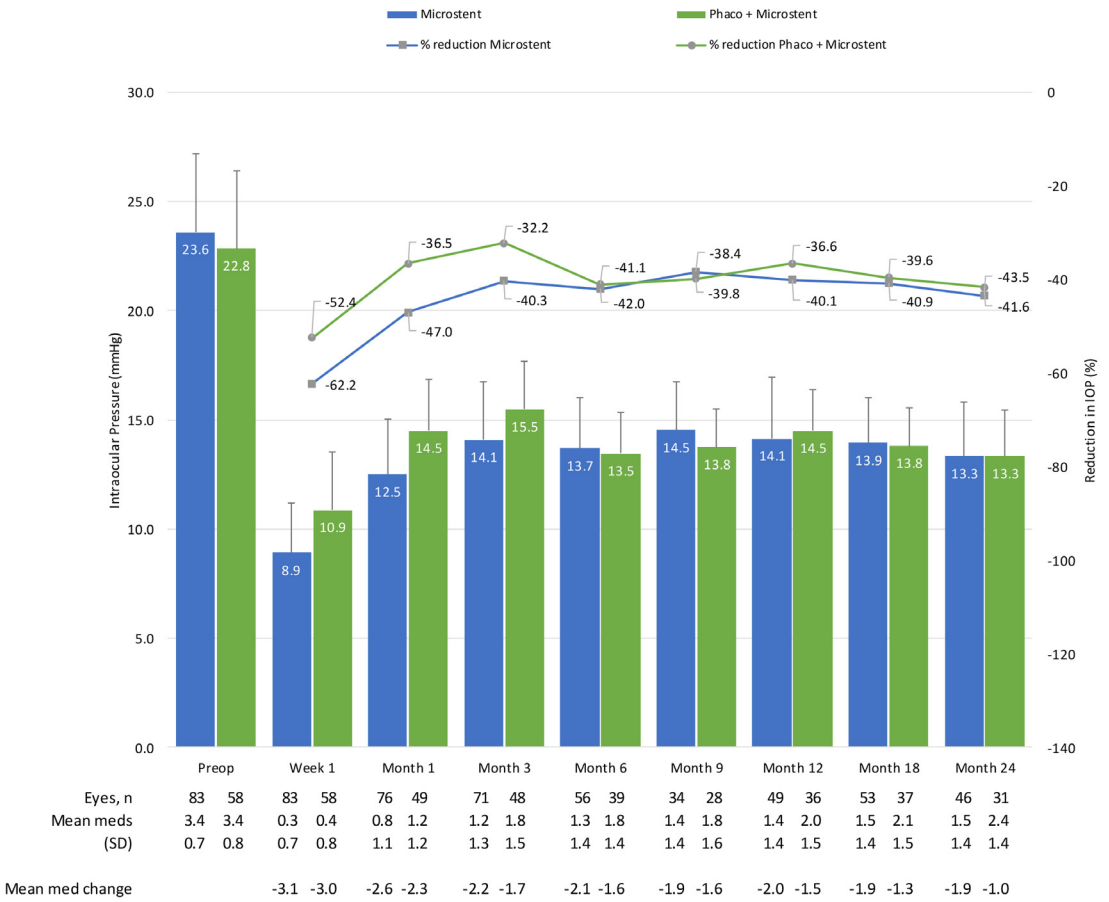

Fig. 1—Intraocular pressure (IOP) and medication use before and after gelatin microstent implantation. Bar graph of mean IOP in eyes with implant alone and combined implant with phacoemulsification. Lines represent percent reduction in mean IOP from baseline at each timepoint. Error bars = SD. IOP median/mean IOP and medications are significantly lower than baseline at all time points in each group ($p < 0.05$). There was no significant difference in IOP reduction between implant alone and cases combined with phacoemulsification.

Note: **Patients were excluded after having undergone repeated glaucoma surgery, which resulted in a lower (n) in later timepoints.**

medications were used in the phaco-microstent group than in the microstent group ($p < 0.001$), most importantly at 24 months (1.5 versus 2.4 classes, $p < 0.005$). There was no difference in IOP between groups ($p = 0.22$).

Mean visual acuity improved from 0.3 ± 0.04 logMAR at baseline to 0.14 ± 0.06 logMAR at 24 months in the phaco-microstent group. There was no significant change in visual acuity over time for the microstent group ($p > 0.05$). Visual acuity was improved in the phaco-microstent group compared with the microstent alone group at 24 months (0.14 ± 0.06 logMAR versus 0.3 ± 0.05 logMAR, $p = 0.03$).

