



Long-Term Treatment Outcomes of Micropulse Transscleral Cyclophotocoagulation in Primary and Secondary Glaucoma: A 5-Year Analysis

Ronald M. P. C. de Crom · Stefani Kujovic-Aleksov · Carroll A. B. Webers ·

Tos T. J. M. Berendschot · Henny J. M. Beckers

Received: August 21, 2024 / Accepted: November 26, 2024
© The Author(s) 2024

ABSTRACT

Introduction: To investigate 5-year outcomes on intraocular pressure (IOP) and safety of micropulse transscleral cyclophotocoagulation (TSCPC) in patients with glaucoma.

Methods: Patients with mild to advanced glaucoma who underwent a standardized micropulse TSCPC procedure at the University Eye Clinic Maastricht from November 2016 to February 2019 were included.

Results: A total of 165 eyes were included, with outcomes for 112 eyes available after 5-year follow-up. Mean age was 67.3 ± 13.9 years; 58.2% were male. Glaucoma subtypes were primary glaucoma ($n=108$) and secondary glaucoma ($n=57$). Prior glaucoma surgery was performed in 65 of 165 eyes (39.4%). In the primary glaucoma group, mean preoperative IOP was 20.7 ± 7.1 mmHg. Mean postoperative IOP at 1, 2, 3, 4, and 5 years significantly reduced to 15.2 ± 6.5 , 14.3 ± 5.0 , 14.0 ± 4.9 , 13.5 ± 4.1 , and 12.9 ± 4.3 mmHg, respectively. Preoperatively, the mean number of IOP-lowering medications

was 3.3 ± 1.3 , which changed to 2.8 ± 1.3 , 2.8 ± 1.2 , 2.8 ± 1.2 , 2.9 ± 1.2 , and 2.7 ± 1.3 at 1, 2, 3, 4, and 5 years, respectively. In the secondary glaucoma group, mean preoperative IOP was 28.7 ± 10.3 mmHg, dropping significantly to 19.3 ± 10.4 , 18.6 ± 11.3 , 17.8 ± 9.8 , 18.1 ± 12.0 , and 15.5 ± 7.6 mmHg at the same intervals. The number of IOP-lowering medication was significantly reduced from 3.5 ± 1.1 to 2.5 ± 1.5 , 2.2 ± 1.5 , 2.6 ± 1.4 , 2.6 ± 1.5 , and 2.5 ± 1.7 . In the total group, mean IOP reduction was 32.5% after 5 years. Postoperative complications included cystic macular edema ($n=3$), fibrinous/uveitic reaction ($n=1$), and rejection of corneal graft ($n=2$), all reversible after treatment. One patient developed late and persisting hypotony. Other adverse events were retinal venous occlusion ($n=1$) and retinal vasculitis ($n=1$), unrelated to the laser treatment. In patients with a preoperative Central Distance Visual Acuity (CDVA) >0.05 on the Snellen chart, more than two lines of visual acuity (VA) loss were attributed to cataract ($n=10$), retinal disease ($n=5$), glaucoma progression ($n=3$), corneal decompensation ($n=2$), or other factors ($n=11$).

Conclusion: Micropulse TSCPC is a safe and effective treatment for reducing IOP and the number of IOP-lowering medications after a 5-year follow-up period. It is a viable alternative for patients after failed incisional glaucoma surgery or high-risk patients.

R. M. P. C. de Crom (✉) · S. Kujovic-Aleksov ·
C. A. B. Webers · T. T. J. M. Berendschot ·
H. J. M. Beckers
University Eye Clinic Maastricht, Maastricht
University Medical Center, P.O. Box 5800,
6202 AZ Maastricht, The Netherlands
e-mail: r.de.crom@mumc.nl

Keywords: Glaucoma; Laser treatment; Micropulse; Transscleral cyclophotocoagulation

Key Summary Points

Why carry out this study?

Despite encouraging results, evidence regarding the long-term efficacy and safety of micropulse transscleral cyclophotocoagulation (TSCPC) remains limited.

There are currently no reports in the literature with a 5-year follow-up period.

In this study, the efficacy, safety, and sustainability of micropulse TSCPC were investigated considering that treatment has limited postoperative complications while offering reduction of intraocular pressure and/or medication.

What was learned from the study?

Micropulse TSCPC can offer a sustained intraocular pressure (IOP) reduction of 32.5% and/or medication reduction after 5 years of follow-up.

Micropulse TSCPC offers a viable alternative for patients with refractory glaucoma and after failed incisional glaucoma surgery.

