Safety and efficacy of concomitant supraciliary microstenting with cataract surgery for treating open-angle glaucoma: 3-year experience

Skuteczność i bezpieczeństwo operacji usunięcia zaćmy z jednoczesnym wszczepieniem nadnaczyniówkowego implantu przeciwjaskrowego – obserwacje 3-letnie

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Abstract. Purpose. This study evaluated the treatment outcomes of supraciliary microstent implantation (CyPass® Micro-Stent, Transcend Medical, USA) in patients with open-angle glaucoma undergoing cataract surgery. Material. Prospective case series. Methods. Twenty patients (mean age: 76.5 ±7.1 years) were evaluated for 36 months after supraciliary microstent implantation combined with cataract surgery. Evaluated outcomes included IOP, best-corrected visual acuity (BCVA), number of required IOP-lowering medications, and adverse events. Results: Baseline mean IOP (16.1 ±3.3 mm Hg) remained well-controlled at 36-months post-surgery (15.8 ±3.4 mm Hg; p =0.070). Baseline BCVA (mean 20/40 Snellen, range 20/25–20/200) was improved after surgery, and the effect was maintained through postoperative 36-months (mean 20/25 Snellen, range 20/20–20/80). All subjects used IOP-drugs at baseline (40% required ≥3 medications), whereas 80% remained medication-free at postoperative 36-months. One stent obstruction resulted in elevated IOP and device explantation. Another subject experienced persistent corneal edema. Adverse events included transiently elevated IOP (20% of eyes) and hypotony (20%). Conclusion. Supraciliary microstenting combined with cataract surgery in open-angle glaucoma results in minimal complications and significantly reduces necessary IOP-lowering medications through postoperative 36-months.
Słowa kluczowe: open-angle glaucoma, phacoemulsification cataract surgery, supraciliary microstent, supraciliary space

Streszczenie. Cel. Ocena wyników leczenia za pomocą mikroimplantu przeciwjaskrowego CyPass® u pacjentów z jaskrą otwartego kąta poddanych usunięciu zaćmy. Materiał. Badanie prospektywne typu case series. Metoda. 20 pacjentów (średnia wieku 76,5 ±7,1 roku) obserwowano przez 36 miesięcy po implantacji mikrostentu do przestrzeni nadnaczyniówkowej wykonanej z usunięciem zaćmy. Oceniano IOP, najlepszą skorygowaną ostrość wzroku (*best-corrected visual acuity* – BCVA), liczbę leków przeciwjaskrowych oraz powikłania. Wyniki. Przedoperacyjne IOP (średnia 16,1 ±3,3 mm Hg) regulowało się w 36-miesięcznym okresie obserwacji (15,8 ±3,4 mm Hg; p =0,070). Przedoperacyjna BCVA (średnia 20/40 wg Snellena, zakres 20/25–20/200) uległa poprawie i po 36 miesiącach wynosiła 20/25 wg Snellena (zakres 20/20–20/80). Wszyscy pacjenci przed zabiegiem stosowali krople przeciwjaskrowe (40% wymagało ≥3 leków), po 36 miesiącach 80% osób nie stosowało żadnych kropli. Jeden pacjent wymagał usunięcia implantu z powodu niedrożności z wysokim IOP. Jeden pacjent miał przewlekły obrzęk rogówki. Inne powikłania to skok IOP (20%) i hipotonia (20%). Wnioski. Zastosowanie mikrostentu nadnaczyniówkowego w połączeniu z usunięciem zaćmy w jaskrze otwartego kąta daje istotną statystycznie redukcję IOP i stosowanych leków przeciwjaskrowych przy niewielkiej liczbie powikłań w 36-miesięcznym okresie obserwacji.
Key words: jaskra otwartego kąta, przestrzeń nadnaczyniówkowa, implant nadnaczyniówkowy, fakoemulsyfikacja zaćmy

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Introduction

Cataracts and glaucoma are the first and second leading causes of blindness worldwide [1]. Both conditions are age-dependent and frequently coexist [1,2]. In the US, for example, nearly 26 million people were estimated to suffer from cataracts in 2014, and this prevalence is expected to increase to 30 million individuals by 2020 due to population aging [2]. In 2014, approximately 2.9 million people in the US had glaucoma, and this number is projected to increase by over 20% to 3.4 million by 2020 [3]. Currently, 3.6 million Americans undergo cataract surgery annually, making it the most commonly performed surgical procedure in the US. Similarly, in the EU, 3.6 million cataract extractions were performed in 2014 [4], and this number will undoubtedly increase with aging population demographics [5,6]. Importantly, approximately 20% of patients receiving cataract surgery also present with a history of concurrent glaucoma [7]. Thus, a significant proportion of patients undergoing cataract surgery remain at risk of vision loss due to coexistent glaucoma. Open-angle glaucoma (OAG) is the most common glaucoma subtype, accounting for 74% of worldwide glaucoma cases [8], and an even larger proportion of US cases [4]. Elevated intraocular pressure (IOP) remains the sole modifiable risk factor for progressive optic neuropathy and vision loss in OAG [9]. Conservative medical therapies to reduce IOP in glaucoma frequently involve simultaneous administration of multiple topical medications to reduce aqueous humor production or increase trabecular and uveoscleral outflow [9]. However, all of these drugs have potentially deleterious side effects [10] that require close follow-up, can be expensive [11], and often require life-long treatment regimens that can be confusing and inconvenient to patients, thereby compromising patient compliance and adherence to dosing schedules [12]. Numerous surgical approaches have been developed in efforts to overcome the need for often complicated and sometimes ineffective medication schedules for controlling ocular hypertension in OAG. Common interventions include laser trabeculoplasty and conventional trabeculectomy [9]. Laser treatment often provides good initial results, but their IOP-lowering effects are highly variable and frequently transient [13]. Conventional trabeculectomy is also an invasive procedure with significant potential side effects [9]. Thus, effective and minimally invasive glaucoma interventions are needed.

