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ORIGINAL RESEARCH

Comparison of Long-Term Effects After Modified CO_2 Laser-Assisted Deep Sclerectomy and Conventional Trabeculectomy in Chinese Primary Open-Angle Glaucoma

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ABSTRACT

Introduction: To compare the long-term effect after modified CO_2 laser-assisted sclerectomy surgery (MCLASS) and conventional trabeculectomy (TRAB) in medically uncontrolled Chinese primary open-angle glaucoma (POAG) patients.This was a retrospective comparative study.

Methods: A total of 87 patients were reviewed, including 45 in the MCLASS group and 42 in the TRAB group. Intraocular pressure (IOP), best-corrected visual acuity (BCVA), and use of supplemental medical therapy were retrospectively compared at baseline, and until 36 months postoperatively.

Results: Patients in both groups achieved a significant IOP decrease from baseline ($P < 0.001$); postoperative IOP in the MCLASS group was significantly lower than that in the TRAB group at 24 and 36 months. The reduced use of medication was statistically significant in both groups, and the number of postoperative medications was significantly more in TRAB group at 24 and 36 months. At 24 and 36 months, the complete success rate was 60% and 53.3% for MCLASS versus 66.7% and 59.5% for TRAB, and the qualified success rate was 91.1% and 88.9% for MCLASS versus 83.3% and 80.9% for TRAB, respectively. BCVA deterioration post TRAB was clinically more serious than that post MCLASS at 24 and 36 months, although the difference was not statically significant at any time point postoperatively. Compared with MCLASS, more complications occurred postoperatively in the TRAB group.

Conclusions: MCLASS is an effective surgical option for Chinese POAG patients. Compared to TRAB, eyes undergoing MCLASS experience a comparable success rate, a greater IOP reduction, fewer medications, and a lower risk of complications up to 36 months.

Keywords: CO_2 laser; Laser surgery; Nonpenetrating deep sclerectomy; Primary open-angle glaucoma; Trabeculectomy

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Key Summary Points

In this study, we found that, compared with conventional trabeculectomy (TRAB), modified CO2 laser-assisted sclerectomy surgery (MCLASS) showed greater intraocular pressure (IOP) reduction.

Compared with TRAB, after MCLASS, patients needed fewer medications.

Compared with TRAB, MCLASS showed similar success rates, but with much lower risk of complications.

MCLASS is an effective surgical option for Chinese primary open-angle glaucoma (POAG) patients.

INTRODUCTION

Since the introduction of Cairns's trabeculectomy (TRAB) in 1968 [1], it has become a widely used treatment in all types of glaucoma. It is still considered to be the gold standard procedure for lowering intraocular pressure (IOP) in patients with primary open-angle glaucoma (POAG). However, this procedure carries a range of potential complications, such as hypotony, hyphema, anterior chamber flattening, choroid detachment, accelerated cataract progression, macular edema, decompression retinopathy, leakage, and infection of the filtration bleb, and some of those may even be sight-threatening [2].

There has recently been renewed interest in nonpenetrating deep sclerectomy (NPDS) for glaucoma [3–5]. NPDS was developed to overcome the severe complications and to improve the safety of conventional filtering procedures, by keeping the inner wall of the trabecular meshwork (TM) intact and by stabilizing the anterior chamber and preventing fluctuation in the IOP [6]. However, the main drawback of NPDS lies in the technical difficulty, which has prevented this technique from gaining popularity among glaucoma surgeons. The most common intraoperative complication of this surgery is perforation of the thin trabeculo–Descemet's membrane during deep sclerectomy dissection. CO_2 laser-assisted sclerectomy surgery (CLASS) is an improved version of the difficult manual procedure of NPDS that uses the unique characteristic of CO_2 laser to ablate only the dry scleral tissue in a precise and efficient manner. Once the outer wall of Schlemm's canal (SC) is opened, the CO_2 laser becomes ineffective due to aqueous percolation; consequently, excessive tissue ablation is prevented and the inner wall of the SC is kept intact, avoiding penetration into the anterior chamber [7].