INTRODUCTION

Glaucoma treatment primarily focuses on reducing intraocular pressure (IOP) [1] to prevent optic nerve damage and vision loss. This is typically achieved through various means, such as topical medications, laser therapy, or surgical procedures aimed at increasing aqueous humor outflow or decreasing its production. Conventional treatments include incisional glaucoma surgery, minimally invasive techniques, or glaucoma tube implantation [2]. For patients with refractory or uncontrolled glaucoma, cyclodestructive procedures like cyclocryocoagulation, cyclodiathermy, or transscleral cyclophotocoagulation (TSCPC) may

be considered as a last resort [3, 4]. However, these procedures have been associated with significant complications [5–7], including persistent hypotony, inflammation, and vision loss, leading many practitioners to reserve them for cases where other options have failed.

Micropulse transscleral cyclophotocoagulation (MP-TSCPC) represents a promising advancement in glaucoma treatment [8]. This laser therapy aims to achieve IOP reduction with minimal damage to the ciliary body, a key component in aqueous humor regulation. Unlike traditional cyclodestructive techniques, micropulse therapy delivers laser energy in short bursts, minimizing thermal injury to collateral ocular tissues. In addition to its destructive effect on the ciliary body, choroidal effusion has been observed [9, 10] to contribute to increased suprachoroidal outflow. Several studies [11–17] have reported favorable outcomes with MP-TSCPC, demonstrating effective IOP reduction and fewer severe complications compared to conventional methods [11]. These findings suggest that MP-TSCPC could potentially be used earlier in the treatment pathway for glaucoma.

Despite encouraging results, evidence regarding the long-term efficacy and safety of MP-TSCPC remains limited. Previous investigations have frequently been characterized by relatively small sample sizes and short follow-up periods, alongside variations in treatment parameters. Moreover, only a limited number of studies have conducted follow-up assessments extending up to 2 years [17–20]. Therefore, there is a need for further investigation into the outcomes of MP-TSCPC in larger cohorts with extended follow-up periods and standardized treatment protocols.

Previously, we conducted a prospective study [17] examining the 2-year outcomes of micropulse treatment. To gain a more extensive understanding and analyze a larger patient cohort, we have now undertaken a retrospective analysis of a larger patient population. This study aims to evaluate the long-term effectiveness and safety of MP-TSCPC in patients with various forms and stages of glaucoma. Through this retrospective review, we aim to provide comprehensive

insights into the outcomes of MP-TSCPC as a treatment option for glaucoma management.

METHODS

This retrospective study analyzed patients with glaucoma treated at the University Eye Clinic of Maastricht University Medical Centre, Maastricht, the Netherlands, between November 2016 and February 2019. This study followed the principles of the Declaration of Helsinki and was approved by the institutional ethics committee (METC) of the Maastricht University Medical Centre+. All patients gave their consent prior to treatment. In this period, patients with mild to advanced glaucoma were offered micropulse transscleral cyclophotocoagulation (MP-TSCPC) as an alternative to standard glaucoma filtration surgery or cyclodestruction; this was only considered if the clinician deemed micropulse TSCP appropriate based on IOP, progression rate, or the patient's unsuitability for incisional surgery. Treatment was considered for cases of uncontrolled glaucoma despite maximal tolerated topical and/or systemic intraocular pressure (IOP)-lowering medications or for cases after previous failed glaucoma surgery or previous glaucoma surgery with insufficient IOP control (performed at least 6 months prior to MP-TSCPC). Additionally, patients with stable advanced glaucoma or high surgical risk were included with the goal of reducing their dependence on IOP-lowering medications in cases side effects from topical and/or especially oral medication (acetazolamide). In eyes without light perception, treatment was aimed at reducing the use of topical medication and/or oral acetazolamide and alleviating pain caused by high preoperative intraocular pressures. Exclusion criteria for treatment included active uveitis with secondary glaucoma, active neovascular glaucoma, or scleral thinning > 1 clock hour.

All patients underwent treatment following a standardized protocol, performed by two glaucoma surgeons (R.d.C, C.S.) in an operating room. After administering sub-Tenon's anesthesia (a mixture of 2% mepivacaine and 75E Hyason), micropulse TSCPC was conducted