This need for effective and minimally invasive non-medical therapies for OAG has led to the introduction of *ab interno* microstent implant technologies that reduce IOP by bypassing areas of high outflow resistance thereby enhancing aqueous humor drainage via natural, physiological pathways [14,15]. These approaches vary with respect to mechanism of action, microstent design, implantation site, and surgical technique for device installation.

The CyPass® Micro-Stent (Transcend Medical, Inc., Menlo Park, CA, USA) is a novel ocular device that was designed to permanently normalize IOP in patients with OAG, by directing unimpeded aqueous humor outflow from the anterior chamber to the supraciliary space (SCS), a part of uveoscleral outflow path. Targeting the uveoscleral pathway as a method to reduce IOP has some potential advantages. The IOP-lowering potential of the suprachoroidal space is well documented through the historical use of the iatrogenic cyclodialysis cleft [16]. Additionally, the prostaglandin analogues that are mainstays of glaucoma medical therapy largely function by enhancing outflow via the uveoscleral route [17].

This study device has been approved for human use in the European Union since 2008, and in 2016 by the US Food and Drug Administration in an Investigational Device Exemption study, although recently it has been withdrawn due to endothelial cell loss after 5 years period [18–20]. The current prospective case series evaluated the 36-month postoperative safety and efficacy profiles of the CyPass device after *ab interno* implantation into OAG patient eyes immediately following phacoemulsification and intraocular lens (IOL) implantation.

Materials and Methods

Study Design

This prospective, open-label, interventional, consecutive case series assessed OAG patient safety and outcomes after receiving a CyPass Micro-Stent implantation after phacoemulsification and IOL implantation. Surgeries were performed between January 2010 and December 2011 by one surgeon (M.R.).

Patients

Inclusion criteria were patients aged ≥18-years-old who required medication to control previously diagnosed primary or secondary OAG, and who had coexistent cataracts that were scheduled for phacoemulsification. One eye of each patient was included in the study; if both eyes qualified, the one with higher IOP values or with worse visual field parameters was selected. If both of these values were comparable, the eye with worse visual acuity was included in the study. The right eye was included in the study if the progression of glaucoma or cataract was comparable in both eyes. Exclusion criteria were prior surgery or laser trabeculoplasty in the eligible eye, clinically significant ocular pathology other than cataract and glaucoma, and diagnosis of acute

angle-closure, narrow-angle, uveitic, neovascular, congenital, traumatic, or normotensive glaucoma in the study eye.

Preoperative Examination

During qualification, medical history concerning prior procedures and treatments was taken. Comprehensive baseline eye examinations assessed IOP (Goldmann tonometry), uncorrected distance visual acuity, best corrected visual acuity (BCVA), retinal cup/disc ratio, central corneal thickness, and axial length. Visual field tests and gonioscopic examination were also conducted.

Surgical Procedure

Anti-glaucoma medications were discontinued on the day of surgery. Topical medications for dilation and cycloplegia were used preoperatively. All surgeries were performed with retrobulbar anesthesia (2% xylocaine, 0.5% bupivacaine, 150 IU hyaluronidase), and patients received bolus intravenous sedation/anxiolysis (50–100 μg fentanyl with 1–2 mg midazolam). Intraoperatively, blood pressure, O_2 saturation, and electrocardiography were monitored.

Phacoemulsification was performed through a 2.2 mm clear-corneal incision, and an AcrySof® IQ IOL (Alcon Laboratories Inc., Fort Worth, TX) was implanted. Irrigation was performed with balanced salt solution containing 100 μg/ml vancomycin. The anterior chamber was filled with viscoelastic (Viscoat®, Alcon Laboratories), and intraocular acetylcholine chloride was administered to maintain pupil constriction and facilitate nasal angle visualization with a Swan-Jacob gonioscope (Ocular Instruments, Bellevue, WA) prior to and during microstent implantation. The implant was loaded onto the retractable guidewire of the applier, inserted into the anterior chamber through the corneal incision, and advanced towards the scleral spur under gonioscopic guidance. The guidewire tip was used to bluntly dissect the ciliary body and create a passageway into the SCS. The microstent was then positioned within the newly created supraciliary duct, the guidewire was retracted, and the applier was withdrawn from the eye. Viscoelastic was evacuated by saline irrigation and aspiration, and the integrity of the corneal incision closure was verified; no patient required corneal incision suturing. Microstents were implanted in the inferionasal quadrant. All patients were prescribed a steroid, NSAID, and antibiotic topical regimen for 1 month postoperatively.