Considering the refractory and scarring characteristics and the specific anatomical features of the anterior chamber in East Asians (including Chinese), we designed a modified CLASS procedure (MCLASS) combined with a preventive laser iris management, including laser peripheral iridotomy (LPI) and argon laser peripheral iridoplasty (ALPI), to prevent iris incarceration and peripheralanterior synechiae (PAS) after surgery, and we demonstrated its long-term efficacy and safety for Chinese POAG patients in our earlier study [8]. Thus far there have been few studies comparing long-term outcomes after CLASS and trabeculectomy. In view of the paucity of existing studies, we designed the current study to compare the efficacy and safety of TRAB with the MCLASS procedure combined with preventive laser iris management in Chinese patients with medically uncontrolled POAG, over the long term.

METHODS

This was a single-center retrospective comparative study. The study protocol was approved by the Institutional Review Board of the Peking Union Medical College Hospital (PUMCH) and was performed according to the tenets of the Declaration of Helsinki.

Forty-five POAG patients who underwent MCLASS and 42 POAG patients who underwent TRAB procedures from 2010 to 2018 were enrolled and followed up postoperatively up to

36 months. Inclusion criteria included IOP out of control despite maximum tolerated doses of pharmacological agents, glaucomatous optic nerve morphology, open angle under gonioscopy, and progressive visual field (VF) loss. Patients were excluded for the following: presence of eye trauma or inflammation, presence of an opacity that might interfere with optic nerve evaluation, other reasons for IOP increase, or previous eye surgery.

Baseline examinations within 2 weeks before surgery and follow-up examinations at 1 week and at 1, 3, 6, 12, 24, and 36 months after surgery were recorded, including best-corrected visual acuity (BCVA), IOP determined with a calibrated Goldman applanation tonometer, slit lamp, and eye fundus. The number of antiglaucoma medications and postoperative complications was also recorded. The inner wall of the TM was assessed by gonioscopy at each follow-up visit. Postoperative ultrasound biomicroscopy (UBM) was performed at 1, 3, 12, 24, and 36 months.

"Complete success" was defined as IOP values ranging between 5 and 18 mmHg and a reduction of $\geq$ 20% without the need for additional hypotensive medications or reoperation for glaucoma. "Qualified success" was defined as the same outcome but including patients who required hypotensive medications postoperatively.

Surgical Technique

Operations were generally performed under surface anesthesia with oxybuprocaine hydrochloride eye drops and subconjunctival anesthesia in the operative field with 2% lidocaine without epinephrine. The patients with a VF radius no greater than 10° or cup-to-disc area ratio $\geq$ 0.9 were performed under general anesthesia.

MCLASS Procedure

MCLASS was performed following the technique described in our earlier study [8]. Gonioscopy was used to evaluate the superior angle. The preferred gonio position was marked for the planned scleral ablation area, where all eyes underwent broad-based peripheral LPI and ALPI surrounding the LPI hole within 1–3 days preoperatively. A superior fornix-based conjunctival flap was created and the Tenon capsule was dissected to expose the sclera. We then created a 5 $\times$ 5 mm rectangular limbal-based flap, of one third to one half partial thickness, and extended by 1 mm into the clear cornea. The CO_2 laser beam was first applied over the posterior scleral bed to create a deep rectangular scleral lake (4 $\times$ 2.2 mm), and was then applied over the surgical limbus to unroof the area of the SC (4 $\times$ 1.5 mm). Lastly, the CO_2 laser beam was moved forward to ablate a 4 $\times$ 1 mm area in trabeculo–Descemet's window (TDW). Following laser ablation, the scleral flap was repositioned and fastened with two adjustable sutures using 10/0 nylon at the top corners. The conjunctiva was secured using buried 10/0 nylon sutures.

TRAB Procedure

TRAB was performed according to the technique described by Cairns. A superior fornix-based conjunctival flap was created to expose the sclera. A one-third-thickness limbal-based 4 $\times$ 4 mm scleral flap was dissected. A block of tissue 1 $\times$ 2 mm was removed just anterior to the scleral spur to enter the anterior chamber, followed by a peripheral iridectomy. The superficial flap was repositioned and sealed with two fixation sutures and two adjustable sutures (10/0 nylon); the conjunctiva was closed with 10/0 nylon sutures to maintain a watertight seal.

Mitomycin C (MMC) was applied by soaked sponges under the scleral flap and conjunctiva in both TRAB and MCLASS groups. If an adequate bleb was not formed or the target pressure was not reached, adjustable sutures were removed earlier within the first 2 weeks after surgery to maintain a smooth outflow during the scar formation stage.