using the MicroPulse P3 probe (Iridex® Cyclo G6 laser system, Mountain View, USA) at 2000 mW with an 80-s duration for IOP < 30 mmHg or 90 s for IOP > 30 mmHg per hemisphere, at a 31.3% duty cycle, based on the settings recommended by the manufacturer. Both hemispheres were treated with continuous movement and steady pressure on the ocular globe, avoiding the 3 and 9 o'clock positions, previous surgical sites, and areas of scleral thinning. For re-treatments, the power was increased to 2100 mW (second treatment) or 2200 mW (third treatment). Postoperative care included topical tobramycin 0.3% combined with dexamethasone 0.1% (Tobradex; Alcon, Fort Worth, TX) eye drops for 9 days, with IOP-lowering medications adjusted as needed. At postoperative visits, IOP and the number of IOP-lowering medications were recorded, and slit-lamp examination was performed to detect treatment complications (e.g. corneal pathology, anterior chamber reaction, cystoid macular edema, choroidal detachment, or other ocular abnormalities). Diamox was included as a glaucoma medication in the calculation of the total number of medications. In the presence of visual complaints, corrected visual distance acuity (CVDA) was measured, and in addition to slit-lamp examination, an optical coherence tomography (OCT) of the macula was performed to confirm or exclude cystoid macular edema. Hypotony was defined as an IOP < 6 mmHg measured at two or more consecutive visits. Patient data were analyzed postoperatively at 1 day, 1 week, and 1, 3, 6, and 12 months and yearly thereafter. All patients with at least 12 months of follow-up were included in this study. In the event that both eyes of one patient needed to be treated, only the first treated eye was included. Partial treatment success was defined as a postoperative IOP reduction of $\geq 20\%$ compared with baseline or a decrease in the number of IOP-lowering medications with stable IOP. Total treatment success was defined as both a postoperative IOP between 6 and 21 mmHg and a postoperative IOP reduction of $\geq 20\%$ compared with baseline and/or a decrease in the number of IOP-lowering medications with stable IOP.

Statistical analyses were performed using IBM SPSS Statistics, version 28.0.0.0. Descriptive

statistics were used to summarize the data, and appropriate statistical tests were conducted to assess the differences between groups.

RESULTS

Baseline characteristics, including age, sex, glaucoma type, previous glaucoma surgery, and lens status, are shown in Table 1.

A total of 165 patients were included in the study; outcomes for 112 eyes were available at the 5-year endpoint: 65 eyes had received only micropulse transscleral cyclophotocoagulation (TSCP), 29 eyes had undergone additional glaucoma surgery, 15 patients had passed away, 3 patients had undergone evisceration or enucleation for reasons unrelated to glaucoma, and 53 patients were lost to follow-up (23, 32, 39, and 53 patients lost to follow-up at 2, 3, 4, and 5 years, respectively). Mean age was 67.3 ± 13.9 (range 18–92) years, 96 were male (58.2%), and 69 were female (41.8%). Primary open-angle glaucoma was diagnosed in 108 patients (65.5%) and secondary glaucoma in 57 patients. Secondary glaucoma included inactive neovascular disease (15 eyes), vitrectomy using silicone oil (13 eyes), uveitis (11 eyes), trauma (8 eyes), a history of complicated cataract surgery (5 eyes), keratoplasty (4 eyes), and elevated episcleral venous pressure (1 eye). No cases of angle closure, pseudoexfoliation, or pigment dispersion glaucoma were included. Prior glaucoma surgery was performed in 65 of 165 patients (39.4%). Prior glaucoma surgery included trabeculectomy (27 eyes), glaucoma drainage device (17 eyes), XEN-gel stent implant (7 eyes), cyclocryocoagulation (3 eyes), Preserflo MicroShunt (2 eyes), or multiple glaucoma surgery (9 eyes). Pseudophakia was present in 84 eyes (50.9%), phakia in 66 eyes (40.0%), and aphakia in 15 patients (9.1%). Pretreatment CDVA was lower than 0.05 Snellen (>1.3 LogMar) in 57 patients, 0.05–0.5 Snellen (1.3–0.3 LogMar) in 38 patients, and better than 0.5 Snellen (<0.3 LogMar) in 70 patients. Preoperative visual field data were available for 119 patients, with a mean deviation of -19.5 ± 7.9 dB. The majority of patients had end-stage glaucoma (63 eyes), followed by

severe glaucoma (35 eyes), moderate glaucoma (13 eyes), and mild glaucoma (8 eyes).

Intraocular Pressure and Glaucoma Medication

IOP results and the number of used glaucoma medications are shown in Fig. 1 and Table 2.

In the primary glaucoma group, the mean preoperative intraocular pressure (IOP) was 20.7 ± 7.1 mmHg, range 11–50 mmHg, $\text{IOP} \leq 21$ mmHg in 70 of 108 patients (64.8%). The mean postoperative IOP dropped significantly ($p < 0.001$) to 14.1 ± 5.1 mmHg at 1 month, 14.3 ± 4.7 mmHg at 3 months, 15.1 ± 5.1 mmHg at 6 months, 15.2 ± 6.5 mmHg at 1 year, 14.3 ± 5.0 mmHg at 2 years, 14.0 ± 4.9 mmHg at 3 years, 13.5 ± 4.1 mmHg at 4 years, and 12.9 ± 4.3 mmHg at 5 years (Fig. 1). The mean number of IOP-lowering medications used preoperatively was 3.3 ± 1.3 . Postoperatively, the mean number of medications used was 3.0 ± 1.4 at 1 month, 2.9 ± 1.3 at 3 months, 2.7 ± 1.3 at 6 months, 2.8 ± 1.3 at 1 year, 2.8 ± 1.2 at 2 years, 2.8 ± 1.2 at 3 years, 2.9 ± 1.2 at 4 years, and 2.7 ± 1.3 at 5 years. The reduction in medication use was statistically significant up to 3 years postoperatively ($p < 0.001$ up to 2 years, $p < 0.01$ at 3 years).

