

Mid-term Clinical Results of CO₂ Laser-assisted Sclerectomy Surgery (CLASS) for Open-Angle Glaucoma Treatment

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Purpose: To evaluate the efficacy and safety of CO₂ Laser-assisted Sclerectomy Surgery (CLASS) in primary and pseudoexfoliative open-angle glaucoma.

Materials and Methods: Single-arm, open-label study included data from 9 medical centers located in 7 countries. Subjects underwent nonpenetrating CLASS procedure with a CO₂ laser system (IOPtiMate). Intraocular pressure (IOP) and number of medications were measured at baseline, 1, 2, 4, and 6 weeks, and 3, 6, 12, 24, and 36 months. Complete success was defined as $5 \leq \text{IOP} \leq 18$ mm Hg and at least 20% IOP reduction with no medications, and qualified success as the same with or without medications at 12, 24, and 36 months.

Results: A total of 111 consecutive eyes were enrolled in the study, 14 were excluded from the study due to protocol deviation or operator error. The mean age was 69.3 ± 12.8 and 73.9% were whites. Percent change in IOP from baseline at 1, 2, and 3 years was, respectively, 45.1%, 46.8%, and 42.5% ($P < 0.001$). Complete success rates after 12, 24, and 36 months were 60.2%, 57.9%, and 47.8%, respectively. Qualified success rates after 12, 24, and 36 months were 79.6%, 91.2%, and 84.8%, respectively. Number of medications dropped from 2.39 ± 1.24 to 0.47 ± 0.84 , 0.53 ± 0.75 , and 0.71 ± 0.89 at 12, 24, and 36 months, respectively ($P < 0.001$).

Conclusions: The CLASS procedure may be a simple and effective treatment for open-angle glaucoma providing extended relief of elevated IOP.

Key Words: glaucoma, filtration, laser surgery, MIGS, CLASS

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Open-angle glaucoma (OAG) is a progressive optic neuropathy, resulting in loss of retinal ganglion cells often leading to progressive damage of the visual field and

blindness.¹ Elevated intraocular pressure (IOP) is a major risk factor for glaucoma and it has been confirmed that reduction of IOP is effective in slowing the disease progression.^{2–5} The individualized setting of a target pressure at which the disease is unlikely to progress is now a key element of glaucoma treatment⁶ and this may be achieved pharmacologically or surgically (lasers or incisional). Trabeculectomy is associated with numerous possible complications, including infection, inflammation, bleb leak, bleb encapsulation, hypotony, cataract, and even vision loss.⁷ Therefore, most ophthalmologists are reluctant to use it as an early intervention⁸ and surgery is usually performed when IOP control is not achieved by medications or laser treatment.⁹ Trabeculectomy, the traditional glaucoma surgery, has hardly evolved since first being described and involves a relatively high complication rate.^{8,10} Glaucoma drainage devices offer an alternative to trabeculectomy in some of the cases, but involve an extensive surgery with a considerable complication rate as well.^{8,10} Nonpenetrating filtration surgery (NPFS) is associated with lower rates of complications, whereas conflicting results exist regarding its efficacy when compared with penetrating surgery.^{11–13} A well-described disadvantage of these procedures is the necessity of high skills and a long learning curve.^{14–16} Perhaps for that reason it did not gain popularity among glaucoma surgeons.

CO₂ Laser-assisted Sclerectomy Surgery (CLASS) was first suggested by Assia et al¹⁷ as a means of simplifying filtration surgery. Advantages of introducing this laser technique as part of the surgical procedure are the CO₂ laser-associated photoablation of dry tissue and coagulation of bleeding vessels, as well as the effective absorption of laser energy by any water or aqueous solution present, even if minimal.¹⁸

Preliminary studies of CLASS in animals and in human cadaver eyes, as well as pilot clinical studies of CLASS with the first model of the CO₂ laser system, OT-133, have demonstrated its efficacy in achieving fluid percolation with significant IOP reduction and a low perforation rate.¹⁷ The safety and performance of a second-generation device for CLASS procedure (OT-134, “IOPtiMate”; IOptima Ltd, Tel Aviv, Israel), utilized in conjunction with a micromanipulating system, was tested in experimental models.¹⁸ The studies confirmed that the novel CLASS technique is a relatively simple and effective operation requiring a short learning curve. Following pre-clinical trials using the OT-134, the safety and efficacy of CLASS technique in lowering IOP were tested in clinical trials in primary open-angle glaucoma (POAG) and in pseudoexfoliative glaucoma (PXFPG). From the preliminary results of the first 37 patients in 3 sites, our group published that the procedure is safe and efficient in lowering IOP.¹⁹ The purpose of the current report is to describe additional

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patients and the mid-term results of the CLASS procedure as studied in 9 sites around the world.