Postoperatively, patients were treated in both groups with 1% prednisolone acetate drops (Pred Forte; Allergan, Irvine, CA) six times daily, and the dose was tapered for at least 4 weeks; the patients also received ofloxacin ophthalmic solution (Santen Pharmaceutical Co., Osaka, Japan) four times daily for 3 weeks.

In the MCLASS group, 2% pilocarpine was administered each night for at least 4 weeks. In the TRAB group, atropine three times daily was added for 1–4 weeks.

In the MCLASS group, if the IOP exceeded 21 mmHg and a severe reduction in the size of the scleral lake was detected by UBM after the procedure, subconjunctival and subscleral 5-fluorouracil (5-Fu; 0.2 mL, 25 mg/mL) was injected. After excluding internal obstacles arising from severe PAS or iris incarceration, laser goniopuncture (LGP) was performed with a Microruptor II neodymium:yttrium–aluminium–garnet (Nd:YAG) laser when IOP exceeded the target level owing to insufficient aqueous percolation through the SC and TDW.

In the TRAB group, postoperative ocular digital massage was carried out when the anterior chamber was formed and IOP was > 12 mmHg. In the case of IOP elevation above 21 mmHg and a filtering bleb that was encysted or showed signs of fibrosis, a needling procedure was carried out followed by a subconjunctival and subscleral injection of 5-Fu (0.2 mL, 25 mg/mL) at the trabeculectomy site.

Statistical Analysis

All analyses were performed using SPSS Statistics Premium v21 (IBM Corp., Armonk, NY, USA). Descriptive statistical results were presented as means ± standard deviation (SD), as medians and interquartile range for continuous variables, or as number and percentage for categorical variables. Data were tested for normality using the Kolmogorov–Smirnov test; parametric or nonparametric tests were then applied accordingly. Univariate associations between two categorical variables were analyzed using the chi-squared test or Fisher's exact test when any cell value was smaller than 5 in cross-tabulations. Mann–Whitney tests and *t* tests were used to compare continuous parameters between the two groups. Repeated measurements of quantitative variables were compared with paired *t* tests (for normally distributed differences in both groups) or Wilcoxon paired signed-rank tests (otherwise). The BCVA was expressed as the standard logarithmic value of VA and was converted to a logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Data were considered to be statistically significant when $P < 0.05$.

RESULTS

A total of 87 eyes of 87 patients were enrolled in the study; 45 eyes underwent MCLASS and 42 eyes underwent TRAB. There was no significant difference between the two groups in age, sex, baseline IOP, BCVA, proportion of VF, or number of preoperative antiglaucoma medications ($P > 0.05$; Table 1).

Patients in both groups achieved a significant IOP decrease from baseline ($P < 0.001$), with a lower IOP in the MCLASS group at 1 week post operation ($P = 0.001$); there was no significant difference between the two groups at 3, 6, and 12 months postoperatively. Postoperative IOP in the MCLASS group was significantly lower than that in the TRAB group at 24 and 36 months (Table 2). The mean IOP reduction fluctuation at 24 and 36 months was 50.7% (95% confidence interval [CI] 37.2–63.8) and 53.2% (95% CI 39.7–66.3) in the MCLASS group, compared to 47.5% (95% CI 36.3–59.3) and 40.0% (95% CI 26.8–53.2) in the TRAB group.

At 24 and 36 months postoperatively, the number of antiglaucoma medication taken per patient was reduced from 3–4 in both groups to 0–1 in the MCLASS group and 0–2 in the TRAB group ($P < 0.05$). There was a significant difference in the number of therapeutic medications taken when compared between the two groups at 24 and 36 months postoperatively (Table 3).

In the MCLASS group, the complete success rates after 24 and 36 months were 60.0% and 53.3%. The qualified success rates after 24 and 36 months were 91.1% and 88.9%. In the TRAB group, the complete success rates after 24 and 36 months were 66.7% and 59.5%, respectively. The qualified success rates after 24 and 36 months were 83.3% and 80.9%, respectively. There was no significant difference in the complete and qualified success rates between the groups at 24 and 36 months postoperatively ($P = 0.519$, 0.561, 0.275, 0.229, respectively).

