Matched Cohort Study of Cataract Surgery With and Without Trabecular Microbypass Stent Implantation in Primary Angle-Closure Glaucoma

ALI SALIMI, MOHAMED ABU-NADA, AND PAUL HARASYMOWYCZ

• **PURPOSE:** **To compare 1-year outcomes of phacoemulsification alone (phaco-only) vs phacoemulsification with implantation of 2 trabecular microbypass stents (iStent or iStent *inject*; phaco-stent) in eyes with primary angle-closure glaucoma (PACG).**

• **DESIGN:** **Retrospective matched clinical cohort study.**

• **METHODS:** **PACG eyes that underwent phaco-only vs phaco-stent at a single ophthalmology center. Groups were matched for baseline intraocular pressure (IOP) and medication use with a tolerance of ±2 mm Hg and ±1 medication, respectively. Primary outcomes included postoperative change in the mean IOP and medications. One-year outcomes were assessed using generalized estimating equations corrected for baseline intergroup differences.**

• **RESULTS:** **One hundred fifty-eight eyes (79 per group) were included. At 1 year, IOP decreased by 13% (from 16.8 ± 3.1 mm Hg preoperatively) in the phaco-only group ($P < .001$) and by 27% (from 17.6 ± 3.2 mm Hg) in the phaco-stent group ($P < .001$). Medication use decreased by 11% (from 1.8 ± 1.3 medications preoperatively) in the phaco-only group ($P < .001$) and by 46% (from 2.2 ± 1.2 medications) in the phaco-stent group ($P < .001$). The phaco-stent group experienced significantly larger reductions in IOP and medications compared with the phaco-only group ($P < .001$). The incidence of IOP spikes was significantly greater in the phaco-only group (18%) compared with the phaco-stent group (4%; $P = .005$). Safety was favorable with few transient postoperative adverse events.**

• **CONCLUSION:** **The results of this study highlight that phacoemulsification with implantation of 2 trabecular microbypass stents is more effective and possibly more protective than phaco-only in PACG eyes, as evidenced by significantly larger IOP and medication reductions and smaller incidences of IOP spikes among the phaco-stent eyes. (Am J Ophthalmol 2021;224:310–320. © 2021 Elsevier Inc. All rights reserved.)**

GLAUCOMA IS THE LEADING CAUSE OF IRREVERSible blindness globally.[1,2] Although approximately three-quarters of glaucoma cases are open-angle glaucoma (OAG) and one-quarter are primary angle-closure glaucoma (PACG), the increased severity of PACG has resulted in near-equal numbers of patients becoming visually impaired from each type.[2] With elevated intraocular pressure (IOP) being the only modifiable risk factor, interventional treatments for PACG focus on widening the anterior chamber angle and reducing IOP. Traditionally this has been achieved with laser peripheral iridotomy,[3] and in recent years the EAGLE study has established cataract surgery as another viable (and possibly even more efficacious) option.[4] Because of the impact of post-phacoemulsification angle widening and reduction in total peripheral anterior synechiae (PAS), postoperative IOP reductions are frequently greater in PACG than in POAG.[5,6]

Despite the angle-widening effect of cataract extraction in PACG, eyes with chronic iridocorneal apposition and elevated IOP often have trabecular damage that cannot be rectified by simply widening the angle; this damage can result in persistently raised IOP even after cataract extraction.[7,8] In these eyes, a glaucoma procedure may be necessary to adequately and sustainably control IOP. Surgical options could include filtration procedures such as trabeculectomy or tube shunt, which result in substantial IOP reductions but also incur significant short- and long-term risks.[9–11] Another surgical option is one of a growing number of procedures in the microinvasive glaucoma surgery (MIGS) category. Over the past decade, MIGS procedures have played an increasing role in glaucoma treatment because of their ability to reduce IOP and medications while avoiding the risks of filtration surgery.[12] Although they do not typically yield the dramatic IOP reductions of filtration surgeries, for many patients, MIGS procedures may offer a more favorable benefit-to-risk profile than more invasive filtration surgeries.

AJO.com Supplemental Material available at AJO.com.

revised and Accepted for publication Dec 28, 2020.

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0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2020.12.032

The first MIGS implant approved by the U.S. Food and Drug Administration, the iStent trabecular microbypass (Glaukos Corp., San Clemente, California, USA), and the more recently introduced second-generation iStent *inject* trabecular microbypass stent (Glaukos Corp.) are indicated in patients with mild to moderate OAG. Both devices create a direct route from the anterior chamber to the Schlemm's canal for the aqueous humor to bypass the damaged trabecular meshwork. Importantly, stent implantation does not disrupt or destroy ocular structures and has consistently shown excellent efficacy and safety in various subtypes and severities of glaucoma, both with and without concomitant cataract surgery.[13–33]

Because of the aforementioned ability of phacoemulsification to lower IOP in PACG eyes, the presence of a control group in PACG studies is particularly important; this applies to studies of any surgical treatments (MIGS or otherwise) as well as to medical or laser procedures. To date, studies of MIGS devices in PACG populations have been relatively sparse. This is possibly because they are "off-label" for the angle-closure indication in most countries, and also because of the aforementioned general perception that phacoemulsification is adequate. To our knowledge, only 1 randomized controlled comparative study has examined outcomes after trabecular microbypass (iStent) with phacoemulsification vs phacoemulsification alone (phaco-only).[18] The study showed a significantly higher success rate in the iStent phacoemulsification group (87.5%) compared with the phaco-only group (43.8%); however, it had a relatively small sample size of 16 eyes per group. To address this gap in the published literature, the present analysis compared 1-year outcomes of phacoemulsification with or without goniosynechialysis (GSL) vs phacoemulsification with implantation of 2 trabecular microbypass stents (iStent or iStent *inject*; phaco-stent) with or without GSL in PACG eyes.