In the secondary glaucoma group, the mean preoperative IOP was 28.7 ± 10.3 mmHg, range 5–56 mmHg, $\text{IOP} \leq 21$ mmHg in 14 of 57 patients (24.6%). The mean postoperative IOP dropped significantly to 20.7 ± 9.3 mmHg at 1 month, 19.9 ± 8.8 mmHg at 3 months, 19.7 ± 6.4 mmHg at 6 months, 19.3 ± 10.4 mmHg at 1 year, 18.6 ± 11.3 mmHg at 2 years, 17.8 ± 9.8 mmHg at 3 years, 18.1 ± 12.0 mmHg at 4 years, and 15.5 ± 7.6 mmHg at 5 years (Fig. 1). The mean number of IOP-lowering medications used preoperatively was 3.5 ± 1.2 . Postoperatively, the mean number of medications used was 2.8 ± 1.5 at 1 month, 2.6 ± 1.4 at 3 months, 2.6 ± 1.6 at 6 months, 2.5 ± 1.5 at 1 year, 2.2 ± 1.5 at 2 years, 2.6 ± 1.4 at 3 years, 2.6 ± 1.5 at 4 years, and 2.5 ± 1.7 at 5 years. Preoperative oral acetazolamide (Diamox) was used in 60 of 165 patients (36.4%) and could be reduced to 23 of 165

Table 1 Demographics of the study population

	Total group	Primary glaucoma	Secondary glaucoma
No. of eyes	165	108	57
Age	67.3 ± 13.9 (range 18–92)	70.8 ± 10.1 (range 35–92)	60.7 ± 17.4 (range 18–89)
Gender	Male 96 (58.2%)	Male 58 (53.7%)	Male 38 (66.7%)
Glaucoma			
Primary	108 (65.5%)	108	–
Secondary	57 (34.5%)	–	57
Neovascular	15	–	15
Post-vitrectomy	13	–	13
Uveitis	11	–	11
Trauma	8	–	8
Complicated phaco procedure	5	–	5
Keratoplasty	4	–	4
Elevated episcleral venous pressure	1	–	1
Patients with prior glaucoma surgery	65 (39.4%)	57 (52.8%)	8 (14.0%)
Trabeculectomy	27	24	3
Glaucoma drainage device	17	14	3
XEN implant	7	7	–
Trabeculectomy + GDD	6	6	–
Cyclo cryocoagulation	3	1	2
Preserflo microshunt implant	2	2	–
GDD + cryocoagulation	1	1	–
TE + GDD + cryocoagulation	1	1	–
Preserflo + GDD	1	1	–
Lens status			
Pseudophakic	84 (50.9%)	62 (57.4%)	22 (38.6%)
Phakic	66 (40.0%)	45 (41.7%)	21 (36.8%)
Aphakic	15 (9.1%)	1 (0.9%)	14 (24.6%)