Table 1 Demographic characteristics

	MCLASS	TRAB	*P* value
N (%)	45 (51.7%)	42 (48.3%)	
Male *N* (%)	25 (55.6%)	23 (78.6%)	0.556[a]
Age	55.1 ± 11.5	54.2 ± 13.5	0.425[b]
Pre-IOP (mmHg)	28.2 ± 9.6	29.5 ± 10.3	0.552[b]
Pre-medications	3.5 (3, 4)	3 (3, 4)	0.668[c]
Pre-Op BCVA (logMAR)	0.3 (0.1, 0.5)	0.2 (0.0, 0.5)	0.208[c]
Pre-Op VF			
Mild	6	9	0.318
Moderate	14	9	0.306
Advanced	25	24	0.881

MCLASS modified CO_2 laser-assisted sclerectomy surgery, *TRAB* trabeculectomy, *IOP* intraocular pressure, *BCVA* best-corrected visual acuity, *VF* visual field
[a]Chi-squared test
[b]*t* test (age and IOP are normally distributed in both groups)
[c]Wilcoxon two-sample test (medications are non-normally distributed in both groups)

Table 2 IOP at baseline, 1 week, and 3, 6, 12, 24, and 36 months following MCLASS and TRAB

IOP (mmHg)	MCLASS (mean ± SD)	TRAB (mean ± SD)	*P* value
Preoperatively	28.2 ± 9.6	29.5 ± 10.3	0.552
1 week	8.1 ± 3.2	11.1 ± 4.9	0.001
3 months	14.8 ± 5.5	13.1 ± 4.0	0.117
6 months	12.8 ± 3.3	14.1 ± 4.7	0.166
12 months	13.3 ± 2.7	14.6 ± 4.9	0.124
24 months	13.9 ± 2.5	15.5 ± 3.7	0.039
36 months	13.4 ± 2.9	17.7 ± 4.1	< 0.001

MCLASS modified CO_2 laser-assisted sclerectomy surgery, *TRAB* trabeculectomy, *IOP* intraocular pressure, *SD* standard deviation

In the TRAB group, the BCVA (logMAR) decreased significantly at 1 week and 12 months postoperatively, $P < 0.05$. Visual acuity returned to 0.3 (0.1, 1.0) at 24 and 36 months, with no significant difference from preoperative BCVA. In the MCLASS group, the BCVA (logMAR) decreased significantly from 0.3 (0.1, 0.5) to 0.7 (0.2, 1.0) at 1 week postoperatively ($P < 0.001$). Visual acuity returned to 0.2 (0.1, 0.6) within 12 months after surgery and remained stable over the following 36 months ($P > 0.05$) (Table 4). BCVA deterioration after TRAB seemed clinically more serious than that after MCLASS at 24 and 36 months. However, no statistically significant differences were

Table 3 Number of antiglaucoma medications before and after surgery in the MCLASS and TRAB groups

Glaucoma medications	MCLASS [median (Q1, Q3)]	TRAB [median (Q1, Q3)]	*P* value
Preoperatively	3.0 (3, 4)	3.5 (3, 4)	0.688
24 months	0 (0, 1)	1 (0, 1)	0.023
36 months	0 (0, 1)	1.5 (1, 2)	< 0.001

Wilcoxon paired signed-rank test between baseline and post-baseline values
MCLASS modified CO_2 laser-assisted sclerectomy surgery, *TRAB* trabeculectomy, *Q1* lower quartile, *Q3* upper quartile

Table 4 LogMAR BCVA at baseline, 1 week, and 12, 24, and 36 months postoperatively

BCVA (logMAR)	MCLASS [median (Q1, Q3)]	TRAB [median (Q1, Q3)]	*P* value
Preoperatively	0.3 (0.1, 0.5)	0.2 (0.0, 0.5)	0.208
1 week	0.7 (0.2, 1.0)	0.35 (0.1, 1.0)	0.148
12 months	0.2 (0.1, 0.6)	0.45 (0.2, 0.5)	0.237
24 months	0.2 (0.1, 0.6)	0.3 (0.1, 1.0)	0.472
36 months	0.25 (0.1, 0.6)	0.4 (0.1, 1.2)	0.059

BCVA best-corrected visual acuity, *MCLASS* modified CO_2 laser-assisted sclerectomy surgery, *TRAB* trabeculectomy, *Q1* lower quartile, *Q3* upper quartile