METHODS

• **STUDY DESIGN AND ELIGIBILITY CRITERIA:** This retrospective matched-cohort study compared the 1-year outcomes of phaco-stent to phaco-only in PACG eyes. Inclusion criteria consisted of eyes from patients >18 years of age; eyes with posterior trabecular meshwork not visible for ≥180 degrees on gonioscopy with or without PAS; glaucomatous damage evidenced on retinal nerve fiber layer (RNFL) imaging, ganglion cell analysis, or visual field; presence of cataracts; the need for reduction of IOP or glaucoma medications in that eye; and availability of ≥12 months of follow-up data. All eyes that met the above criteria and had undergone phacoemulsification cataract surgery between 2009 and 2019 at our ophthalmology center were included as part of the phaco-only group. Patients in the phaco-stent group were matched to those in the phaco-only group through an automated algorithm using the SPSS statistical package case-control matching (IBM Corp., Chicago, Illinois, USA).[34–36] Matching was performed according to the preoperative IOP with a tolerance of ±2 mm Hg and glaucoma medication use with a tolerance of ±1 medication. Exclusion criteria included patients with secondary forms of angle-closure, elevated episcleral venous pressure, and acute or chronic intraocular inflammation. The decision to implant iStent was made preoperatively by the surgeon based on a combination of factors, including achieving a lower target IOP and reducing medication burden to aid in compliance and ocular surface symptoms. All procedures were performed by the same surgeon, at a single ophthalmology center in Montreal, Quebec, Canada. The study was approved by the ethics committee of the Hôpital Maisonneuve-Rosemont (Montreal, Quebec, Canada) and all procedures were performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

• **SURGICAL TECHNIQUE:** All procedures were performed under topical anesthesia and sterile conditions. For those in the phaco-only group, standard phacoemulsification was performed through a temporal clear corneal incision, nasal GSL was performed if nasal PAS were present, and a foldable intraocular lens was successfully implanted in the posterior capsule of all eyes. For those in the phaco-stent group, the implantation of stents preceded the cataract surgery, as follows. Through a clear temporal clear incision and under the direct visualization of the angle using gonioscopy, GSL was performed nasally if PAS were present, and then 2 first- or second-generation trabecular microbypass stents (iStent or iStent *inject*) were inserted ab interno to the nasal trabecular meshwork, separated at least 2 clock hours apart. For a greater postoperative IOP reduction, the stents were placed close to the collector channel ostia (areas with greater trabecular meshwork pigmentation[37] or with evidence of focal blood reflux[38]), as previously described.[13,14]

The standard postoperative regimen consisted of oral acetazolamide (500 mg on the first evening), topical moxifloxacin ophthalmic solution 0.5% (3 times a day for 1 week), topical nepafenac ophthalmic suspension 0.1% (3 times a day for 1 month), and topical loteprednol etabonate 0.5% for 2 weeks (tapered from 4 times a day). Glaucoma medications were not routinely stopped postoperatively and were adjusted, on a case-by-case basis, at the surgeon's discretion according to the preoperative IOP, disease severity, tolerance of the eye drops, desired target IOP and the glaucoma medication used in the contralateral eye.

• **OUTCOME MEASURES AND DATA ANALYSIS:** Demographic, baseline clinical characteristics, and postoperative data at postoperative months 1, 3, 6, and 12 were extracted from patients' medical records. The efficacy measures included the change in mean IOP and glaucoma medication use at 1 year postoperatively. In addition, the following proportional analyses were performed for each group: eyes with IOP ≤18 mm Hg, IOP ≤15 mm Hg, and IOP ≤12 mm Hg; eyes with increase, maintenance, or reduction in their antiglaucoma medication use vs their preoperative regimen; and medication-free eyes. IOP was measured by the same surgeon using a calibrated Goldmann applanation tonometer, and antiglaucoma medication use was scored based on the number of active pharmacologic classes.[39–41]

Safety measures consisted of any intra- and postoperative adverse events, along with postoperative changes in best-corrected visual acuity (BCVA), cup-to-disc ratio (CDR), visual field mean deviation (VF MD), early postoperative IOP spikes (increased IOP by >10 mm Hg or 50% from baseline IOP[39,41]), and secondary glaucoma interventions or surgeries. BCVA scores were converted to logarithm of minimal angle of resolution (logMAR). Glaucoma severity was classified according to the Hodapp-Anderson-Parrish visual field criteria, with VF MD better than −6 dB classified as mild, between −6 to −12 dB classified as moderate, and worse than −12 dB classified as severe.[42]

The Shapiro-Wilk test verified the normality of the data. Baseline differences between groups' demographics and clinical characteristics were assessed using the independent Student *t* test (continuous variables with normal distribution), the Mann-Whitney *U* test (continuous variables without normal distribution), and the χ^2 test (categorical variables). The 1-year efficacy and safety outcomes were evaluated using generalized estimating equations with the group (phaco-only vs phaco-stent) being the between-subject factor and the model corrected for baseline variables that were different between the 2 groups. Effect of time (within-subject variable) evidenced the postoperative outcomes of each surgery separately, while the time–group interaction compared the outcomes of 2 groups. Additional analyses were performed including only 1 eye of each patient. For those with both eyes included, 1 eye was randomly selected for this supplementary analysis using Excel (Microsoft, Redmond, Washington, USA) to generate "1" or "2" randomly, in which "1" represented the right eye and "2" represented the left eye. All statistical analyses were performed using SPSS software (version 26.0; IBM Corp., Chicago, Illinois, USA) with α set at 0.05 for statistical significance.