Device Description

The CyPass® Micro-Stent (Transcend Medical, Inc., Menlo Park, CA) is constructed of flexible polyimide and is 6.35 mm long, with its largest external diameter measuring 0.51 mm and an internal diameter of 0.31 mm. The microstent has 76 µm-diameter fenestrations along its distal length to facilitate aqueous humor flux, and possesses three protruding retention rings at the proximal end for device stabilization within the SCS. The CyPass device is a supraciliary tube designed to permanently enhance aqueous humor outflow from the anterior chamber to the SCS. The device is provided by the manufacturer mounted on a curved introducer guidewire with a blunt dissection tip to facilitate insertion along the scleral curvature. When the guidewire is retracted after gonioscopy-guided device positioning within the angle and SCS, the CyPass device's natural elasticity causes slight rebound straightening that further anchors the microstent to surrounding tissues. The device has received the Conformité Européenne mark and is available for clinical use in Europe. The CyPass Micro-Stent is also the focus of an ongoing multicenter, randomized, controlled trial that is registered in the US [20].

Postoperative Protocol

Follow-up ophthalmological examinations were performed on postoperative Days 1 and 7, and Months 1, 3, 6, 12, 18, 24, and 36. Eye exams determined IOP, CDVA, and visual field, and the anterior and posterior segments were evaluated. Post-operative analyses included the occurrence of complications and the number of applied anti-glaucoma medications needed to maintain target IOP (*i.e.*, <21 mm Hg). Safety-related outcome measures included intra-operative and postoperative adverse events (AEs). Effectiveness outcomes assessed during follow-up included changes from baseline of IOP, BCVA, and number of glaucoma medications required to maintain target IOP in the operated eye.

Statistical Analyses

Descriptive statistics and paired two-tailed Student's t-tests were used to evaluate the data, which are provided as numbers and percentages of the patient population, and means ± standard deviation (SD) or 95% confidence intervals (95% CIs), with p-values <0.05 considered indicative of statistically significant differences between comparator groups. Statistical analyses were performed using Excel 2010 (Microsoft Corp., Redmond, WA) and Prism® v.5.03 statistical and graphing software (GraphPad Software, Inc., San Diego, CA).

Results

Patient demographics

This study included 20 eyes of 20 patients with OAG; 17 were primary OAG and 3 were secondary OAG. Group demographic data are given in Table 1. The cohort consisted of 19 females (95%) and 1 male (5%), with a mean age of 76.5±7.1 years at enrollment. Some patients missed follow-up visits for personal reasons unrelated to the study, so that N-values at postoperative 1, 2, and 3 year time points numbered 18 (90%), 16 (80%), and 15 (75%) eyes.

Intraocular pressure control and visual acuity

Mean preoperative medicated IOP was 16.1 ±3.3 mm Hg. Following surgery, IOP was significantly decreased by approximately 13% and 12% at respective 6, and 12 month follow-ups (p =0.0082, and 0.0425; paired t-tests) (Figure 1A-B). At postoperative 2 and 3 years, respective IOP values were decreased *vs* baseline values by 9% (15.1 ±1.9 mm Hg) and 2% (15.8 ±3.4 mm Hg), though these differences were no longer statistically distinct (Figure 1B). Preoperative BCVA averaged 0.48±0.23 Units (≈20/40 Snellen) on the decimal scale (range 0.06–0.90 Units). After cataract replacement with an IOL and microstent implantation, BCVA significantly improved in a progressive fashion. The percentage of subjects with 20/25 or better BCVA was markedly increased from 10% of the cohort at baseline 72%, 81%, and 80% of study subjects at postoperative 1, 2, and 3 years, respectively (p <0.001 at all time points by Fisher's exact test) (Figure 1C). Acuity increased immediately in 90% of patients by 1 week postoperatively (not shown). In 90% of cohort, BCVA had significantly increased at postoperative 1 month versus preoperative values, and this acuity either stabilized or continued to improve through the 36-month follow-up. Of the two patients whose BCVA had decreased at the 1-month examination, one patient displayed a negligible decrease from 0.6 to 0.5 Units (from 20/32 to 20/40 Snellen), which improved to 0.8 Units (20/25 Snellen) by 6 months. The second exception presented with a preoperative BCVA of 0.6 Units, which fluctuated postoperatively to a low of 0.2 Units (20/100 Snellen) at 3 6 months and returned to 0.4 Units (20/50 Snellen) at 12 months. However, this patient's decreased acuity appeared in concert with early-onset corneal edema (Day 1) and later-onset macular edema (Month 3). Acuity continued to improve, and stabilized at 0.50 Units through the 2- and 3-year time points.