MATERIALS AND METHODS

Throughout the first year the study was conducted prospectively and data beyond the first year were collected retrospectively.

This was an open-label, multinational, multicenter clinical research study, conducted in accordance with the Declaration of Helsinki with the approval of the Human Research Committee of the participating medical centers with applicable regulations pertaining to Good Clinical Practice. All participating patients or their legal guardians signed an informed consent document before enrollment. The clinical trials were carried out in 9 medical centers located in 4 different continents between December 2007 and February 2011: Mexico City, Mexico (Drs Gil-Carrasco and Turati), Madanapalle, India (Drs Thomas and Naveen), Moscow, Russia (Dr Anisimova), Ancona, Italy (Dr Mariotti), Valencia, Spain (Dr Muñoz), Genève, Switzerland, (Dr Shaarawy), Lausanne, Switzerland, (Dr Mermoud), Ramat Gan, Israel (Dr Melamed), and Kfar Saba, Israel, (Dr Geffen).

Patients were recruited and eligible candidates were adults (18 y old or older) of both sexes, with POAG or PXFG in the eye scheduled for surgery (only 1 eye included for each participant). Criteria for glaucoma diagnosis were an open-angle and glaucomatous appearance of the optic nerve head, including thinning or notching of the neuroretinal rim, accompanied by localized or diffuse retinal nerve fiber layer loss, cup/disc ratios being higher vertically as compared with horizontally, and a correlating typical glaucomatous visual field loss. Primary filtration surgery was indicated in each participant, all of whom were on maximal tolerated ocular hypotensive medications and had an IOP in the study eye of 18 mm Hg or higher, as measured with a Goldmann applanation tonometer during 3 consecutive visits over a 90-day period before enrollment. Additional inclusion criteria were a phakic or pseudophakic study eye with no other ocular disorders other than cataract, and no prior surgical or laser intervention in the study eye other than uneventful clear corneal incision cataract surgery with posterior intraocular lens implantation.

Excluded from the trial were patients with a history of previous intraocular surgery other than clear corneal cataract extraction, a history of ocular laser procedures, or a history of severe eye trauma. Patients with any media opacity that may interfere with optic nerve evaluation were excluded, as well as individuals with a pupillary dilation diameter of <2 mm, patients with a best-corrected visual acuity of $\leq 20/200$ in the fellow eye, candidates with known allergy to the study medications, severe systemic disease or disabling conditions, and pregnant or nursing women. Patients in which the surgical procedure deviated from protocol were excluded from the efficacy analysis although included in the safety analysis. Data from participants who were followed up for <3 months were excluded from the efficacy analysis although included in the safety analysis.

Throughout the first year the study was conducted prospectively and all patients at all 9 sites underwent a baseline examination within 2 weeks before surgery, and 1 day, 1, 2, 4, and 6 weeks, and 3, 6, and 12 months following surgery. Patient data regarding follow-up visits at 24

months ± 4 weeks and 36 months ± 4 weeks were retrospectively collected from 7 out of 9 sites as well.

Baseline examination included refraction, best-corrected visual acuity measured with a Snellen chart, comprehensive biomicroscopy, IOP assessment with a calibrated Goldmann applanation tonometer (average of 3 repeated measurements taken at the same time of the day ± 1 h), and fundus examination including optic disc evaluation. Patients also underwent gonioscopy, assessment of central corneal thickness (average of 3 repeated measurements), and 3 consecutive threshold 24-2 Humphrey perimetry tests, the last of which was performed within 2 weeks before surgery.

Complications, both intraoperative and postoperative (early, through day 7, and late, beyond 1 wk), were classified according to severity and their relationship to the studied device. Also recorded was the incidence of intraoperative macroperforations, defined as perforations accompanied by iris prolapse or intraoperative anterior chamber shallowing or both. Microperforations, in contrast, were defined as small trabeculo-Descemet holes with no loss of depth of the anterior chamber, and no iris prolapse as such were not considered to be an adverse event.