RESULTS

• **DEMOGRAPHICS:** The study consisted of a total of 158 PACG eyes of 107 patients—79 eyes of 50 patients in the phaco-only group and 79 eyes of 57 patients in the phaco-stent group. Phacoemulsification with GSL accounted for 44 eyes (56%) among the phaco-only group and 41 eyes (52%) among the phaco-stent group, without any intergroup differences ($P = .63$) The average preoperative IOP was 16.8 ± 3.1 mmHg in the phaco-only group and 17.6 ± 3.2 mm Hg in the phaco-stent group ($P = .11$) and the mean number of glaucoma medications was 1.8 ± 1.3 and 2.2 ± 1.2 medications in each group ($P = .08$), respectively. The demographics and baseline clinical characteristics of each group are presented and compared in Table 1. History of laser peripheral iridotomy was the only baseline measure that was significantly different between the 2 groups, present among a larger proportion of phaco-only eyes (91%) compared with phaco-stent eyes (66%; $P < .001$). No significant differences were found in the remaining baseline demographic and clinical measures including age, sex, laterality, axial length, anterior chamber depth, presence of plateau iris configuration ("double-hump" appearance on indentation gonioscopy during preoperative examination), prevalence of significant baseline PAS requiring intraoperative GSL, gonioscopy (Shaffer grading), central corneal thickness, baseline IOP and glaucoma medication use, BCVA, CDR, visual field measures, RNFL thickness, and ganglion cell inner plexiform layer (GCIPL) thickness. In addition to the VF MD, the categorical distribution of glaucoma severity (mild, moderate, or severe) was not statistically different between the 2 groups ($P = .74$). The phaco-only group consisted of 56% mild, 25% moderate, and 19% severe glaucoma cases compared with the phaco-stent group which included 59% mild, 27% moderate, and 14% severe glaucoma cases. None of the eyes in either group had a history of acute primary angle-closure during the 6 months preceding the surgery.

• **EFFICACY:** Both cataract surgery as a standalone procedure and combined with implantation of trabecular microbypass stents led to significant reductions in IOP and glaucoma medication use at 1 year postoperatively (Table 2); however, compared with cataract surgery alone, concurrent implantation of trabecular microbypass stents with cataract surgery resulted in significantly greater reductions in both postoperative IOP ($P < .001$) and medication use ($P < .001$).

In the phaco-only group, average IOP significantly decreased by 2.2 mm Hg (13% relative reduction), from 16.8 ± 3.1 mm Hg preoperatively to 14.6 ± 2.5 at 1 year of follow-up ($P < .001$). This contrasts with the phaco-stent group, in which IOP decreased by 4.7 mm Hg (27% relative reduction), from 17.6 ± 3.2 mm Hg preoperatively to 12.9 ± 2.3 mm Hg at 1 year of follow-up ($P < .001$; Figure 1). Comparing the degree of IOP reduction between the 2 groups revealed a significantly larger IOP reduction in the phaco-stent group compared with the phaco-only group ($P < .001$; Table 2). According to the proportional analyses shown in Figure 2, compared with the phaco-only group a smaller proportion of eyes in the phaco-stent group had preoperative IOPs ≤18 mm Hg, ≤15 mm Hg, and ≤12 mm Hg; however, at 1 year of follow-up, a larger proportion

TABLE 1. Demographic and Preoperative Ocular Characteristics of Phaco-Only and Phaco-Stent Groups

Variable	Phaco-Only (n = 79)	Phaco-Stent (n = 79)	*P* Value
Age at time of surgery (y)	68.1 ± 11.2	69.2 ± 8.0	.45[a]
Sex (male:female), n (%)	27 (34):52 (66)	24 (30):55 (70)	.73[b]
Laterality (OD:OS), n (%)	40 (51):39 (49)	41 (52):38 (48)	1.00[b]
Previous laser peripheral iridotomy, n (%)	72 (91)	52 (66)	<.001[b]
Peripheral anterior synechiae requiring intraoperative goniosynechialysis, n (%)	44 (56)	41 (52)	.63[b]
Plateau iris, n (%)	24 (30)	25 (32)	.86[b]
Axial length (mm)	23.0 ± 0.8	23.2 ± 1.0	.16[a]
Anterior chamber depth (mm)	2.7 ± 0.4	2.7 ± 0.3	.60[a]
Gonioscopy (Shaffer grade)	1.5 ± 0.9	1.5 ± 0.8	.91[c]
Central corneal thickness (μm)	549.3 ± 32.6	546.6 ± 41.2	.65[a]
Intraocular pressure (mm Hg)	16.8 ± 3.1	17.6 ± 3.2	.11[a]
No. of glaucoma medications	1.8 ± 1.3	2.2 ± 1.2	.08[c]
Corrected distance visual acuity (logMAR)	0.29 ± 0.43	0.21 ± 0.19	.11[a]
Cup-to-disc ratio	0.66 ± 0.16	0.70 ± 0.13	.15[c]
Visual field, mean deviation (dB)	−7.3 ± 6.6	−5.9 ± 5.5	.15[a]
Visual field, pattern standard deviation (dB)	4.8 ± 2.5	4.7 ± 2.9	.39[c]
Retinal nerve fiber layer thickness (μm)	80.1 ± 16.9	75.6 ± 14.4	.08[a]
Ganglion cell and inner plexiform layer thickness (μm)	72.8 ± 11.4	70.1 ± 9.8	.12[a]

LogMAR = logarithm of minimal angle of resolution; OD = oculus dexter; OS = oculus sinister; phaco-only = phacoemulsification alone; phaco-stent = phacoemulsification with implantation of 2 trabecular microbypass stents.