Table 1. Patient demographics and baseline clinical parameters
Tabela 1. Wyjsciowe dane demograficzne i kliniczne

N=20 eyes from 20 patients	
age, years, mean ±SD	**76.5 ±7.1**
female, n (%)	19 (95%)
male, n (%)	1 (5%)
glaucoma type, n (%)	**20 (100%)**
primary OAG	17 (85%)
secondary OAG	3 (15%)
baseline IOP, mm Hg, mean ±SD	**16.1 ±3.3**
≥21 mm Hg, n (%)	2 (10%)
<21 mm Hg, n (%)	18 (90%)
range	11–22 mm Hg
glaucoma medications, n, mean ±SD	**2.3 ±0.9**
3+ meds, n (%)	8 (40%)
2 meds, n (%)	8 (40%)
1 med, n (%)	4 (20%)
0 meds, n (%)	0 (0%)
prior glaucoma surgery/laser, n (%)	**0 (0%)**

Medications

Significantly fewer anti-glaucoma medications were used after surgery than before the procedure, throughout the entire 3-year follow-up (Figure 2). Mean preoperative anti-glaucoma drug use numbered 2.3 ±0.9 medications. At the 12-month follow-up, this number had been significantly reduced to 0.2 ±0.4 drugs (p<0.0001 *vs* baseline; paired t-test) (Figure 2A). At 2 and 3 years after intervention, mean glaucoma medication use remained significantly reduced at 0.4 ±0.5 and 0.5 ±0.6 drugs, respectively (p <0.0001 at both time points). No subject was anti-glaucoma drug-free at study entry. However, at 1, 2, and 3 years after microstent implantation, 83%, 81%, and 80% of our cohort did not require any glaucoma medications (p <0.0001 *vs* baseline for all follow-up points) (Figure 2B). At 1 year postoperatively, only 1 anti-hypertensive medication was required in the 17% of subjects that resumed drug use. At postoperative 2 and 3 years, of the ≈20% of subjects that required supplemental medication, none required more than 2 drugs.

At baseline, every study subject was using glaucoma medication to control IOP. After surgery, over 80% of the cohort was able to maintain IOP ≤21 mm Hg without medication through 3 years, and 67% realized a drug-free IOP ≤18 mm Hg (Figure 2C). At postoperative 3 years, 47% of study subjects presented IOP ≤15 mm Hg without medication. Whereas 75% of the baseline population had IOP within the clinically targeted 6–18 mm Hg range,