All patients underwent a CLASS procedure using the same surgical technique previously described by us (Fig. 1).¹⁹ Combining the CLASS procedure with additional surgery (eg, cataract surgery) was forbidden and the surgeons were instructed accordingly. The surgical technique involves a scleral flap creation followed by repeated laser applications, which cause progressive ablation of thin layers of scleral tissue until aqueous percolation is achieved. The percolating fluid absorbs the laser energy, preventing it from reaching the remnant sclera. The ablation therefore stops and penetration through the remaining thinned scleral wall is avoided. Application of mitomycin C (MMC), its concentration (0.02% to 0.04%), and duration (1 to 3 min) were left to the surgeon's discretion. Surgeons were permitted to convert to conventional trabeculectomy at any stage of the operation according to their judgment. Spacer implants were not placed underneath the scleral flap. Patients were treated postoperatively with prednisolone acetate 1% drops (Pred Forte; Allergan, Irvine, CA) 6 times daily for at least 4 weeks and moxifloxacin 0.5% drops (Vigamox; Alcon Laboratories, Fort Worth, TX) 4 times daily for 2 weeks. Any further treatment was left to the surgeon's discretion.

Postoperative Safety Analysis

Safety issues were determined in terms of device malfunctions, device-related macroperforations, or all other procedure-related adverse events. To properly assess the safety of the CLASS procedure, any patient who underwent CO₂ laser treatment was included in the safety analysis. Therefore, patients who experienced perforation by knife and underwent trabeculectomy (without ever being exposed to CO₂ laser) were not included in the safety or efficacy analysis.

Postoperative Efficacy Analysis

"Complete success" was defined as IOP values measured at the 12, 24, and 36 months visit ranging between 5 and 18 mm Hg and IOP reduction $\geq 20\%$ as compared with baseline IOP without hypotensive medications or repeat surgery. The same parameters, but including also subjects who required hypotensive medications postoperatively, were

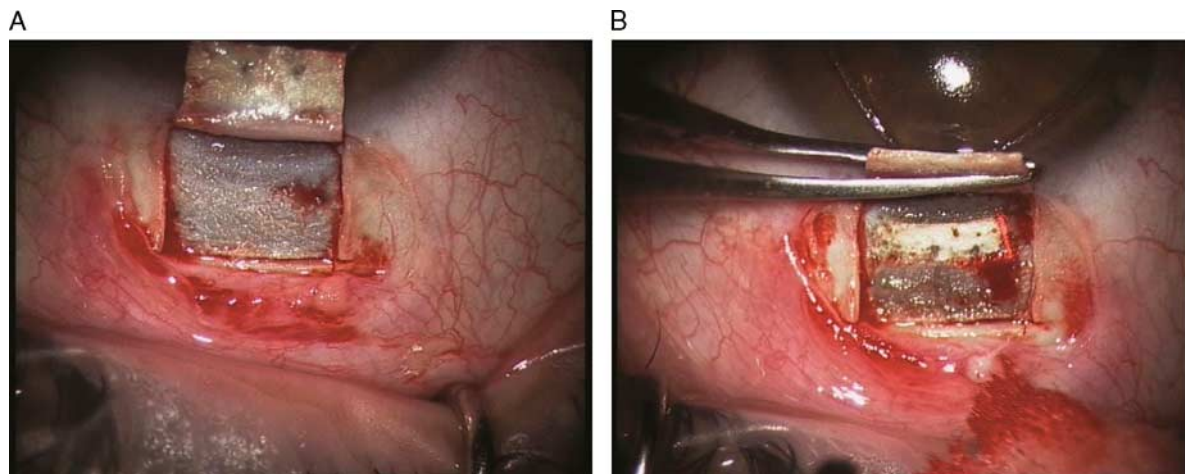


FIGURE 1. Surgical steps. A, A partial thickness (one third to one half) rectangular limbal-based 5 × 5-mm superior scleral flap was dissected at the limbus into the clear cornea. B, Ablation has been initiated over Schlemm's canal.

defined as “qualified success.” Failure was defined as an IOP value ≤ 5 or > 18 mm Hg, IOP reduction of $< 20\%$ as compared with baseline IOP, severe loss of vision, intraoperative device-related macroperforations, or the need to undergo additional glaucoma procedures other than goniopuncture or bleb needling. Goniopuncture and bleb needling revision were not considered to be failures or adverse events, as both are commonly used post-NPFS interventions to maintain or augment the operative results.^{20–22} The number of hypotensive medications being used by each patient at each visit was compared with the baseline situation.