Survival analysis and risk factors for failure

Complete and qualified surgical success over time is demonstrated in Figure 2. From 24-month survival analysis estimates, 34.1% of microstent eyes maintained complete success versus 20.7% of eyes with combined phacoemulsification ($p = 0.02$; Fig. 2A); 79.1% versus 75.1% maintained qualified success, respectively ($p = 0.86$; Fig. 2C). At 24 months, 33.3% versus 20.7% of eyes maintained an IOP of 6–15 mm Hg without medication ($p = 0.03$; Fig. 2B); 65.1% versus 64.0% maintained an IOP of 6–15 mm Hg allowing medications, respectively ($p = 0.29$; Fig. 2D).

Cox regression analysis revealed an increased risk of failure in eyes combined with phacoemulsification versus microstent alone (Hazard ratio [HR] = 1.6, 95% CI 1.1–2.1, $p = 0.02$). A higher risk of failure also was found in eyes with normal-tension glaucoma compared with POAG (HR = 2.3, 95% CI 1.2–4.4, $p = 0.01$) and patients with diabetes (HR = 1.7, 95% CI 1.0–2.9, $p = 0.04$). Two of 3 patients with pseudoexfoliation required tube shunt implantation 1–2 years after microstent implantation. Other factors, such as age, sex, disease severity, previous glaucoma surgery, number of medications, preoperative IOP, and the surgeon's learning curve, did not have a statistically significant effect on surgical success (Table 2). There was a trend for pseudophakic status in the microstent group to have a lower rate of failure (HR = 0.7, 95% CI 0.4–1.1, $p = 0.13$).