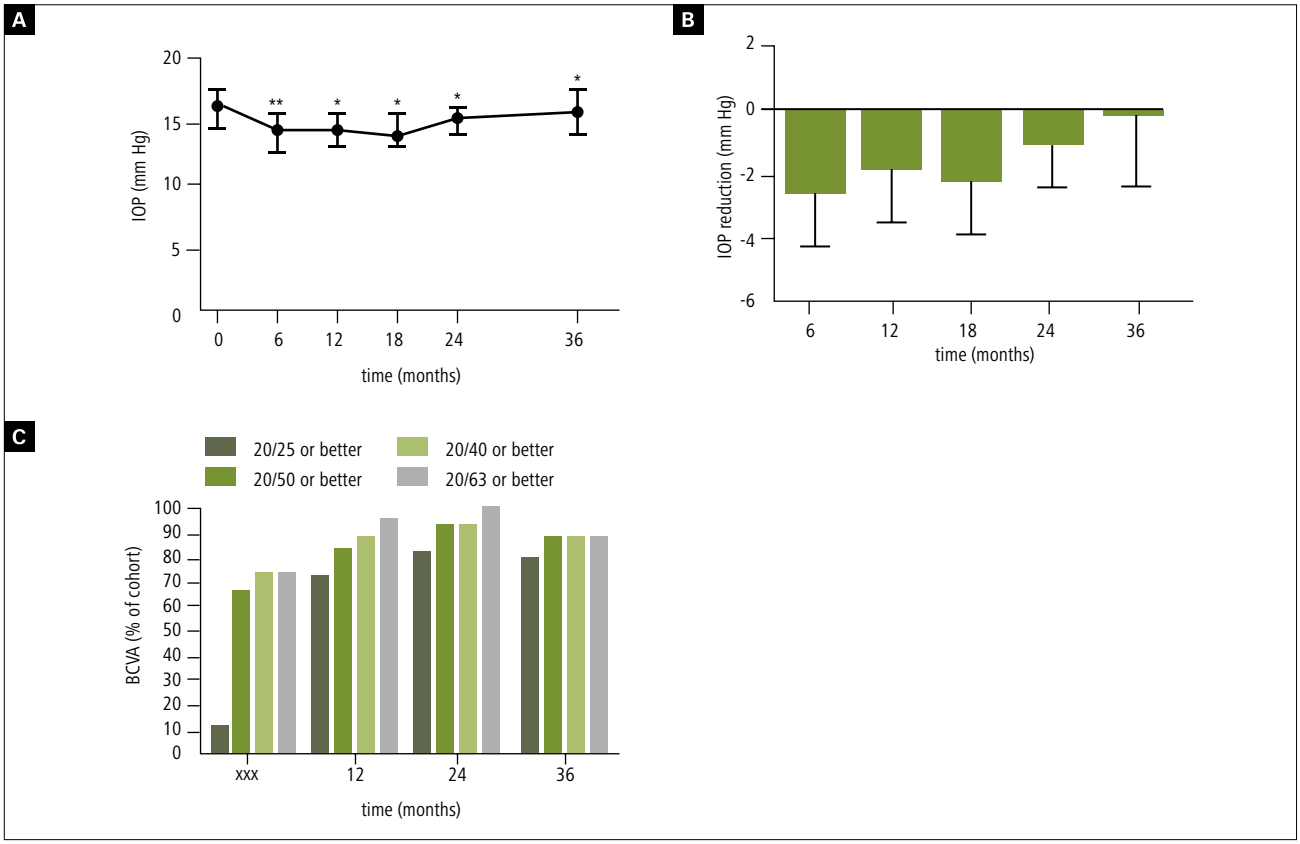

Figure 1. Intraocular pressure (IOP) and best corrected visual acuity (BCVA). **A.** Preoperative mean medicated IOP was 16.1 ±3.3 mm Hg (95% CI: 14.6–17.6 mm Hg). After CyPass Micro-Stent implantation with phacoemulsification cataract extraction, IOP significantly decreased by ≈12% through postoperative 18 months. At the 3-year study terminus, mean ±SD IOP was 15.8 ±3.4 mm Hg (95% CI: 13.9–17.7 mm Hg), which was not significantly different from baseline values ($p > 0.05$ by paired two-tailed t-test). **B.** IOP was significantly reduced for 18 months following surgery, and did not exceed baseline levels through postoperative 3 years. **C.** The percentage of subjects with 20/25 or better BCVA was markedly increased from 10% of the cohort at baseline 72%, 81%, and 80% of study subjects at postoperative 1, 2, and 3 years, respectively ($p < 0.001$ at all time points by Fisher's exact test). Values shown in Panels A and B are means with 95% confidence intervals (95% CIs)

Rycina 1. Ciśnienie wewnątrzgałkowe (IOP) i najlepsza skrygowana ostrość wzroku (BCVA). **A.** Przedoperacyjna średnia wartość IOP wynosiła 16,1 ±3,3 mm Hg (95% CI: 14,6–17,6). Po implantacji mikrostentu CyPass w połączeniu z fakoemulsyfikacją zaćmy IOP uległo znaczącej redukcji o około 12% w okresie 18-miesięcznej obserwacji. Po 3 latach średnia wartość IOP wynosiła 15,8 ±3,4 mm Hg (95% CI: 13,9–17,7) i nie była statystycznie różna od wartości przedoperacyjnych ($p > 0,05$). **B.** IOP uległo znaczącej redukcji po 18 miesiącach od operacji i nie przekraczało przedoperacyjnych wartości wyjściowych w czasie 3 lat obserwacji. **C.** Odsetek przypadków grupy badanej z BCVA 20/25 lub lepszą wyraźnie się zwiększył z 10% przed operacją do 72%, 81% i 80% przypadków odpowiednio w 1., 2. oraz 3. roku obserwacji ($p < 0,001$). Wartości pokazane na wykresach A oraz B są średnimi z 95% przedziałami ufności (95% CI).

all of these individuals required medication to do so (Figure 2D). At postoperative 2 years, 100% of participants maintained IOP within this aspirational pressure range, although only 19% were using glaucoma drugs. This effect was maintained through the 3-year follow-up, when 80% of subjects stayed within the target IOP range without supplemental medication.

Complications

Clinically significant adverse events (AEs) occurred in two patients (10%) during follow-up (Table 2). In the first case, stent obstruction with blood in the angle was noted at 2 weeks following surgery, with associated elevated IOP. Non-penetrating deep sclerectomy was performed in this subject with concurrent explantation of the microstent at the time of surgery, with no additional sequelae. The second case consisted of persistent corneal edema (>3 months duration) starting 1 day after surgery. This subject also had an episode of macular edema 3 months postoperatively, which was medically managed and resolved within 2 weeks following onset. Other anticipated minor AEs included transient elevated IOP (defined as IOP >30 mm Hg inclusive and more than 10 mm Hg higher than baseline IOP) in 4 patients (20%), and transient hypotony (pressure <6 mm Hg), also in 4 patients (20%), all resolving within 1 month.

Table 2. Adverse events
Tabela 2. Powikłania

*N=20 eyes from 20 patients	•(% of cohort)*
high IOP (>30 mm Hg & B/L +10 mm Hg)	4 (20%)
≤1 mo. (Transient)	4 (20%)
>1 mo. (Persistent)	0 (0%)
hypotony (<6 mm Hg)	4 (20%)
≤1 mo.	4 (20%)
>1 mo.	0 (0%)
hyphema	**1 (5%)**
≤1 mo.	1 (5%)
>1 mo.	0 (0%)
corneal edema	**1 (5%)**
≤1 mo.	0 (0%)
>1 mo.	1 (5%)
macular edema	**1 (5%)**
≤1 mo.	1 (5%)
>1 mo.	0 (0%)
BCVA loss ≥2 Snellen lines	**0 (0%)**
microstent parameter requiring intervention	**1 (5%)**
malpositioned	0 (0%)
migrated	0 (0%)
obstruction requiring explantation	1 (5%)
miscellaneous	**1 (5%)**
anterior chamber shallowing	0 (0%)
cataract	0 (0%)
endothelial touch	0 (0%)
glaucoma disease progression	0 (0%)
macular changes, other than edema	0 (0%)
retinal disease progression	0 (0%)
secondary glaucoma surgery	1 (5%)

*One subject had two adverse events in the study eye (corneal edema and macular edema)
IOP – intraocular pressure, B/L – baseline, BCVA – best corrected visual acuity