Statistical Methods

Statistical analyses were performed using statistical program SAS version 9.1 (SAS Institute, Cary, NC). Data are presented as mean \pm SD or median (range) as appropriate for continuous variables or as n (%) for categorical variables. The change in IOP from baseline at each follow-up evaluation was analyzed using repeated measures ANOVA (analysis of variance) and then further analyzed with Student *t* tests with the conservative Bonferroni correction for multiple comparisons. In addition, repeated measurement analyses (MMRM) for IOP measures adjusted for use of MMC and needling/goniopuncture procedures were performed. Kaplan-Meier life-table curves for efficacy were built to demonstrate the duration of success as previously defined.

RESULTS

Overall, 111 consecutive eyes of 111 subjects were enrolled. Of those 108 were included in the safety analysis and 97 for efficacy analysis. The mean age was 69.3 ± 12.8 years and 55.9% (n = 62) were of male sex. POAG was the diagnosis in 76.6% of the cases and PXFG in the rest. This heterogeneous group consisted of white (73.9%), Hispanic (12.6%), Indian (11.7%), and African (1.8%) subjects. The mean C/D ratio was 0.8 ± 0.14 and the mean CCT 546.8 ± 33.9 μ m.

Three patients were excluded from safety analysis due to perforation by knife without any CLASS treatment. Fourteen patients were excluded from the efficacy analysis for the following reasons: perforation by surgical knife

(n = 3), a thick scleral flap created with a knife (more than one half of scleral thickness) followed by a macroperforation (n = 2), a thin scleral flap (less than one third of scleral thickness) (n = 1), narrow angles (n = 4), prior laser iridectomy (n = 1), and an insufficient follow-up period (n = 3). Two of the 3 patients with an insufficient follow-up period were lost to follow-up (4 and 6 wk after the procedure) and the third died 4 weeks after the procedure, from causes unrelated to the glaucoma surgery (complications of longstanding severe diabetes mellitus).

Safety Analysis

Data on all 108 enrolled participants who received CLASS treatment (exposed to CO₂ laser) were used in the analysis of safety outcomes. No technical device malfunctions occurred. There were 5 CLASS procedure-related macroperforations (4.6% of patients) that occurred as a result of excessive scleral tissue ablation. The recorded complications in this study are presented in Table 1.

The following complications required surgical interventions: 2 patients with bleb leaks underwent revision of the blebs, 2 patients with choroidal detachments underwent choroidal effusion drainage, 6 patients with incarcerated iris underwent successful Nd:YAG laser iridoplasty, and another 3 required iris repositioning. One patient who was diagnosed with malignant glaucoma was treated with pars plana vitrectomy and 1 patient with peripheral anterior synechia underwent synechiolysis. One patient lost 4 Snellen lines due to macular edema associated with post-operative hypotony resulting in permanent retinal damage. The rest of the complications were mild, treated conservatively, and resolved shortly after. Shallow diffuse blebs were observed with no late bleb-related complications.

Efficacy Analysis

Ninety-seven subjects were included in the final efficacy analysis. The preoperative IOP of 25.8 ± 5.4 mm Hg (mean \pm SD) dropped to 13.5 ± 3.8 , 13.5 ± 4.1 , 13.0 ± 3.1 , and 14.2 ± 2.9 mm Hg at 6, 12, 24, and 36 months, respectively (Fig. 2). The mean percent IOP reduction at 6, 12, 24, and 36 months was $45.8\% \pm 16.8\%$ (95% CI, 42.24–49.40), $45.1\% \pm 19.5\%$ (95% CI, 40.8–49.38), $46.8\% \pm 15.5\%$ (95% CI, 42.48–51.04), and $42.5\% \pm 14.4\%$ (95% CI, 38.0–47.1),

TABLE 1. Procedure-related Complications

Complications	N (%)
Early bleb leak*	9 (8.3)
Iris incarceration	9 (8.3)
Peripheral anterior synechia	6 (5.6)
Shallow anterior chamber	6 (5.6)
HypHEMA	5 (4.6)
Corneal complications†	4 (3.8)
Choroidal detachment	3 (2.8)
Hypotony	3 (2.8)
Malignant glaucoma	2 (1.9)
Macular edema	1 (0.9)
Reduced visual acuity‡	1 (0.9)

*Early bleb leak: diagnosed at the early postoperative period (up to 1 wk from surgery).