Table 5 Surgical complications associated with MCLASS or TRAB during the 36-month follow-up period

Complications	MCLASS *n* (%)	TRAB *n* (%)	*P* value
Hyphema	2 (4.4)	9 (21.4)	0.018
Hypotony	0	3 (7.1)	0.068
Shallow anterior chamber	0	4 (9.5)	0.034
Choroidal detachment	0	3 (7.1)	0.068
Iris incarceration	0	0	1.000
Macular edema	0	1 (2.4)	0.298
Peripheral anterior synechiae	8 (17.7)	8 (19)	1.000
Cataract development and progression	5 (11.1)	12 (28.6)	0.040
Endophthalmitis	0	0	1.000
Total number patients with complications	15 (33.3)	40 (95.2)	< 0.001

MCLASS modified CO_2 laser-assisted sclerectomy surgery, *TRAB* trabeculectomy

observed between the two groups at any of the time points postoperatively.

The overall rate of complications in the TRAB group was significantly higher than that in the MCLASS group (95.2% vs. 33.3%, $P < 0.001$; Table 5). In the TRAB group, all eyes received postoperative ocular digital massage, and subconjunctival injections of 5-FU were performed in 15 eyes (35.7%). Nine eyes (21.4%) suffered from early hyphema, seven eyes (16.7%) experienced filtering bleb leakage, four eyes (9.5%) developed flattening of the anterior chamber, three eyes (7.1%) suffered from choroidal detachment, three eyes (7.1%) were found to have postoperative hypotony accompanied by flat anterior chamber and choroidal detachment, filtering bleb fibrosis was observed in 13 eyes (30.9%), and cataract progression was seen in 12 eyes (28.6%) during the 36-month follow-up period.

In the MCLASS group, subconjunctival injections of 5-FU were performed in 12 eyes (26.7%). LGP was performed with the Nd:YAG laser in 21 eyes (46.6%). Two eyes (4.40%) suffered from early hyphema, eight eyes (17.70%) experienced PAS (six eyes were treated with Nd:YAG laser and two eyes received goniosynechialysis), filtering bleb fibrosis was found in five eyes (11.1%), and cataract progression was seen in five eyes (11.1%) during the 36-month follow-up period. Notably, no case was complicated by iris incarceration, bleb leak, or infection during the 36-month follow-up.

DISCUSSION

Conventional penetrating TRAB is associated with a high rate of postoperative complications. NPDS was developed as a safer and more acceptable surgical intervention for patients compared to conventional procedures; however, it has been reported to be technically more difficult [9, 10]. In more recent years, with the use of CO_2 lasers, CLASS has been implemented to overcome the technical difficulty and eliminate the prolonged learning curve which is characteristic of manual NPDS, and can be confidently performed by surgeons with a wide range of experience in filtration surgery. The efficacy of the CLASS procedure was found to be at least comparable to that reported in a series of studies using manual NPDS [11]. However, some preliminary studies have suggested that the incidence of associated complications was unsatisfactory, and the incidence of PAS and iris incarceration was relatively high following CLASS, which has limited its successful use in east Asian POAG patients.

Considering the characteristics of Chinese POAG patients, we developed a modified CLASS procedure combined with preventive laser iris management, and confirmed its long-term effectiveness and safety in our previous study [8]. The MCLASS approach highlighted several key points. (1) Based on gonioscopy, the widest superior angle position with sparse or uniform pigmentation where blood reflux in the SC was to be was chosen in priority that corresponded to the scleral site for ablation. (2) Broad-based and peripheral LPI was performed as close as possible to the root of the iris and centered in the expected percolation area. ALPI was then applied, surrounding the LPI hole (at least 500 μm in width) within 1–3 days prior to the surgical procedure. (3) During surgery, we created a larger scleral flap (5 × 5 mm compared to a regular 4 × 4 mm flap) and a scleral lake that was large and deep enough to ensure an increased level of drainage and percolation of aqueous humor. (4) We not only revealed the SC during surgery, but also used the CO_2 laser to extend the area of ablation forward to create a TDW. (5) At the end of the surgery, we sutured the scleral flap tightly using adjustable sutures.