Discussion

Managing ocular hypertension in OAG patients is critical in mitigating vision loss and blindness. Pharmacological treatment, when effective, frequently involves multiple topical medications that must be self-administered on complicated schedules [9], resulting in poor patient compliance [12]. These IOP-lowering drugs are also expensive [11], must be used for a lifetime, and are not without side effects [10]. Conventional surgical approaches for enhancing aqueous drainage to correct IOP in OAG such as the gold standard trabeculectomy are invasive procedures that have a high rate of adverse events including visual acuity instability and loss, typically require close follow-up, often require adjunctive pharmacological therapy, and are prone to failure requiring re-operation [9,13–15]. The CyPass Micro-Stent is implanted in a minimally invasive *ab interno* procedure that aims to overcome standard OAG treatment shortcomings by exploiting the unconventional uveosceleral outflow pathway. This microstent device is approved for clinical use in Europe and is currently undergoing phase III clinical trials in the US [18,19]. Our OAG cohort received microstent implantation concurrent with phacoemulsification cataract surgery. Baseline IOP was generally well-controlled and target IOP was maintained for at least 36 months postoperatively. Importantly microstented eyes maintained the clinically-targeted IOP range in lieu of markedly decreased numbers of IOP medications required during follow-up. Cataract phacoemulsification surgery itself has been shown to lower IOP in primary OAG eyes, likely by forming a deeper anterior chamber, but this effect appears modest in magnitude. Indeed, a 2014 report of 157 OAG patients indicated that, although mean baseline IOP in patients that underwent phacoemulsification decreased during 1-year follow-up, 38% of eyes with medication-controlled OAG had worsened IOP control after surgery, with 24% requiring additional drugs or laser trabeculoplasty [21]. Another long-term study indicated no significant difference in IOP medication use in OAG eyes 3 and 5 years after cataract surgery [22], whereas another group reported that phacoemulsification reduces hypotensive medication use in OAG patients by 0.4 ±0.9 medications at 24 months [23]. Thus, consensus remains to be established regarding variable IOP responses to cataract surgery in OAG patients. Garcia-Feijoo et al. show that CyPass Micro-Stent surgery without cataract removal effectively lowers IOP, precluding the need for more invasive glaucoma surgery in over 80% of patients at 1 year, thereby reducing postoperative glaucoma surgical complications. There were no serious intraoperative adverse events. The most common adverse events included IOP increases >30 mm Hg (11%), transient hyphema (6%), and cataract progression (12%). Mean IOP was reduced by 34.7%. Mean medication usage was also reduced from baseline 2.2 (±1.1) to a mean of 1.4 ±1.3 at 12 months [24]. The multicenter, prospective case series (136 eyes with OAG) shows that no sight-threatening adverse events occurred within the 24-month postoperative period after CyPass Micro-Stent implantation combined with phacoemulsification. The most common adverse events were transient (≤1 month onset) hypotony (15.4%) and micro-stent obstruction (8.8%), typically due to iris tissue overgrowth.