Age in mean years ± SD

GDD glaucoma drainage device; TE trabeculectomy

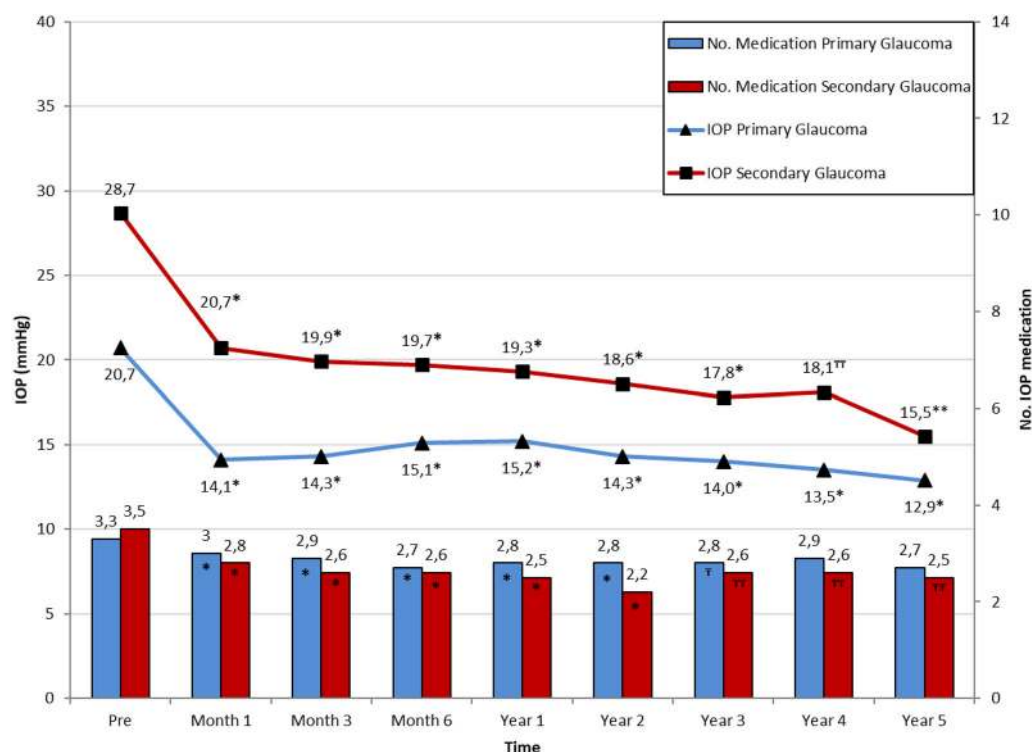


Fig. 1 IOP and number of glaucoma medications in total patient cohort. Intraocular pressure (IOP) in mean mmHg, number of medications in mean, *significant $p < 0.001$ compared with preoperative values, **significant $p < 0.005$

compared with preoperative values, [†]Significant $p < 0.01$ compared with preoperative values, ^{††}Significant $p < 0.05$ compared with preoperative values

patients (13.9%) after 1 year, meaning 61.7% of patients could stop this medication.

Both pre- and postoperative IOP levels were significantly lower in the primary glaucoma group compared to the secondary glaucoma group ($p < 0.0001$), but there were no significant differences in postoperative treatment effect/IOP change between the two groups. Additionally, no significant IOP differences were found in postoperative IOP between the different subgroups with secondary glaucoma or between different lens conditions. The treatment effect did not significantly differ between patients with a history of glaucoma surgery and those without such a history. There was a significant correlation of preoperative IOP and IOP-lowering effect at 1–5 year postoperatively (Pearson's correlation 0.359–0.505, $p < 0.001$). We did not find a correlation between postoperative IOP change and age or preoperative number of IOP-lowering medication.

Further analysis was done of the 65 eyes which only received micropulse TSCP during the 5 year follow-up. In this 5-year completers cohort (see Table 3), the preoperative IOP of 20.3 ± 7.2 mmHg significantly decreased to 14.0 ± 4.6 mmHg at 1 year and remained stable at 13.7 ± 5.6 mmHg up to 5 years postoperatively (statistically significant ($p < 0.001$) at all points), an IOP reduction of 32.5%. An IOP reduction of at least 20% was achieved in 64.6%, 66.2%, 67.7%, 69.2%, and 63.1% after 1, 2, 3, 4, and 5 years, respectively. In this cohort, 47.7%, 55.4%, 44.6%, 43.1%, and 44.6% of patients needed fewer glaucoma medications after treatment after 1, 2, 3, 4, and 5 years, respectively. In this group, oral acetazolamide was used in 26 of 65 patients (40.0%) preoperatively and in 10 of 65 patients (15.4%) after 1 year, meaning 61.5% of patients could stop the acetazolamide. This number also remained stable with 10 of 65 patients (15.4%) using oral acetazolamide after

Table 2 Treatment results in total patient cohort

	Pre	Month 1	Month 3	Month 6	Year 1	Year 2	Year 3	Year 4	Year 5
Primary glaucoma									
No. eyes	108	107	105	104	100	74	67	62	45
IOP	20.7 ± 7.1	14.1 ± 5.1*	14.3 ± 4.7*	15.1 ± 5.1*	15.2 ± 6.5*	14.3 ± 5.0*	14.0 ± 4.9*	13.5 ± 4.1*	12.9 ± 4.3*
No. medications	3.3 ± 1.3	3.0 ± 1.4*	2.9 ± 1.3*	2.7 ± 1.3*	2.8 ± 1.3*	2.8 ± 1.2*	2.8 ± 1.2 [†]	2.9 ± 1.2	2.7 ± 1.3
No. retreated eyes	–	–	8/108 (7.4%)	23/108 (21.3%)	32/108 (29.6%)	35/108 (32.4%)	38/108 (35.2%)	40/108 (37.0%)	41/108 (38.0%)
No. glaucoma surgery	–	–	–	–	6/108 (5.6%)	7/108 (6.5%)	8/108 (7.4%)	11/108 (10.2%)	14/108 (13.0%)
Secondary glaucoma									
No. eyes	57	57	54	53	49	34	27	20	20
IOP	28.7 ± 10.3	20.7 ± 9.3*	19.9 ± 8.8*	19.7 ± 6.4*	19.3 ± 10.4*	18.6 ± 11.3*	17.8 ± 9.8*	18.1 ± 12.0 ^{††}	15.5 ± 7.6 ^{**}
No. medication	3.5 ± 1.2	2.8 ± 1.5*	2.6 ± 1.4*	2.6 ± 1.6*	2.5 ± 1.5*	2.2 ± 1.5*	2.6 ± 1.4 ^{††}	2.6 ± 1.5 ^{††}	2.5 ± 1.7 ^{††}
No. retreated eyes	–	–	9/57 (15.8%)	14/57 (24.6%)	19/57 (33.3%)	23/57 (40.4%)	24/57 (42.1%)	24/57 (42.1%)	26/57 (45.6%)
No. glaucoma surgery	–	–	–	3/57 (5.2%)	8/57 (14.0%)	11/57 (19.3%)	12/57 (21.1%)	14/57 (24.6%)	15/57 (26.3%)