Although both groups achieved a significant IOP decrease from baseline, there was a trend toward better IOP outcomes with MCLASS, and postoperative IOP in the MCLASS group was significantly lower than that in the TRAB group at 24 and 36 months. The MCLASS group achieved better IOP reduction at 24 and 36 months (50.7% vs. 47.5% and 53.2% vs. 40%, respectively). The extent of IOP reduction contrasted with that reported by Jankowska–Szmul [12]. We think this is due to the modifications that we made of a larger scleral flap and a deeper scleral lake.

The results of MCLASS in our study were encouraging, with complete success rates of 60.0% at 24 months and 53.3% at 36 months, respectively, and qualified success rates of 91.1% at 24 months and 88.9% at 36 months, respectively. While such results are consistent with those of a previous multicenter study, which showed a complete success rate of 57.9% after 24 months and a qualified success rate of 91.2% after 24 months [13], it is worth noting that more than 85% of the patients in the multicenter study were white and Hispanic, and the preoperative IOP and the extent of IOP reduction were both lower than those in the current study. We have reason to believe that MCLASS is more suitable for more advanced and refractory Chinese POAG patients, and can achieve better IOP lowering effects and success rates.

There was no statistically significant difference when comparing the complete success rate and qualified success rate in the MCLASS group with the TRAB group. The complete success rate in the TRAB group was slightly higher than that in the MCLASS group, whereas the qualified success rate of the TRAB group was lower, because there was a smaller number of patients who required IOP-lowering medications after MCLASS. In our study, the decrease in the number of antiglaucoma medications compared favorably with previous studies of CLASS [14]. Meanwhile, there was significant difference in the number of therapeutic medications taken when comparing between the two groups at 24 and 36 months postoperatively. MCLASS patients, compared with TRAB patients, required fewer medications to maintain the target IOP and a satisfactory range of IOP reduction.

BCVA deterioration after TRAB seemed more serious than that after MCLASS at 24 and 36 months. In previous studies, cataract was also more commonly reported after TRAB. Although the preoperative BCVA in the MCLASS group was lower than that in the TRAB group, the long-term visual acuity in the MCLASS group was better than that in the TRAB group, primarily because of less surgery-related cataract development and progression after MCLASS. This finding may be explained by the non-perforation of the eye, which greatly minimizes the effects of anterior chamber inflammation, medications, and sudden IOP fluctuations on the lens.

In nonpenetrating surgery, the peeling of the inner wall of the SC and the use of Nd:YAG goniopuncture in the follow-up can control the IOP. LGP was suggested as a standard adjunctive practice to transform the technique from a nonpenetrative approach into a micro-perforation approach, as this will extend the increased flow of aqueous humor. Previous studies on LGP following NPDS report an LGP rate of 41–63% [15–17]. In current study, LGP was performed with the Nd:YAG laser in 21 eyes (46.6%). The modified procedure of the successful creation of a TDW during MCLASS surgery is a prerequisite for LGP. Although transforming to perforations theoretically, LGP was applied carefully in terms of the site and the number of laser shots to ensure making only a micro-perforation, which rarely causes sudden hypotony, flat anterior chamber, iris incarceration, or PAS.

In previous studies, complications were more common in the TRAB group. Similarly, in this study, complications caused by early postoperative overfiltration and filtering bleb fibrosis were almost inevitably encountered in the TRAB group, despite our technique of using adjustable sutures to tighten the scleral flap during the early phases and the use of MMC during the operation. MCLASS has the obvious advantage of minimizing the complication of overfiltration and its sequelae; no MCLASS-treated eye showed hypotony or flat anterior chamber, even after LGP, whereas three eyes (7.1%) experienced hypotony, four eyes (9.5%) presented with a shallow anterior chamber, and three eyes (7.1%) suffered from choroidal detachment in the TRAB group. MCLASS-treated eyes also had a significantly lower incidence of hyphema (4.4%) compared with TRAB (21.4%).