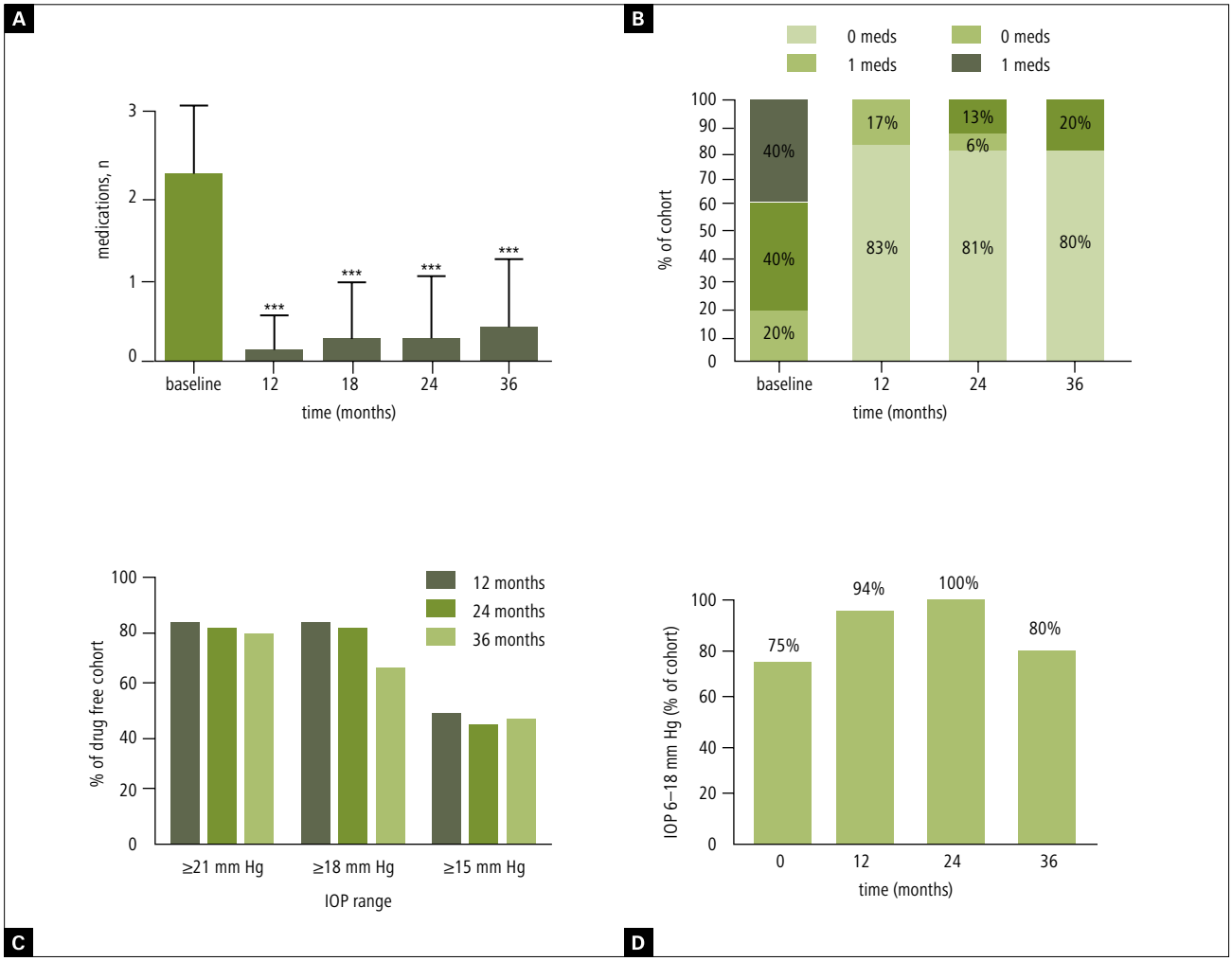

Figure 2. Topical anti-hypertensive glaucoma medication use. A. The average number of preoperative IOP-lowering medications used by this cohort was 2.3 ±0.9 drugs (95% CI: 1.9–2.6 drugs), and no patient was drug-free before cataract extraction and microstent implantation surgery. Glaucoma medications were dramatically reduced to 0.2 ±0.4 drugs (95% CI: 0.0–0.4 drugs) at 12 months, and maintained at 0.4 ±0.8 (95% CI: −0.1–0.9 drugs) through 36 months following surgical intervention with microstent implantation (***p<0.001 at both follow-up times *vs* baseline, unpaired t-test; shown are mean ±SD). **B.** Before surgery, no subject was IOP drug-free, and 40% were using ≥3 drugs. At 12-months follow-up, a significantly increased 83% of patients were drug-free, and the remaining 17% were using only one IOP-reducing medication (p<0.001 by Fisher's exact test). At postoperative 3 years, 80% of the cohort remained medication-free. **C.** Through 3 years, surgical intervention resulted in similarly elevated proportions of subjects having stably improved IOP control in the operated eye while remaining medication-free. **D.** Microstenting with cataract surgery increased the proportion of subjects, with or without anti-glaucoma medication use, to maintain IOP in the 6–18 mm Hg range.

Rycina 2. Liczba stosowanych leków przeciwjaskrowych. A. Średnia liczba przedoperacyjnych leków obniżających IOP stosowanych w grupie badanej wynosiła 2,3 ±0,9 leku (95% CI: 1,9–2,6), nie było żadnego pacjenta bez miejscowej terapii przeciwjaskrowej przed operacją usunięcia zaćmy i implantacji mikrostentu. W ciągu 12 miesięcy liczba stosowanych leków przeciwjaskrowych uległa znacznej redukcji do 0,2 ±0,4 (95% CI: 0,0–0,4) i utrzymywała się na poziomie 0,4 ±0,8 (95% CI: -0,1–0,9) przez 36 miesięcy (*** p <0,001 w obu okresach obserwacji w stosunku do wartości wyjściowej, test t Studenta dla prób niezależnych, pokazano średnią ±SD). **B.** Przed operacją w badanej grupie nie było żadnego pacjenta bez miejscowej terapii przeciwjaskrowej, a aż 40% stosowało co najmniej 3 leki. W 12-miesięcznym okresie obserwacji istotnie zwiększył się odsetek pacjentów bez leków do 83%, a pozostałe 17% stosowało tylko jeden lek (p <0,001). W 3. roku obserwacji 80% badanej grupy pozostało bez leków. **C.** Przez 3 lata obserwacji przeprowadzona procedura chirurgiczna skutkowała zwiększeniem odsetka osób z dobrze kontrolowanym IOP w operowanym oku bez konieczności stosowania miejscowych leków przeciwjaskrowych. **D.** Implantacja mikrostentu w połączeniu z chirurgią zaćmy zwiększa odsetek pacjentów z lekami przeciwjaskrowymi lub bez leków z dobrze kontrolowanym IOP w zakresie 6–18 mm Hg.