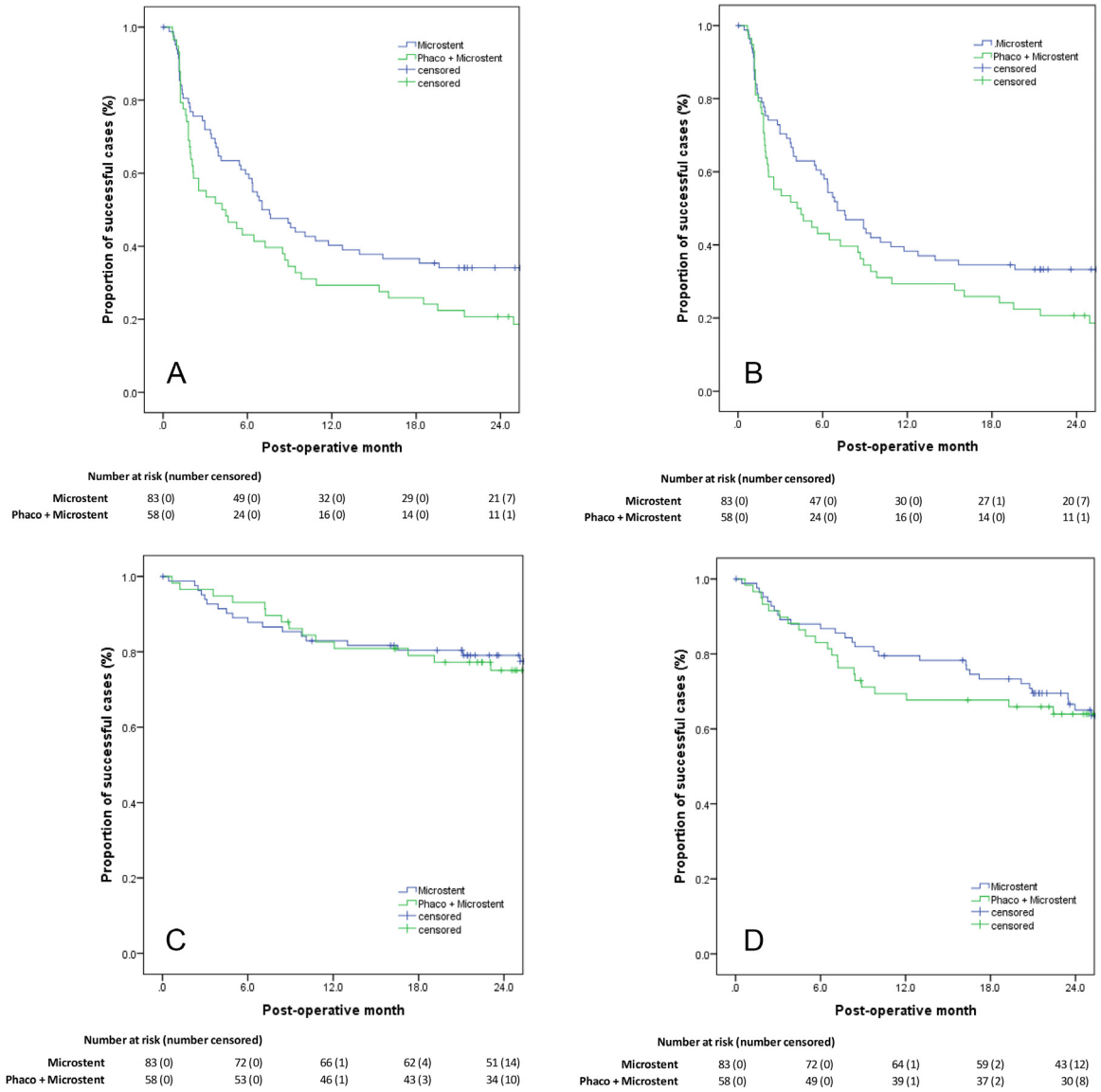

Fig. 2—Surgical success following gelatin microstent implantation. (A) Complete surgical success, defined as an intraocular pressure (IOP) of 6–18 mm Hg with a minimum 20% reduction in IOP from baseline and no medications. (B) IOP of 6–15 mm Hg with a minimum 20% reduction in IOP from baseline and no medications. (C) Qualified surgical success, defined as an IOP of 6–18 mm Hg with a minimum 20% reduction in IOP from baseline allowing for medications. (D) IOP of 6–15 mm Hg with a minimum 20% reduction in IOP from baseline and allowing for medications.

Complications, interventions, and reoperations

Cumulative incidences of early and late postoperative complications and interventions are summarized in Table 3. Most complications occurred during the first postoperative month. The most frequent were hypotony (microstent n = 13,15.7% versus phaco-microstent n = 1, 1.2%, $\varphi < 0.01$, $p < 0.01$) and hyphema (n = 6, 7.2% versus n = 2, 3.4%, $\varphi = 0.73$, $p > 0.05$), which occurred more frequently in eyes with the microstent alone and resolved within 1 month. In the microstent group, 8 eyes (57.1%) with hypotony were phakic. Hypotony maculopathy occurred in 4 eyes (2.8%) and caused persistent decreased vision despite normalization of pressure. There was no significant difference in other complications between groups. Stent exposure occurred in 2 eyes (1.4%) in the first month and 2 eyes (1.4%) afterward (n = 4, 2.8%). There was one stent blockage in the AC due to synechiae formation that cleared after YAG laser treatment and another with blood that cleared spontaneously. One stent broke after needling. Two stents migrated toward the conjunctiva and one toward the AC. One stent was repositioned with forceps at the slit lamp; the other required explantation and bleb revision. There were no other vision-threatening complications.

The most common intervention was needling of MMC or 5-FU, which occurred in 54 eyes (38.3%). Subconjunctival injection of MMC or 5-FU alone was performed in 36 eyes (25.5%). Most subconjunctival injections were in the first

Table 2—Preoperative features associated with failure after microstent implantation

Preoperative Factor	Interval	Hazard ratio	95% CI		*p* Value	n
			Lower	Upper		
Demographics						
>75 years of age	vs ≤75 years of age	1.1	0.7	1.7	0.67	34
Female	vs male	0.9	0.6	1.4	0.72	68
Left eye	vs right eye	1.1	0.8	1.6	0.58	75
Medical comorbidities						
Diabetes*	vs no diabetes	**1.7**	**1.0**	**2.9**	**0.04**	**19**
Hypertension	vs no hypertension	0.9	0.6	1.5	0.74	26
Combined with phacoemulsification	vs implant alone	**1.6**	**1.1**	**2.3**	**0.02**	**58**
Pseudophakic status	vs phakic (microstent group alone)	0.7	0.4	1.1	0.13	57
Disease severity						
Mild disease		0.8	0.5	1.2	0.20	53
Moderate disease		1.1	0.7	1.7	0.69	34
Advanced disease		1.2	0.8	1.8	0.34	54
Preoperative medications						
1 Medication class		2.1	0.5	8.5	0.30	2
2 Medication classes		0.9	0.5	1.9	0.86	10
3 Medication classes		0.8	0.6	1.2	0.37	54
4 Medication classes		1.2	0.8	1.8	0.30	73
Preoperative IOP >21 mm Hg	vs IOP <21	1.1	0.7	1.6	0.76	70
Preoperative IOP >30 mm Hg	vs IOP <30	1.1	0.6	2.0	0.68	19
Previous LPI	vs no LPI	0.7	0.4	1.3	0.30	20
Previous SLT	vs no SLT	0.8	0.5	1.2	0.24	48
Previous glaucoma surgery	vs primary surgery	1.2	0.7	2.2	0.51	15
Glaucoma subtype						
Pigment dispersion	vs primary open angle	1.1	0.5	2.4	0.79	7
Primary angle closure		0.8	0.4	1.6	0.52	9
Combined mechanism		1.2	0.5	2.9	0.62	13
Uveitic		0.8	0.3	2.6	0.71	6
Normal tension		**2.3**	**1.2**	**4.4**	**0.01**	**11**
Learning curve						
11–20 Cases	vs first 10 cases	0.6	0.3	1.2	0.14	26
21–30 Cases		0.9	0.5	1.8	0.85	27
31 Cases onward		1.0	0.6	1.7	0.95	64