†Corneal complications recorded included dellen and superficial punctate keratopathy.

‡Reduced visual acuity: loss of ≥ 2 Snellen lines as documented on 2 consecutive visits 3 months postsurgery.

respectively ($P < 0.001$). The patterns of IOP reduction were similar in all 9 surgical centers.

The complete success rates (defined as $5 < \text{IOP} \leq 18$ and $\geq 20\%$ IOP reduction without a need for postoperative hypotensive medications) after 12, 24, and 36 months were 60.2% (95% CI, 0.50-0.70), 57.9% (95% CI, 0.44-0.71), and 47.8% (95% CI, 0.33-0.63), respectively. The qualified success rates (also defined as $5 > \text{IOP} \leq 18$ and 20% IOP reduction or more but with a need for postoperative hypotensive medications) after 12, 24, and 36 months were 79.6% (95% CI, 0.70-0.87), 91.2% (95% CI, 0.81-0.97), and 84.8% (95% CI, 0.71-0.94), respectively. Kaplan-Meier survival curves for probability of CLASS success, censored for time of loss, are presented in Figure 2.

MMC was used in 88.8% of the procedures at a concentration of 0.02% to 0.04% for duration of 1 to 3 minutes. The complete success rates with and without MMC at 12, 24, and 36 months were 62% (51/82) versus 64% (7/11) ($P = 0.81$), 62% (33/53) versus 0% (0/5) ($P = 0.03$), and 52% (22/42) versus 0% (0/4) ($P = 0.14$), respectively. The qualified success rates with and without MMC at 12, 24, and 36 months were 78% (64/82) versus 82% (9/11) ($P = 0.92$), 91% (48/53) versus 80% (4/5)

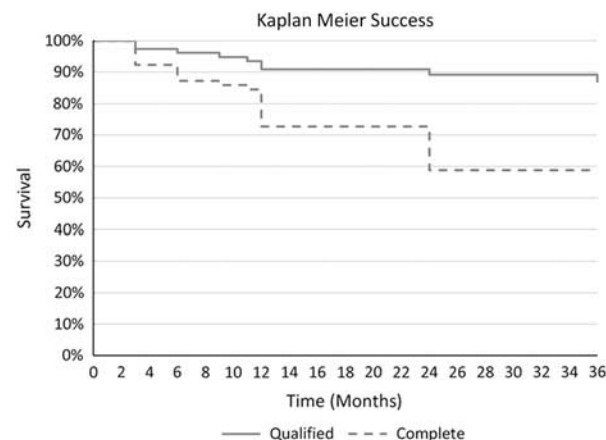


FIGURE 2. Kaplan-Meier curves of the 3-year survival, censored for time of loss.

($P = 0.97$), and 86% (36/42) versus 75% (3/4) ($P = 0.87$), respectively.

The preoperative use of hypotensive medications per patient significantly dropped from an average of 2.39 ± 1.24 to 0.47 ± 0.84 , 0.53 ± 0.75 , and 0.71 ± 0.89 at 12, 24, and 36 months, respectively ($P < 0.001$).

Goniotomy was performed in 18 (18.5%) patients. Needling was performed in 12 (12.4%) patients. Goniotomy and bleb needling procedures were performed in the first year of the study and no procedure-related complications were reported.

In the repeated measurement analysis of IOP, adjusted for the use of MMC and any needling/goniotomy, the reduction in IOP at all time points when compared with baseline was significant ($P < 0.001$).