4.4% of eyes required secondary incisional glaucoma surgery. High IOP (>30 mm Hg and ≥baseline IOP + 10 mm Hg) occurred in 4.4% and 11% of eyes needed secondary glaucoma surgery. At 24 months, there was a sustained effect on involving reduction of both medication usage and IOP reduction [25]. In the two-year COMPASS trial 374 eyes had cataract surgery with cypass implantation, unmedicated IOP

decreased from 24 ±2.8 mm Hg before surgery to 17.0 ±3.4 mm Hg. The surgery significantly reduces hypotensive ocular medication usage from baseline 1.4 ±0.9 to 0.2 ±0.6 after 24 months. 84.8% of subjects were medical free after 24 months which is similar to our results. 39% of eyes had transient complications like visual acuity loss ≥2 Snellen lines, iritis, corneal edema, hypotony, and cyclodialysis cleft. Nearly all resolved by the end of the trial. Moreover, the complication rate was not significantly higher than in phacoemulsification alone group. The authors did not notice any vision-threating microstent-related adverse events [26]. The iStent (Glaukos Corp., Laguna Hills, CA) is a metal microstent that is implanted within the Schlemm's canal to enhance trabecular outflow [27]. The iStent main efficacy endpoint in a 2012 reporting of results from concurrent microstenting with cataract surgery was the proportion of subjects with IOP ≤21 mm Hg without needing IOP medication [28]. At postoperative 2 years, this criterion was achieved by 61% of iStented subjects. Though our study did not employ washout IOP measurements, 100% of our cohort was medication-dependent at baseline, with 40% using ≥3 drugs. This was sustainedly reduced to 17–20% of participants requiring drugs at postoperative 1–3 years. At the 2-year comparator point, 81% of our cohort was IOP medication-free, and all subjects maintained IOP within a more stringent 6–18 mm Hg range. The Hydrus appliance (Ivantis Inc., Irvine, CA) is another metal microstent that targets Schlemm's canal. A 2015 report on OAG subjects undergoing microstenting with cataract surgery indicated a medication-free rate of 73% at postoperative 2 years [29], similar to the 81% rate we currently report with the CyPass Micro-Stent. The Hydrus cohort required 2.0 mean medications at baseline, which decreased to 1.0 drugs in microstented subjects at 2 years; in the current CyPass study, mean medication use was reduced from 2.3 at baseline to 0.4 drugs at postoperative 2 years, a value that remained stable (0.5 medications) through 3 years. In our trial, microstent implantation performed concurrently with phacoemulsification markedly and sustainedly reduced the need for medications to control IOP in subjects with OAG. Here, 80% of participants maintained target IOP values while remaining entirely drug-free through 3 years of follow-up, whereas all patients were anti-glaucoma drug-dependent before intervention.Visual acuity significantly improved after dual cataract extraction/microstent implantation, and this effect was observed as early as postoperative 1-month, with continued improvement and maintenance through the 3-year follow-up. Thus, we have no evidence that contraindicates installing the CyPass device during routine cataract surgery because of vision degradation. Future prospective studies comparing phacoemulsification alone to combined cataract surgery with microstent implantation will provide more definitive assessments of potential microstent treatment effects on visual acuity. No surgical procedure is entirely devoid of potential complications. Two patients experienced serious AEs in our cohort. One case of microstent obstruction associated with hyphema, elevated IOP (transient; maximum 45 mm Hg), and blood in the angle necessitated device explantation at postoperative 3 weeks. A prior iStent report indicated a similar 4.3% incidence of microstent obstruction through 24 months of follow-up [28]. In our study, another patient experienced a single transient (<2 weeks) instance of macular edema that began at postoperative 3 months; this patient also displayed persistent corneal edema with immediate postoperative onset that lasted 6 months. Though the aforementioned iStent RCT reported a cumulative 17.2% rate of diverse anticipated minor AEs through 24 months [28], their published results do not detail the specific incidence of corneal edema alone. The Hydrus study reported a low AE rate; however they observed focal peripheral anterior synechiae in 19% of microstented subjects [29], that did not occur in our cohort. Minor AEs in our study comprised transiently elevated IOP and hypotony. Limited patient numbers may have skewed our true AE rate; indeed, another recent clinical trial of 184 patients that underwent dual phacoemulsification/CyPass Micro-Stent implantation reported no serious AEs though 6 months follow-up [19].

Conclusions

Implanting the supraciliary CyPass Micro-Stent concurrent with cataract surgery is a safe and minimally-invasive open-angle glaucoma treatment option that reduces necessary intraocular pressure-lowering medications through postoperative 36 months. Study limitations include a relatively small cohort size and the single-arm protocol that precluded assessing the potential impact of cataract surgery on stent-mediated OAG outcomes. The lack of a medication "wash-out" at baseline visit was the limitation too. Nonetheless, this efficacy and safety study is related to a much larger multicenter clinical trial still in progress [20], and provides important new information regarding the utility of concomitant microstent implantation during routine cataract surgery. The microinvasive nature of this procedure holds significant promise in effectively treating ocular hypertension in OAG, in this case using the same clear corneal incision created for cataract extraction. Given the unpredictable outcomes of more invasive OAG surgical interventions, and the already high yet still-increasing cost of IOP-lowering medications [11], the supraciliary CyPass device may prove to be an effective minimally-invasive glaucoma treatment option that reduces or precludes the need for pharmacological support.

Ethical approval

This study was conducted under the auspices of the Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients before the procedure.

Conflict of interests

Apart from receiving study funding from Transcend Medical, no author has any conflict of interest, financial or otherwise, to declare.

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