Intraocular pressure (IOP) in mean mmHg ± SD, number (No.) of medications in mean ± SD

*Significant $p < 0.001$ compared with preoperative values, **significant $p < 0.005$ compared with preoperative values, [†]significant $p < 0.01$ compared with preoperative values, ^{††}significant $p < 0.05$ compared with preoperative values

5 years. No correlations were found between the number and class of preoperative medications and the postoperative IOP-lowering effect.

In the primary glaucoma group, treatment success at 1, 2, 3, 4, and 5 years was achieved in 70 of 108 patients (64.8%), 60 of 78 patients (76.9%), 53 of 71 patients (74.6%), 42 of 64 patients (65.6%), and 30 of 45 patients (66.7%), respectively. In the secondary glaucoma group, treatment success at 1, 2, 3, 4, and 5 years was achieved in 37 of 57 patients (64.9%), 28 of 36 patients (77.8%), 20 of 29 patients (69.0%), 18 of 23 patients (78.3%), and 16 of 20 patients (80.0%), respectively. In the 5-year completers cohort (Table 3), partial treatment success was achieved in 75.4%, 80.0%, 76.9%, 73.8%, and 70.8% after 1, 2, 3, 4, and 5 years, respectively. Complete treatment success in this cohort was achieved in 73.8%, 80.0%, 73.8%, 73.8%, and 69.2% at 1, 2, 3, 4, and 5 years, respectively. In this cohort, subgroup analysis of patients with a preoperative IOP of 6–21 mmHg showed complete success in 69.8%, 74.4%, 74.4%, 74.4%,

and 72.1% after 1, 2, 3, 4, and 5 years, respectively. Subgroup analysis of patients with a preoperative IOP of >21 mmHg showed complete success in 81.8%, 90.9%, 72.7%, 72.7%, and 63.6% at 1, 2, 3, 4, and 5 years, respectively.

Complications

A preoperative CDVA > 0.05 on the Snellen chart was present in 109 of 165 patients, 43 of 165 eyes had a preoperative CDVA < 0.05 on the Snellen chart (range light perception-finger counting), and 13 of 165 eyes had no light perception preoperatively. Evaluation of postoperative CDVA was done in eyes with a preoperative CDVA > 0.05 on the Snellen chart. Postoperative CDVA at 1 year of follow-up was available in 86 of 108 patients with a preoperative CDVA > 0.05 (1.3 LogMar) on the Snellen chart. In this group, mean LogMar VA was 0.29 (range –0.08–1.00) preoperatively and 0.39 (range 0–1.30) after 1 year of follow-up. In this group,

Table 3 Treatment results in 5-year completers cohort

	Pre	Year 1	Year 2	Year 3	Year 4	Year 5
No. Eyes	65	65	65	65	65	65
IOP	20.3 ± 7.2	14.0 ± 4.6*	14.0 ± 4.6*	13.8 ± 5.1*	13.9 ± 5.6*	13.7 ± 5.6*
No. medications	3.2 ± 1.3	2.5 ± 1.4*	2.4 ± 1.4*	2.5 ± 1.3*	2.7 ± 1.4**	2.6 ± 1.4**
Mean IOP reduction	–	31.0%	31.0%	32.0%	31.5%	32.5%
% Patients with oral acetazolamide	40.0%	15.4%	12.3%	15.4%	18.4%	15.4%
% Eyes with retreatments	–	30.8%	32.3%	33.8%	35.4%	38.5%
% Eyes with IOP 6–21 mmHg	66.2%	93.8%	95.4%	93.8%	89.2%	90.8%
% Eyes with > 20% IOP reduction	–	64.6%	66.2%	67.7%	69.2%	63.1%
% Eyes with medication reduction	–	47.7%	55.4%	44.6%	43.1%	44.6%
IOP reduction > 20% AND medication reduction	–	32.3%	32.3%	29.2%	26.2%	26.2%
IOP reduction > 20% OR medication reduction	Total group	75.4%	80.0%	76.9%	73.8%	70.8%
	IOP 6–21 mmHg (<i>n</i> = 43)	69.8%	74.4%	76.7%	74.4%	72.1%
	IOP > 21 mmHg (<i>n</i> = 22)	86.4%	90.9%	77.3%	72.7%	68.2%
Postoperative IOP 6–21 mmHg	Total group	73.8%	80.0%	73.8%	73.8%	69.2%
	IOP 6–21 mmHg (<i>n</i> = 43)	69.8%	74.4%	74.4%	74.4%	72.1%
IOP reduction > 20% OR medication reduction	IOP > 21 mmHg (<i>n</i> = 22)	81.8%	90.9%	72.7%	72.7%	63.6%