Mean ± standard deviations are presented and statistically compared.

[a]Independent *t* test.

[b]χ^2 test.

[c]Mann-Whitney *U* test.

of eyes among the phaco-stent group achieved such IOPs in each category. More specifically, 97% of eyes in the phaco-stent group achieved IOP ≤18 mm Hg compared with 89% in the phaco-only group, 76% achieved IOP ≤15 mm Hg compared with 43% in the phaco-only group, and 24% achieved IOP ≤12 mm Hg compared with 16% in the phaco-only group.

In the phaco-only group, antiglaucoma medications significantly decreased by 11% from a mean of 1.8 ± 1.3 medications preoperatively to 1.6 ± 1.4 at 1 year of follow-up (*P* = .034; Figure 3). In the phaco-stent group, the use of antiglaucoma medications significantly decreased by 46% from 2.2 ± 1.2 medications preoperatively to 1.2 ± 1.0 at 1 year (*P* < .001; Figure 3). The degree of medication reduction was significantly greater in the phaco-stent group compared with the phaco-only group (*P* < .001; Table 2). The proportional analysis also echoed this finding; at 1 year postoperatively, glaucoma medications were maintained or reduced among 96% of the phaco-stent group compared with 81% in the phaco-only group (Figure 4). In other words, only 4% of the in the phaco-stent group experienced an increase in their glaucoma medication use at 1 year postoperatively, which contrasts with 19% in the phaco-only group (Figure 4). While preoperatively a larger proportion of phaco-only eyes were medication-free (13% compared with 8% in the phaco-stent group), at 1 year a greater proportion of eyes in the phaco-stent group were medication-free (37% compared with 27% in the phaco-only group; Figure 5).

• **SAFETY MEASUREMENTS:** All eyes successfully underwent phacoemulsification with or without implantation of 2 stents (either iStent or iStent *inject*). No evidence of intraoperative complications was noted. Postoperatively, BCVA improved significantly in both groups (*P* < .001) with no intergroup differences (*P* = .24). Within the first postoperative year, disease stability was maintained in each group with no significant differences between the 2 groups with regard to postoperative changes in CDR (*P* = .37), VF MD (*P* = .20), and the thickness of RNFL (*P* = .09) or GCIPL (*P* = .26; Table 2).

Postoperative adverse events were rare and transient without sight-threatening sequelae. Early postoperative IOP spikes occurred in 17 eyes (11%), the majority within the first postoperative day (n = 10 eyes) and the remaining within the first postoperative month (n = 7 eyes). Among these eyes, 6 underwent anterior chamber tap and the rest were managed medically. Intergroup analysis revealed that

TABLE 2. One-Year Outcomes in Efficacy and Safety Measures in Phaco-Only and Phaco-Stent Groups

Variable	Preoperative		12-Month Follow-Up	Postoperative Change	*P* Value
Intraocular pressure (mm Hg)					
Phaco-only (n = 79)	16.8 ± 3.1		14.6 ± 2.5	−2.2	<.001
Phaco-stent (n = 79)	17.6 ± 3.2		12.9 ± 2.3	−4.7	<.001
Group–time interaction		*P* < .001			
Glaucoma medications					
Phaco-only (n = 79)	1.8 ± 1.3		1.6 ± 1.4	−0.2	.034
Phaco-stent (n = 79)	2.2 ± 1.2		1.2 ± 1.0	−1.0	<.001
Group–time interaction		*P* < .001			
BCVA (logMAR)					
Phaco-only (n = 79)	0.29 ± 0.43		0.19 ± 0.40	−0.10	<.001
Phaco-stent (n = 79)	0.21 ± 0.19		0.06 ± 0.09	−0.15	<.001
Group–time interaction		*P* = .24			
Cup-to-disc ratio					
Phaco-only (n = 79)	0.66 ± 0.16		0.67 ± 0.16	0.01	.53
Phaco-stent (n = 79)	0.70 ± 0.13		0.70 ± 0.13	0.00	.51
Group–time interaction		*P* = .37			
VF MD (dB)					
Phaco-only (n = 62)	–6.3 ± -6.3		–6.4 ± 6.9	−0.1	.08
Phaco-stent (n = 69)	–5.7 ± 5.1		–5.8 ± 4.9	−0.1	.83
Group–time interaction		*P* = .20			
RNFL thickness (μm)					
Phaco-only (n = 69)	80.1 ± 16.9		78.6 ± 16.4	−1.5	.06
Phaco-stent (n = 79)	75.6 ± 14.4		75.7 ± 14.0	0.1	.86
Group–time interaction		*P* = .09			
GCIPL thickness (μm)					
Phaco-only (n = 69)	72.8 ± 11.4		72.5 ± 12.1	−0.3	.55
Phaco-stent (n = 79)	70.1 ± 9.8		70.4 ± 9.7	0.3	.26
Group–time interaction		*P* = .26			

BCVA = best-corrected visual acuity; GCIPL = ganglion cell and inner plexiform layer; logMAR = logarithm of minimal angle of resolution; phaco-only = phacoemulsification alone; phaco-stent = phacoemulsification with implantation of 2 trabecular microbypass stents; RNFL = retinal nerve fiber layer; VF MD = visual field mean deviation.