IOP, intraocular pressure; LPI, laser peripheral iridotomy; SLT, Selective laser trabeculoplasty.
Bold value indicates statistical significance at $p < 0.05$.
*$p<0.05$

postoperative month (84.2%) and used 5-FU (93.8%; Table 3). Most needlings were performed after the first postoperative month (67.2%) and used MMC (94.9%). There was a higher rate of needling in eyes combined with phacoemulsification (microstent n = 26, 31.1% versus phaco-microstent n = 28, 48.3%; χ^2 [1, N = 141) = 4.2; $p = 0.04$). Most interventions were performed in the first postoperative month (Table 3). Stent repositioning was performed in 3 eyes (2.1%).

There were 35 additional glaucoma surgeries (24.8%) performed in 33 eyes (23.4%) (Table 4), including tube shunt (n = 28, 19.9%), trabeculectomy (n = 3, 2.1%), and repeat microstent implantation (n = 4, 2.8%). There were 9 eyes (6.4%) that underwent micropulse CPC and 5 (3.5%) that underwent G-Probe CPC. There was no difference in reoperation rate between groups ($p = 0.58$).

Discussion

In our cohort, implantation of a gelatin microstent decreased the mean IOP of all patients by 42.7% (23.3 mm Hg preoperatively to 13.3 mm Hg at 24 months) and decreased the mean number of glaucoma medications by 1.5 classes (3.4 classes preoperatively to 1.9 classes at 24 months). Our findings seem to be consistent with the available literature (Table 5).

Using the established definition of complete surgical success, maintaining an IOP of 6–18 mm Hg and ≥20% reduction from baseline on no IOP-lowering medications,[19] there was increased failure of microstent implantation when combined with phacoemulsification. This effect was also seen in other retrospective[20] and prospective studies.[29] This is likely due to the implant creating a subconjunctival drainage pathway, much like a trabeculectomy. There is evidence suggesting that combined phacoemulsification with trabeculectomy may have poorer long term IOP reduction than trabeculectomy alone,[17] despite having similar IOP reduction in the short term.[30,31] This could be explained by the longer duration of AC inflammation after cataract extraction compared with trabeculectomy,[32] and the release of such inflammatory mediators may stimulate bleb fibrosis leading to failure. This is supported by a higher rate of needling in eyes with combined phacoemulsification in our cohort.

Phacoemulsification alone reduces IOP by a variety of mechanisms, including widening of the iridocorneal angle,[33] biochemical changes of the trabecular meshwork,[34] and increased aqueous humour outflow due to changes in the uveal tract.[35] A meta-analysis showed that phacoemulsification alone decreases IOP by 13% in patients with POAG.[16]

Table 3—Eyes with early (≤1 month) and late (>1 month) complications and interventions following microstent implantation