Late drainage failure has been well documented after TRAB, with subconjunctival fibrosis being strongly implicated [18]. In the current study, subconjunctival injections of 5-FU were performed in 15 eyes (35.7%) in the TRAB group and in 12 eyes (28.6%) in the MCLASS group; all eyes received postoperative

ocular digital massage in the TRAB group, but not in the MCLASS group. Despite aggressive bleb revision, 13 eyes (30.9%) showed subconjunctival fibrosis resulting in the disappearance of subconjunctival blebs in patients after TRAB, compared to only five eyes (11.1%) in the MCLASS group. We observed that filtering bleb fibrosis was rare after MCLASS surgery, although the majority of filtration blebs were flat and nonfunctional. This may be related to the mechanism of aqueous drainage in nonpenetrating trabecular techniques, although it has not been fully elucidated. It has been postulated that drainage may either go through the subconjunctival pathway, but more primarily through the SC and episcleral veins, via increased uveoscleral outflow from intrascleral and suprachoroidal pathways, after CLASS [19, 20]. In our previous study, we found that once the intrascleral lake had formed, the IOP was not dependent upon the overlying blebs. We believe that because more drainage channels were present after MCLASS than TRAB, once the subconjunctival space collapsed, TRAB would have a greater impact on postoperative IOP increase, and IOP would then be more difficult to controlled.

Stegmann et al. postulated that failure of drainage after a nonpenetrating surgical procedure might occur because of PAS formation over the TDW or excessive fibrosis reducing drainage through the window or closing the ostia of the SC [21]. The incidence of PAS and iris incarceration has been shown to be relatively high following CLASS. By modifying the procedures and performing preventive LPI + ALPI within the percolation area, ablating further forwards the TDW but without penetration, and administering pilocarpine as postoperative treatment, we effectively prevented iris incarceration and PAS after surgery. No case was complicated by iris incarceration, and only eight eyes (17.70%) experienced PAS. We recommend careful postoperative examinations, including gonioscopy and UBM, to recognize and treat scleral lake fibrosis early and to prevent PAS or iris incarceration in order to avoid surgical failure and reoperation. The incidence of postoperative complications was significantly lower after MCLASS. This group showed no incidence of reoperation related to choroidal detachments, flat anterior chambers, or hypotony, and had less hyphema than the TRAB group. A similar lower rate of complications was also described by El Sayyad et al. [22].

To the best of our knowledge, this is the first comparative study of MCLASS versus conventional TRAB over the long term. In our study, MCLASS achieved a significant IOP decrease from baseline, a reduction in the number of medications, and a lower number of complications compared to TRAB up to 36 months. This highly promising technique can be considered a valid alternative to the classical method. However, there are several limitations to our study that need to be considered. First, this was a single-center retrospective comparative study. A randomized prospective study with longer follow-up is required to further evaluate and substantiate the safety and long-term efficacy of the MCLASS procedure and to compare the outcomes to standard TRAB. Second, we did not compare the non-modified CLASS with TRAB. In our pilot unpublished study, considering the high incidence of PAS and iris incarceration of up to 80%, and the resulting uncontrolled IOP and surgical failure, for ethical reasons we resolutely modified the surgical procedures, and we chose not to set up a non-modified CLASS as a control group in the follow-up study, as we had reason to believe that MCLASS is safer and more effective for a Chinese population based on our previous study [8].

CONCLUSION

In conclusion, the MCLASS procedure was found to be as efficient as TRAB in terms of the success rates at 36 months. Of paramount importance is the finding that MCLASS is associated with greater IOP reduction, fewer medications, and a lower risk of complications compared to TRAB.

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Disclosures. Yang Zhang, Jin Mao, Qi Zhou, Lüe Li, Shunhua Zhang, Ailing Bian and Gangwei Cheng have no conflicts of interest to declare.

Compliance with Ethics Guidelines. This study was approved by the Institutional Review Board of Peking Union Medical College Hospital and conformed to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects after an explanation of the nature of the study before entry into this study.

Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Cairns JE. Trabeculectomy. Preliminary report of a new method. Am J Ophthalmol. 1968;66(4):673–9.
2. Song A, Scott IU, Flynn HW Jr, Budenz DL. Delayed-onset bleb-associated endophthalmitis: clinical features and visual acuity outcomes. Ophthalmology. 2002;109(5):985–91.
3. Bylsma S. Nonpenetrating deep sclerectomy: collagen implant and viscocanalostomy procedures. Int Ophthalmol Clin. 1999;39(3):103–19.
4. Krasnov MM. Symposium: microsurgery of the outflow channels. Sinusotomy. Foundations, results, prospects. Trans Am Acad Ophthalmol Otolaryngol. 1972;76(2):368–74.
5. Fyodorov SN, Kozlov VI, Timoshkina NT. Nonpenetrating deep sclerectomy in open angle glaucoma. Ophthalmosurgery. 1990;3:52–5.
6. Bochmann F, Kaufmann C, Kipfer A, Thiel MA. Corneal patch graft for the repair of late-onset hypotony or filtering bleb leak after trabeculectomy: a new surgical technique. J Glaucoma. 2014;23(1):e76-80.
7. Assia EI, Rotenstreich Y, Barequet IS, Apple DJ, Rosner M, Belkin M. Experimental studies on non-penetrating filtration surgery using the CO_2 laser. Graefes Arch Clin Exp Ophthalmol. 2007;245(6):847–54.
8. Zhang Y, Cheng G. Modified CO_2 laser-assisted sclerectomy surgery in Chinese patients with primary open-angle glaucoma and pseudoexfoliative

glaucoma: a 2-year follow-up study. J Glaucoma. 2020;29(5):367–73.

9. Cheng JW, Xi GL, Wei RL, Cai JP, Li Y. Efficacy and tolerability of nonpenetrating glaucoma surgery augmented with mitomycin C in treatment of open-angle glaucoma: a meta-analysis. Can J Ophthalmol. 2009;44(1):76–82.

10. Russo V, Scott IU, Stella A, Balducci F, Cosma A, Barone A, et al. Nonpenetrating deep sclerectomy with reticulated hyaluronic acid implant versus punch trabeculectomy: a prospective clinical trial. Eur J Ophthalmol. 2008;18(5):751–7.

11. Hondur A, Onol M, Hasanreisoglu B. Nonpenetrating glaucoma surgery: meta-analysis of recent results. J Glaucoma. 2008;17(2):139–46.

12. Jankowska-Szmul J, Dobrowolski D, Wylegala E. CO_2 laser-assisted sclerectomy surgery compared with trabeculectomy in primary open-angle glaucoma and exfoliative glaucoma. A 1-year follow-up. Acta Ophthalmol. 2018;96(5):e582–91.

13. Geffen N, Mimouni M, Sherwood M, Assia EI. Mid-term clinical results of CO_2 laser-assisted sclerectomy surgery (CLASS) for open-angle glaucoma treatment. J Glaucoma. 2016;25(12):946–51.

14. Yu X, Chen C, Sun M, Dong D, Zhang S, Liu P, et al. CO_2 laser-assisted deep sclerectomy combined with phacoemulsification in patients with primary open-angle glaucoma and cataract. J Glaucoma. 2018;27(10):906–9.

15. Al Obeidan SA. Incidence, efficacy and safety of YAG laser goniopuncture following nonpenetrating deep sclerectomy at a university hospital in Riyadh, Saudi Arabia. Saudi J Ophthalmol. 2015;29(2):95–102.

16. Shaarawy T, Mansouri K, Schnyder C, Ravinet E, Achache F, Mermoud A. Long-term results of deep sclerectomy with collagen implant. J Cataract Refract Surg. 2004;30(6):1225–31.

17. Anand N, Pilling R. Nd:YAG laser goniopuncture after deep sclerectomy: outcomes. Acta Ophthalmol. 2010;88(1):110–5.

18. Hitchings RA, Grierson I. Clinico pathological correlation in eyes with failed fistulizing surgery. Trans Ophthalmol Soc U K. 1983;103(Pt 1):84–8.

19. Mavrakanas N, Mendrinos E, Shaarawy T. Postoperative IOP is related to intrascleral bleb height in eyes with clinically flat blebs following deep sclerectomy with collagen implant and mitomycin. Br J Ophthalmol. 2010;94(4):410–3.

20. Chiou AG, Mermoud A, Underdahl JP, Schnyder CC. An ultrasound biomicroscopic study of eyes after deep sclerectomy with collagen implant. Ophthalmology. 1998;105(4):746–50.

21. Stegmann R, Pienaar A, Miller D. Viscocanalostomy for open-angle glaucoma in black African patients. J Cataract Refract Surg. 1999;25(3):316–22.

22. El Sayyad F, Helal M, El-Kholify H, Khalil M, El-Maghraby A. Nonpenetrating deep sclerectomy versus trabeculectomy in bilateral primary open-angle glaucoma. Ophthalmology. 2000;107(9):1671–4.