Mean ± standard deviations are presented and statistically compared using generalized estimating equations corrected for previous history of laser peripheral iridotomy.

the incidence of IOP spikes was significantly greater in the phaco-only group (14 eyes; 18% of the group) compared with the phaco-stent group (3 eyes; 4% of the group; $P =$ .005). Posterior capsular opacification was noted among 16 eyes (10%), 9 of which were in the phaco-only group and 7 in the phaco-stent group. Rebound iritis occurred in 4 eyes (3 in the phaco-only group and 1 in the phaco-stent group), all of which occurred within the first postoperative month and were managed with topical steroids. Stent-specific adverse events included the formation of PAS over the stents in 2 eyes, in 1 covering both stents and in the other covering only 1 of the 2 stents; both eyes had normal angle configuration (no plateau iris). In the phaco-only group, 1 eye underwent pars plana vitrectomy for aqueous misdirection syndrome at postoperative month 3. Notably, there were no incidences of iris trauma or prolapse, iridodialysis, persistent corneal edema or decompensation, hypotony, choroidal detachment, stent extrusion, myopic shift, or endophthalmitis.

Within the 1-year follow-up, 6 eyes (4%) underwent selective laser trabeculoplasty, half of which belonged to the phaco-only group and the other half to the phaco-stent group. Importantly, no eye needed to undergo incisional secondary glaucoma surgeries during the follow-up period.

• **SUPPLEMENTARY ANALYSES:** The eyes in the phaco-stent group received 2 trabecular microbypass stents of either the first-generation (iStent) or the second-generation (iStent *inject*) model. Thus, we compared the efficacy outcomes of iStent (n = 53) vs iStent *inject* (n = 26) within this group. IOP decreased from 17.6 ± 3.5 mm Hg preoperatively to 12.9 ± 2.4 mm Hg at 1 year of follow-up among eyes that received iStent and from 17.5 ± 2.7 mm Hg to 13.0 ± 2.3 mm Hg in those that received iStent *inject*.

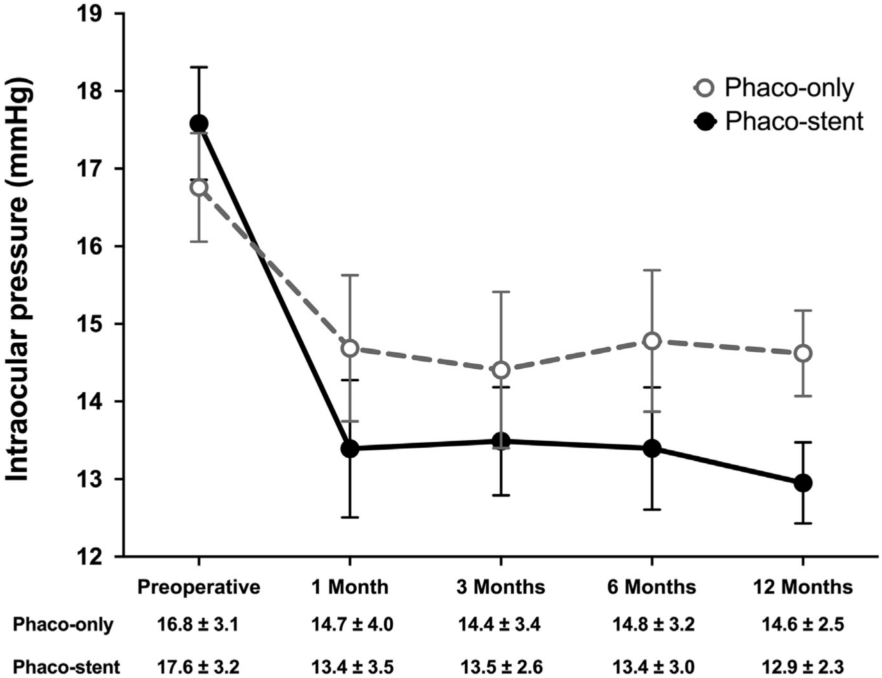

FIGURE 1. Postoperative change in intraocular pressure. At 1 year postoperatively, the average intraocular pressure significantly decreased in both groups ($P < .001$); however, the phacoemulsification with implantation of 2 trabecular microbypass stents (phaco-stent) group (solid black lines) experienced significantly larger reductions in intraocular pressure compared with the phacoemulsification alone (phaco-only) group (dotted gray lines; $P < .001$). Error bars represent 95% confidence intervals. Mean ± standard deviations are shown.