Complications	Early (≤1 month)				Late (>1 month)				Total			
	Microstent	Percent total (n = 83)	Phaco-microstent	Percent total (n = 58)	Microstent	Percent total (n = 83)	Phaco-microstent	Percent total (n = 58)	Microstent	Percent total (n = 83)	Phaco-microstent	Percent total (n = 58)
Hypotony	13	15.7%	1	1.7%	1	1.2%	0	0.0%	14‡	16.9%	1‡	1.7%
Hypotony maculopathy*	4	4.8%	0	0.0%	0	0.0%	0	0.0%	4	4.8%	0	0.0%
Hyphema	6	7.2%	2	3.4%	0	0.0%	1	1.7%	6	7.2%	3	5.2%
Choroidal detachment	4	4.8%	0	0.0%	0	0.0%	0	0.0%	4	4.8%	0	0.0%
Shallow AC	3	3.6%	0	0.0%	0	0.0%	0	0.0%	3	3.6%	0	0.0%
Seidel-positive bleb/suture leak	1	1.2%	0	0.0%	2	2.4%	1	1.7%	2	2.4%	1	1.7%
Macular edema	0	0.0%	0	0.0%	3	3.6%	3	5.2%	3	3.6%	3	5.2%
Dellen	0	0.0%	0	0.0%	1	1.2%	0	0.0%	1	1.2%	0	0.0%
Vitreous hemorrhage	1	1.2%	1	1.7%	0	0.0%	0	0.0%	1	1.2%	1	1.7%
Endophthalmitis	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Bullous keratopathy	0	0.0%	0	0.0%	1	1.2%	0	0.0%	1	1.2%	0	0.0%
Microstent-specific complications†												
Exposed Microstent	2	2.4%	0	0.0%	1	1.2%	1	1.7%	3	3.6%	1	1.7%
Other	3	3.6%	2	2.4%	2	2.4%	0	0.0%	5	6.0%	2	2.4%
Interventions												
Needling												
MMC	6	7.2%	8	13.8%	18	21.7%	19	32.8%	24§	28.9%	24§	41.4%
5-FU	1	1.2%	4	6.9%	1	1.2%	1	1.7%	2	2.4%	4	6.9%
Subconjunctival injection alone												
MMC	2	2.4%	0	0.0%	3	3.6%	1	1.7%	5	6.0%	1	1.7%
5-FU	14	16.9%	16	27.6%	1	1.2%	1	1.7%	14	16.9%	16	27.6%
Bleb revision	2	2.4%	1	1.7%	6	7.2%	8	13.8%	7	8.4%	9	15.5%
AC re-formation	5	6.0%	1	1.7%	0	0.0%	0	0.0%	5	6.0%	1	1.7%
AC tap	2	2.4%	3	5.2%	1	1.2%	1	1.7%	3	3.6%	4	6.9%
Stent reposition	3	3.6%	0	0.0%	1	1.2%	0	0.0%	3	3.6%	0	0.0%
Laser to stent	2	2.4%	0	0.0%	0	0.0%	0	0.0%	2	2.4%	0	0.0%
Stent explantation	1	1.2%	1	1.7%	1	1.2%	0	0.0%	2	2.4%	1	1.7%

AC, anterior chamber; MMC, mitomycin C; 5-FU, 5-fluorouracil.

Note: If an eye had multiple interventions in the late and early periods, this was counted as one eye in the total column. Thus total eyes may be less than the sum of early and late cases.

*Hypotony maculopathy was defined as decreased visual acuity due to hypotony that did not return to baseline after 3 months (baseline acuity ± 1 line).

†Other microstent complications: Early complications (≤1 month) in the microstent group included blocked stent (n = 1), migrated stent (n = 1), and synechiae formation around the stent (n = 1). Early complications in the phaco-microstent group included blocked stent (n = 1) and migrated stent (n = 1). There was 1 microstent that broke and 1 that migrated in the microstent group 1 month postoperatively.

‡$p < 0.001$.

§$p < 0.05$.

Table 4—Eyes with reoperations after microstent implantation

Reoperations	Microstent alone	Percent total	Phaco + microstent	Percent total	Total	Percent total
Baerveldt glaucoma device	12	14.5%	8	13.8%	20	14.2%
Micropulse CPC	5	6.0%	4	6.9%	9	6.4%
Ahmed glaucoma valve	3	3.6%	5	8.6%	8	5.7%
CPC	4	4.8%	1	1.7%	5	3.5%
Repeat gelatin stent implantation	2	2.4%	2	3.4%	4	2.8%
Trabeculectomy	1	1.2%	2	3.4%	3	2.1%
iStent	1	1.2%	0	0.0%	1	0.7%

CPC, cyclophotocoagulation.
Note: There were no significant differences in reoperations between groups.