Intraocular pressure (IOP) in mean mmHg mean ± SD, number (No.) of medications in mean ± SD

*Significant $p < 0.001$, **significant $p < 0.005$, †significant $p < 0.01$ compared with preoperative values

14 of 86 patients (16.3%) lost one lines of VA. Loss of two or more lines of VA was seen in 30 of 86 eyes (34.9%), caused respectively by cataract (10 eyes), retinal disease (5 eyes), progression of glaucoma (3 eyes), corneal decompensation (2 eyes), other non-glaucoma surgery (3 eyes), and unexplained vision loss (7 eyes). Among the ten patients with cataract, three underwent cataract surgery, resulting in an improvement in visual acuity in all cases, achieving at least preoperative levels. Postoperative CDVA at 1 year of follow-up was available in 12 of 36 patients with a preoperative CDVA ≤ 0.05 on the Snellen chart. In this group, 5 of 12 patients (41.7%) lost one or more

line because of progression of glaucoma (2 eyes), retinal disease (1 eye), and unexplained visual lost (2 eyes). In this group, no changes were seen in patients with preoperative light perception (7 patients).

In the early postoperative period (<3 months), the following complications occurred in 8 of 165 patients (complication rate 4.8%): cystoid macular edema (*n* = 3), rejection of corneal graft (*n* = 2), and fibrinous anterior chamber reaction (*n* = 1), all reversible after treatment (prolonged use of topical steroid treatment). Other adverse events were retinal venous occlusion (*n* = 1) and retinal vasculitis (*n* = 1), both not related to the

laser treatment. In the late postoperative period, one patient (0.5%) developed a hypotony with an IOP of 3 mmHg. This patient had a history of congenital cataract, aphakia, vitrectomy with use of silicon oil (and oil removal) after retinal detachment, and neovascular glaucoma and developed a numerical hypotony 2 months after second treatment. No visual complaints and no signs of hypotony maculopathy were present in this patient.

Retreatments

Sixty-seven of 165 eyes (40.6%) received 78 retreatments. After 1 year, retreatments were performed in 51 of 165 eyes (30.9% retreatment rate). Among all the retreatments performed in this study, the 25th percentile was 80 days, the median (50th percentile) was 140 days, and the 75th percentile was 343 days. In the 5-year completers cohort, retreatment was performed in 20 of 65 (30.8%), 21 of 65 (32.3%), 22 of 65 (33.8%), 23 of 65 (35.4%), and 25 of 65 (38.5%) eyes after 1, 2, 3, 4, and 5 years, respectively, with a mean number of retreatments of 1.28 per eye (32 retreatments in 25 eyes). There were no significant differences in need for retreatment in patients with primary compared with secondary glaucoma. No significant correlations were found between preoperative IOP or preoperative number of medications and the need for retreatment. Additionally, lens status, history of glaucoma surgery, and the interval between treatment and retreatment were not significant predictors of the need for retreatment. Conversion to other glaucoma surgery in the total group was necessary in 29 of 165 eyes (17.6%). Conversion to other glaucoma surgery was performed in 20 of 67 retreated patients (9 cyclocryotherapy/continuous wave laser, 7 glaucoma drainage devices, 1 trabeculectomy, 1 Preserflo MicroShunt, and 2 phacoemulsification with iStent implantation) with a mean time to conversion in this group of 546 (range 105–1452) days after primary laser treatment. Conversion to other glaucoma surgery was done in nine eyes with no retreatment (2 cyclocryotherapy/continuous wave laser, 4 phacoemulsification with iStent implantation, 4 glaucoma drainage devices, and

1 vitrectomy) with a mean time to conversion of 1075 (range 273–1841) days after primary laser treatment. There was a significant correlation between the preoperative IOP and the need for additional glaucoma surgery ($p=0.012$). A higher preoperative IOP was associated with a higher likelihood of needing extra glaucoma surgery. No significant correlations were found between the preoperative number of medications and the need for additional glaucoma surgery. There were also no differences regarding lens status.