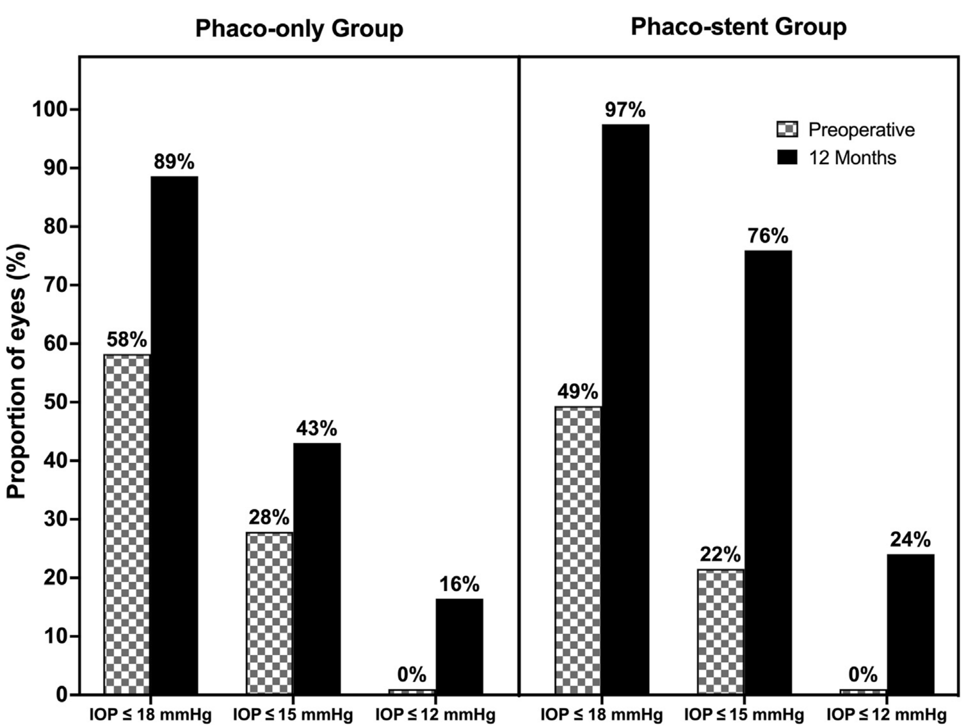

FIGURE 2. Percentages of eyes with intraocular pressure (IOP) ≤18, ≤15, and ≤12 mm Hg preoperatively (checked gray bars) and at 1 year postoperatively (solid black bars). The left and right panels represent the results of phacoemulsification alone (phaco-only) and phacoemulsification with implantation of 2 trabecular microbypass stents (phaco-stent) groups, respectively.

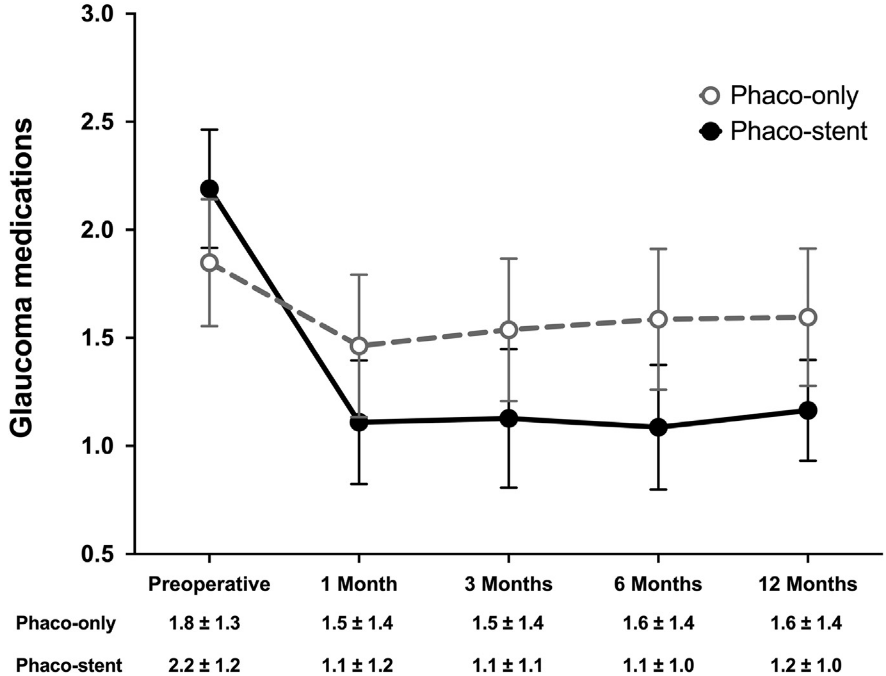

FIGURE 3. Postoperative change in the number of glaucoma medications. At 1 year postoperatively, the average number of glaucoma medications significantly decreased in both groups ($P < .001$); however, the phacoemulsification with implantation of 2 trabecular microbypass stents (phaco-stent) group (solid black lines) experienced significantly larger reductions in glaucoma medication use compared with the phacoemulsification alone (phaco-only) group (dotted gray lines; $P < .001$). Error bars represent 95% confidence intervals. Mean ± standard deviations are presented.

Antiglaucoma medication use decreased from 2.2 ± 1.2 medications to 1.1 ± 1.1 among iStent eyes and from 2.2 ± 1.3 medications to 1.3 ± 0.8 among iStent *inject* eyes. No differences were found between the eyes with iStent and iStent *inject* with respect to the degree of reductions in IOP ($P = .90$) and medication use ($P = .35$).

Given that both eyes of some patients (29 in the phaco-only group and 22 in the phaco-stent group) were included in the study, we performed supplementary analyses including only 1 eye of each patient, selected at random as described in the Methods section. A total of 50 eyes of 50 patients in the phaco-only group and 57 eyes of 57 patients in the phaco-stent group were included. The demographic and baseline clinical characteristics of the 2 groups are presented in Supplemental Table 1 (Supplemental Material available at AJO.com). The postoperative outcomes of this subanalysis were generally similar to those of the whole cohort and are presented in Supplemental Table 2. IOP significantly decreased in both groups ($P < .001$); however, the degree of reduction was significantly larger in the phaco-stent group (4.5 mm Hg) compared with the phaco-only group (2.0 mm Hg; $P < .001$). The use of antiglaucoma medications remained stable in the phaco-only group (0.2 medications reduced; $P = .16$) but significantly decreased in the phaco-stent group (1.0 medication reduced; $P < .001$). BCVA improved in both groups ($P < .001$), and no significant differences were observed between the 2 groups in terms of postoperative changes in CDR ($P = .52$), VF MD ($P = .59$), and the thickness of RNFL ($P = .35$) or GCIPL ($P = .63$) (Supplemental Table 2).