Table 5—Review of large cohort studies using the ab-interno gelatin microstent

Author	Study details	Preoperative	12 months	Percentage reduction			
		IOP (mmHg)	Drops	IOP (mmHg)	Drops	IOP (%)	Drops (%)
Szigiato et al. (this study)	141 eyes (both solo and combined)	23.3	3.4	14.3	1.6	38.6	51.3
Reitsamer et al.[15]	202 eyes (both solo & combined)	21.4	2.7	14.9	0.9	29.3	66.7
Widder et al.[20]	261 eyes (both solo and combined)	24.3	2.6	16.8	0.2	30.9	92.3
Karimi et al.[21]	259 eyes (both solo and combined)	19.3	2.6	14.2	0.8	26.4	69.3
Heidingeret al.[14]	199 eyes (both solo and combined)	22.8	2.9	17.1	1.8	22.7	37.9
Hengerer et al.[22]	148 eyes (both solo and combined)	32.2	3.13	14.24	0.3	55.8	90.4
Smith[23]	68 eyes (both solo and combined)	22.1	2.9	14.8	1.1	33.0	62.1
Galal et al.[24]	13 eyes (both solo and combined)	16.0	1.9	12	0.3	25.0	84.2
Fea[25]	12 eyes (both solo and combined)	21.8	2.92	14.9	0.5	31.7	82.9
Grover[26]	65 eyes (only solo)	25.1	3.5	15.9	1.7	36.76	51.4
Tan[27]	39 eyes (only solo)	24.9	3.0	14.5	0.7	41.8	76. 7
Perez-Torregrosa[28]	30 eyes (only combined)	21.2	3.07	15.03	0.17	29.1	94.5
De Gregorio et al.[12]	41 eyes (only combined)	22.5	2.5	13.1	0.4	41.8	84.0

IOP, intraocular pressure.

Canal-based MIGS devices combined with cataract surgery benefit from this IOP-lowering effect.[36,37] However, it appears that bleb-based MIGS devices such as the XEN-45 may have a different outcome from canal-based MIGS when combined with phacoemulsification.

Appropriate needling of fibrosing blebs is a key to successful postoperative management. Our rates of needling were similar to those by Mansouri et al. (37%),[29] Galal et al. (30.7%),[24] and Widder et al. (34%).[20] Antimetabolites such as MMC and 5-FU both have been proven to reduce the scarring process in subconjunctival filtering surgeries,[38,39] with intraoperative MMC having greater lowering of IOP with a slightly better safety profile.[40]

The majority of complications in our cohort were transient and did not require intervention. Hypotony and hyphema were the most common complications and resolved spontaneously within 1 month. We hypothesize that there was less postoperative hypotony in eyes combined with phacoemulsification because of dispersive ophthalmic viscosurgical devices retained in the AC that may have reduced flow through the trabecular meshwork in the early postoperative period. Only cohesive ophthalmic viscosurgical devices were used in microstent cases without phacoemulsification, which were completely removed. The only sight-threatening complications observed during follow-up were 4 cases of hypotony maculopathy with decreased visual acuity despite normalization of pressure. We did not observe any case of endophthalmitis. This study did not directly compare the 2 surgical modalities, but the complication rates of trabeculectomy reported in the literature are higher, including hyphema (24.6%), bleb leak (17.6%), cataract progression (20.2%), and endophthalmitis (0.2%).[41]

Exposure of the microstent remains a long-term risk of the device. Four eyes (2.8%) were exposed during the first 2 years, and this stresses the importance of regular follow-up to avoid blebitis or endophthalmitis, considering that half of patients were minimally symptomatic despite their stent exposure. Repair can include sutured closure, removal of the microstent, and bleb revision with conjunctival pulldown, amniotic membrane, or scleral patch graft. Our reoperation rate (23.4%) is greater than those of other studies (6.0%–14.1%),[13,14,21,29] which may be explained by longer follow-up in our cohort.

Our study did not detect a significant increase in failure in a surgeon's first 10 cases compared with subsequent cases, which suggests a rapid learning curve. Notably, these were glaucoma surgeons with many years of experience in a variety of glaucoma surgeries including MIGS, skills that were similar to microstent implantation.[42]

Strengths and limitations

The retrospective study design increased selection bias and confounding factors, including a higher number of patients with previous CPC and angle surgery in the microstent-only group. To ensure adequate 2-year follow-up, we excluded patients with less than 1 year of follow-up from analysis (n = 6). A small proportion of the remaining patients did not attain 2 years of follow-up (n = 8 of 141) but should have minimal influence on the results. There

was no standardized protocol for postoperative management. It was at the ophthalmologist's discretion when to restart medications, perform needling/injection, or reoperate.

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Footnotes and Disclosure

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