DISCUSSION

Glaucoma is the second leading cause of blindness worldwide and affects approximately 70 million people.^{23,24} Reduction of IOP is the only proven method to treat the disease. Treatment includes ocular hypotensive drops, laser trabeculoplasty, and surgery. The search for the optimal glaucoma surgical treatment has led to a spectacular revolution in recent years and has changed the paradigm of surgical glaucoma treatment. Trabeculectomy with MMC and tube-shunt surgery are viable surgical options for managing glaucoma but both may be accompanied with possible complications and failure.²⁵ NPFS is another surgical option. The justification for NPFS procedures is based on a greater safety profile when compared with trabeculectomy,²⁶ thus NPFS may be an appropriate option for patients at high risk of developing complications.⁴ A recent systematic review by the Cochrane Eye and Vision Group comparing NPFS versus trabeculectomy for OAG reported that control of IOP is better with trabeculectomy than some of the NPFS procedures such as viscocanalostomy although the data regarding deep sclerectomy was inconclusive.¹¹ This may reflect surgical difficulties in performing nonpenetrating procedures and the need for surgical experience.

As the ideal surgical solution for glaucoma has yet to be found, many research groups around the globe are trying to develop novel techniques and devices that require a short learning curve, aiming for a higher safety profile, rapid recovery, and higher efficacy. New procedures and devices collectively termed minimally invasive glaucoma surgery (MIGS) pursue the goal of reducing IOP with the lowest possible rate of complications, attempting to overcome those inherent to conventional surgery.²⁷ However, many of the MIGS procedures produce only a limited IOP reduction and are reserved for use in glaucoma patients with early to moderate disease and are often combined with cataract surgery.²⁸ In addition, some of the MIGS require a significant learning curve of its performers.²⁹

The CLASS procedure attempts to overcome some of the safety issues related to penetrating procedures such as trabeculectomy and tube-shunt surgery while achieving adequate IOP control, better than the one achieved using NPFS and currently available MIGS.

The CO₂ laser is the most commonly used laser in laser-assisted operations.³⁰ It has been utilized for tissue dissection in filtration procedures using either a continuous-wave or a rapid super-pulse mode.³¹

This multinational study of 111 eyes found CLASS to be relatively safe and effective procedure for the treatment of OAG. No device malfunctions occurred.

Although this was an open-label series of consecutive procedures, we can compare the outcome with data available in the literature for trabeculectomy. According to the Cochrane systematic review the reported adverse events rates were 17% and 65% in the NPFS and trabeculectomy groups, respectively.¹¹ Two adverse events reported by all of the studies included in the Cochrane review were hyphema and hypotony. The reported rates of hyphema in the review were 4.6% and 13% and those of hypotony were 2.6% and 15.6% in the NPFS and trabeculectomy groups, respectively. The rates of hyphema and hypotony in our study were 4.6% and 2.8%, respectively, therefore much lower than in trabeculectomy and similar to those of the NPFS.

Macroperforation rate in our study was 4.6% and cases were successfully converted to trabeculectomy. The rate of macroperforation in NPFS varies greatly as during the initial learning phase a surgeon can expect a 30% perforation rate, which after experience may be lowered to approximately 3%.²⁶ It is worth noting that the CLASS procedure also has a learning curve, and that in this study we report results of surgeons who performed the procedure while at the beginning of their learning phase.

A relatively high rate of iris incarceration was witnessed in this study (9 cases accounting for 8.3%). Six of these cases (5.6% of total adverse events and 67% of the specific events) occurred in the same site (40% of the 15 subjects operated in that site), and may have been a result of the surgeon's technique. Also, in this specific site, gonioscopy was performed on the first day following surgery, which may also have contributed to the high rate of iris incarceration.

All incarcerations recorded in that site were successfully treated with YAG laser iridoplasty. The other 3 incarcerations that were recorded in the other sites (3.2% of the 93 subjects operated in the other 8 centers) were successfully treated with surgical iris repositioning. Previous studies have reported iris incarceration to occur in 0% to 5.5% of eyes undergoing NPFS.^{11,32}