DISCUSSION

IN THIS STUDY, WE PRESENT A MATCHED-COHORT COMPARison of eyes undergoing phacoemulsification as a standalone procedure or with concomitant implantation of 2 trabecular microbypass stents (either 2 iStents or iStent *inject*) by a single surgeon at an academic ophthalmology center in Montreal, Quebec, Canada. To date, the iStent and iStent *inject* have been studied predominantly in eyes with POAG, with increasing numbers of reports in ocular hypertension, pseudoexfoliative glaucoma, normal tension glaucoma, and pigmentary glaucoma. However, the available data in PACG have been relatively sparse. The current study contributes some of the first data yet available of trabecular microbypass in PACG, and because of its inclusion of an equally sized phaco-only control group, the specific impact of stent implantation vs cataract extraction can be discerned. In addition, the cohort included a substantial portion of eyes with moderate and severe glaucoma—populations that are less commonly represented in MIGS studies.

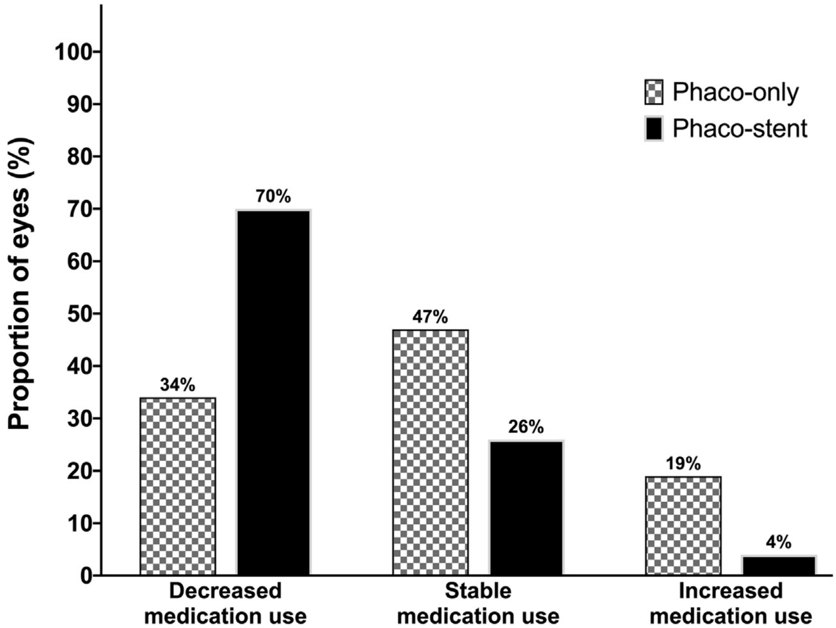

FIGURE 4. Percentage of eyes with decreased, stable, and increased glaucoma medication use at 1 year postoperatively. The checked gray bars and solid black bars represent phacoemulsification alone (phaco-only) and phacoemulsification with implantation of 2 trabecular microbypass stents (phaco-stent) groups, respectively.

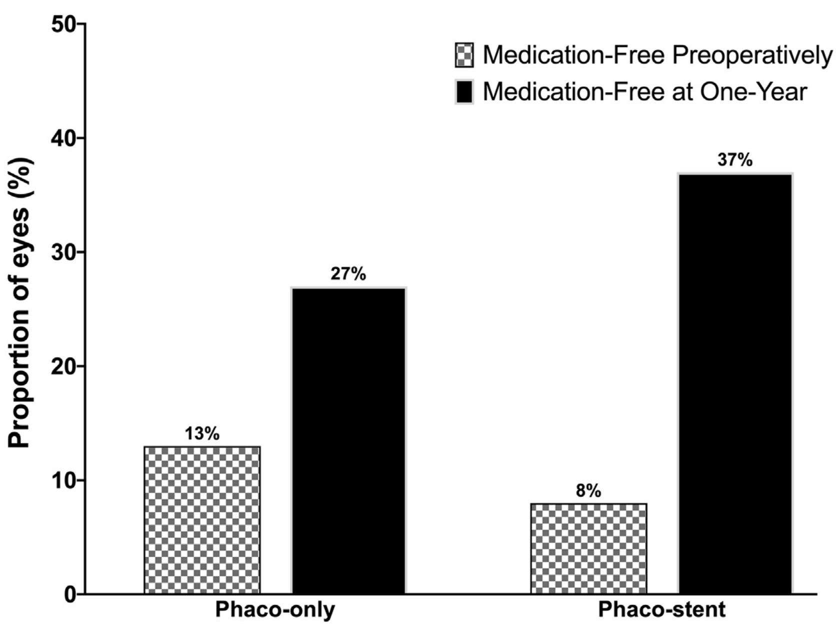

FIGURE 5. Percentage of medication-free eyes preoperatively and at 1 year postoperatively. The checked gray bars and solid black bars represent the preoperative and 1-year follow-up periods, respectively. Phaco-only = phacoemulsification alone; phaco-stent = phacoemulsification with implantation of 2 trabecular microbypass stents.

The angle-widening effect of phacoemulsification cataract extraction is well-documented[43–46]; the resultant IOP reductions are known to be greater in PACG than in POAG because of the impact of postphacoemulsification angle widening and reduction in total PAS.[5,6] To differentiate the IOP-lowering contribution of phacoemulsification vs that of glaucoma surgery, 2 previous randomized controlled studies evaluated combined phacoemulsification and trabeculectomy vs phaco-only. The data showed significant additional IOP and medication reductions in the combined phacoemulsification-trabeculectomy group, but also demonstrated some of the risks associated with filtration procedures.[8,47]

A number of real-world studies have included modest numbers of appositional ACG or patients with narrow-angle glaucoma in their overall cohorts.[13,25,28,29] However, sample sizes were not sufficient for subgroup analyses, and because of the absence of a phaco-only control group, it was not possible to distinguish the effect of stent implantation vs cataract extraction in these eyes. One retrospective cohort study[48] did include a control group, but all patients had combined-mechanism glaucoma (not ACG). To our knowledge, 1 study to date has evaluated iStent implantation plus phacoemulsification vs phaco-only; the study showed significantly greater IOP and medication reductions with the combined intervention vs phaco-only, as highlighted above in our article.[18]

Our efficacy data are consistent with the findings of Chen and associates,[18] with both studies showing significant treatment benefit of stent implantation plus phacoemulsification over phaco-only. Specifically, our study showed an approximately twofold increase in the amount (in mm Hg) of IOP reduction, and an approximately threefold increase in the number of medications reduced, in eyes undergoing stent-phacoemulsification surgery vs phaco-only. In addition, significantly greater proportions of stent-phacoemulsification eyes vs phaco-only eyes achieved 1 year IOP measurements of ≤18 mm Hg, ≤15 mm Hg, and ≤12 mm Hg, while a smaller proportion increased their glaucoma medication use and a larger proportion maintained or decreased their glaucoma medication use compared with their preoperative regimen. Notably, there were significantly fewer IOP spikes postoperatively in the phaco-stent group, highlighting the protective effect of stent implantation against postoperative IOP spikes, consistent with previous evidence in OAG.[49,50] Prevention of IOP spikes is particularly important in more advanced glaucoma cases where the optic nerve is more susceptible to insults.[51,52]

Of note, our cohort included a considerable number of eyes with plateau iris configuration, in which the anterior chamber angle is known to remain crowded even after cataract surgery.[53] This configuration theoretically could limit the amount of IOP reduction experienced after phacoemulsification, as well as predispose to stent occlusion by the peripheral iris.[53] In our cohort, the IOP reductions in phaco-stent eyes were still significantly greater than in phaco-only eyes, and the 2 isolated cases of stent occlusion were both in eyes with normal angle configuration. This suggests that trabecular bypass stenting could be effective and safe in eyes regardless of their preoperative angle configuration.

The safety profile of the stents was highly favorable. Postoperative adverse events were rare and transient in both the phaco-stent and phaco-only groups, with no sight-threatening sequelae; there were no between-group differences in postoperative CDR, VF MD, or thickness of RNFL or GCIPL. No eyes underwent incisional secondary glaucoma surgery. Visual acuity improved significantly in both groups, indicating that stent implantation does not detract from the expected visual benefits of cataract surgery. There were no occurrences of complications seen with filtering surgery, such as hypotony, choroidal detachment, bleb-related complications, or endophthalmitis.[9–11]

The study has certain limitations. The global burden of glaucoma is high, with PACG playing a particularly large role in East Asian populations[54,55]; however, information on race was not available in this study, so it is unclear to which population the results can be most directly applied (Asian or otherwise). Also, data regarding the extent of preoperative PAS were unavailable. To address this shortcoming, we compared the rate of intraoperative GSL between the 2 groups, as a proxy for existence of clinically significant baseline PAS. While there were no significant differences in the rate of GSL performed between the 2 groups, one should interpret the results with this limitation in mind. A larger proportion of eyes in the phaco-only group had undergone laser peripheral iridotomy. Although all analyses we corrected for this intergroup difference, we cannot rule out the possibility that some of the eyes in phaco-stent group had different mechanisms of IOP elevation and that bypassing the trabecular meshwork through implantation of the stents could have allowed them to achieve greater IOP reductions. There was no preoperative medication washout, as this would not have been appropriate in this real-world clinical setting and population. Our phaco-stent group included eyes with iStent and iStent *inject*. While the subgroup analyses of these 2 stents revealed comparable efficacy, it may be possible that this subanalysis was underpowered. Thus, we encourage future studies to compare the outcomes of iStent and iStent *inject* in larger samples of PACG eyes.

CONCLUSION

THIS STUDY CONTRIBUTES SUBSTANTIVE AND NOVEL DATA in our understanding of microinvasive glaucoma surgery in angle-closure eyes. The results showed that phacoemulsification with implantation of 2 trabecular microbypass stents produced significantly greater IOP and medication reductions vs phaco-only, with a comparably favorable safety and sustained duration of treatment effect. The inclusion of a matched control group enables the discernment of the stents' effects from those of phaco-only treatment—a distinction that is particularly important in the setting of angle-closure, where cataract extraction is known to yield sizable IOP reductions. The outcomes shed light on a relatively rarely examined indication in MIGS research—angle-closure disease—and suggest that iStent and iStent *inject* could be viable options for treating these patients.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST. Funding/Support: This study received no funding. Financial Disclosures: P.H. is a consultant for Allergan, Glaukos, Ivantis, J and J Vision, and Santen. All authors attest that they meet the current ICMJE criteria for authorship.

Acknowledgments: We thank the participants in this study. A.S. was responsible for conceptualization, design, data acquisition, data analysis and interpretation, and drafting of the manuscript. M.A-N. was responsible for data acquisition and interpretation and review and editing of the manuscript. P.H. was responsible for conceptualization, design, data interpretation, drafting and editing the manuscript, and supervision. This study was approved by the Ethics Committee of the Hôpital Maisonneuve-Rosemont in Montreal, Quebec, Canada. All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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