Despite the potential advantages of the high safety profile provided by NPFS procedures,²⁶ there are contradictory reports regarding their efficacy, specifically when compared with trabeculectomy.^{11,33} A systematic review for the US Preventive Task Force reported that trabeculectomy decreases IOP better than NPFS procedures.³³ In the current study, the reduction in average IOP, from 25.8 ± 5.4 mm Hg at baseline to 13.5 ± 4.1 , 13.0 ± 3.1 , and 14.2 ± 2.9 mm Hg at 12, 24, and 36 months following CLASS procedure, are comparable with those of 3 large studies reporting the efficacy of trabeculectomy.^{7,34} The National Survey study reported a 42.8% reduction in IOP at 12 months following trabeculectomy⁷ and Kirwan et al³⁴ reported a reduction in average IOP from 23 ± 5.5 mm Hg at baseline to 12.4 ± 4 mm Hg at 24 months following trabeculectomy. Finally, the Tube Versus Trabeculectomy study reported a reduction in average IOP from 25.6 ± 5.3 mm Hg at baseline to 13.5 ± 6.9 mm Hg at 36 months following trabeculectomy.³⁵

In this study the complete success rate after 12, 24, and 36 months were 60.2%, 57.9%, and 47.8%, respectively, and the qualified success rates were 79.6%, 91.2%, and 84.8%, respectively. The complete success after 24 months

was lower than reported by Kirwan and colleagues following trabeculectomy when using similar criteria (78% reported by Kirwan and colleagues vs. 57.9% in this study). However, the qualified success rate of the CLASS procedure after 24 months was higher (86% vs. 91.2%).³⁴

In this study, the number of hypotensive medications dropped from a baseline average of 2.4 ± 1.2 to 0.5 ± 0.7 to 0.71 ± 0.89 at 24 and 36 months of follow-up ($P < 0.001$). These results resemble those of Netland and colleagues who reported a drop in the use of hypotensive medications from 3.2 ± 1.1 to 0.7 ± 1.2 at 24 months posttrabeculectomy and those of the Tube Versus Trabeculectomy study that reported a drop from 3.2 ± 1.1 to 1.3 ± 1.3 at 24 and 36 months posttrabeculectomy.^{35,36}

Previous studies have demonstrated the need for a long learning curve when performing NPFS procedures and the limitations of comparing first cases of NPFS with trabeculectomy.¹⁶ Jonescu-Cuyper et al¹⁴ initially reported a success rate of 0% with viscocanalostomy. In a subsequent study of viscocanalostomy, the same group reported a success rate of 30%.¹⁵

The relatively high success rates of our multicenter study that included all surgeries, including the first CLASS procedures performed by most surgeons participating in the study, are an indication of the short learning curve. It is interesting to note the similarity in pressure profile at the various sites. Postsurgery IOP pattern was similar in Hispanic eyes in Mexico, Asian eyes in India, and white eyes in 7 centers in Europe and Israel.

In the current study the MMC group demonstrated significantly higher complete success rates at 24 months ($P = 0.02$) and a nonsignificant trend toward higher success rates at 36 months ($P = 0.14$) as compared with the non-MMC group although the non-MMC group was very small and probably too small for comparison. At both 24 and 36 months follow-up, none of the eyes in which MMC was not applied achieved complete success. This is supported by other publications that have shown that intraoperatively applied MMC during NPFS procedures results in a lower IOP levels and better success rates.^{37,38}

Laser goniopuncture is most frequently associated with nonpenetrating surgery, as an attempt to augment filtration by converting it to a full-thickness procedure with rupture of the trabeculo-Desemet membrane.³⁹ Possible complications of goniopuncture include hypotony, hyphema, peripheral anterior synechia, iris prolapse, and choroidal detachment.^{40,41} The overall rate of goniopuncture in this study was relatively low (18.5%). In a study comparing deep sclerectomy with collagen implant versus trabeculectomy, Ambresin et al⁴² reported performing goniopuncture in 45% of the deep sclerectomy patients.

The main limitation of this study is the absence of a control group, the lack of a control arm in this study precluded subjects' randomization and treatment masking; thus, a direct comparison with the standard-of-care procedure could not be performed. An additional limitation of this study is the loss to follow-up, which reached 58% at 3 years and may have led to selection bias. However, as a patient with uncontrolled glaucoma is more likely to seek medical help or advice than one whose glaucoma is successfully controlled, we feel that such a bias would have been more likely to have underestimated the efficacy of CLASS than to overestimate. Another limitation is that patient data at 24 and 36 months were collected retrospectively further

contributing to the loss to follow-up and potential selection bias. Finally, visual field deterioration was not reported as an outcome of this study.

Therefore, prospective, masked, long-term randomized controlled clinical trials comparing the CLASS procedure to other currently used procedures are required to further evaluate and substantiate the procedure.

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