DISCUSSION

In this study, we investigated the outcomes on intraocular pressure (IOP) and safety following treatment with micropulse transscleral cyclophotocoagulation (MP-TSCPC) in patients with glaucoma. Success, defined as either a $\geq 20\%$ IOP reduction or a stable postoperative IOP with fewer medications, was achieved in 70.8% of patients after 5 years of follow-up. Specifically, an IOP reduction of $\geq 20\%$ was observed in 63.1% of patients, while 44.6% were able to reduce their number of glaucoma medications. Both targets ($>20\%$ IOP reduction and fewer medications) were achieved in 26.2% of patients. During the 5-year follow-up period, both postoperative intraocular pressure (IOP) and the number of medications remained stable. During the 5-year follow-up period, 53 of 165 patients (32.1%) were lost to follow-up. Analysis of these patients showed a significantly higher age (73.1 vs 63.9 years) but no other differences in baseline characteristics (preoperative IOP, glaucoma medications, or glaucoma severity). Furthermore, most of these patients were referred back to ophthalmic centers within our region. However, in case of need for any additional glaucoma treatments, these procedures would again have been performed in our clinic. We therefore assume that the original treatment was probably still successful.

Since this is the first study with a 5-year follow-up period to our knowledge, our data can only be compared with studies of shorter follow-up durations. In the studies by Zaarour et al., Khan et al., Basto et al., and Chen

et al., treatment parameters were similar to our protocol, making these studies highly comparable [15, 18–20]. Zaarour et al. found success rates (IOP between 6 and 21 mmHg or > 20% IOP reduction) of 73.3% and 66% after 12 and 15 months, respectively, similar to our findings. Khan et al. reported a 29.2% IOP reduction and a reduction in oral acetazolamide use but no reduction in topical medications after 2 years. Basto et al. observed a 27.1% IOP reduction after 1 year and a 17.7% reduction after 2 years, with a success rate of 45.5% after 2 years (IOP 6–21 mmHg, >20% IOP reduction or reduction in medication). Chen et al. reported a 46.5% IOP reduction and a success rate of 75% at 2 years (IOP 6–21 mmHg or >20% IOP reduction). Nguyen et al. found that 76.8% of patients achieved a > 20% IOP reduction after 12 months, a higher rate compared to our study [16]. In our study, mean IOP reduction after 5 years of follow-up was 30.8%, higher compared to the studies of Khan and Basto. Studies by Chen, Sarrafour, and Nguyen et al. [16, 19, 21] showed higher IOP reduction percentages (30.3–46%) at 1 year. A potential explanation may lie in the higher energy levels (2000–2500 mW) and prolonged application durations (90 s per hemisphere) employed in the studies by Sarrafpour and Nguyen. It is well established that increased energy levels and extended laser application time are associated with a greater reduction in intraocular pressure (IOP) following micropulse transscleral cyclophotocoagulation (TSCPC). In our study, a standard energy setting of 2000 mW was utilized, with a maximum of 2200 mW applied during a third treatment session. Additionally, variations in patient characteristics might also contribute to the observed outcomes. Our study predominantly included white patients. Although iris color and pigmentation levels were not documented in our study, it is plausible that the laser effects may be more pronounced in heavily pigmented eyes, such as those found in Afro-American, Arabic, or Asian populations, compared to less pigmented eyes. Additionally, a third potential factor contributing to the smaller reduction in intraocular pressure (IOP) observed in our study could be the dual objective in some patients of reducing both IOP and medication usage through micropulse

transscleral cyclophotocoagulation (TSCPC). The use of glaucoma medication decreased in our study from 3.1 preoperatively to 2.6 after 5 years. This reduction is better compared with the study of Khan (0.1 reduction), similar when compared to the studies of Sarrafpour and Basto (0.6 reduction) and Zaarour (0.5 reduction), and is lower compared with the study of Yelen-skiy and Chen (1.0 and 1.2 reduction) [14, 15, 18–21].

The second goal of our study was to evaluate the safety of the MP-TSCPC procedure by assessing the number and duration of postoperative complications. Visual acuity (VA) decreased by more than two lines on the Snellen chart in 34.9% of patients after 1 year. Most VA losses were related to retinal disease, cataract, or glaucoma progression. At 1 year, eight patients experienced unexplained vision loss, which may have been due to variations in VA measurements or decreased CDVA due to (natural) glaucoma progression. Varikuti et al. [22] and Sarrafour et al. [21] found decreases in VA of 20.83% and 18.8% of patients after 12 and 6 months of follow-up, respectively.

In our study, early postoperative complications were observed in 8 out of 165 patients, all of which were reversible following treatment. One patient developed persistent hypotony in the late postoperative period (5 months after the second treatment), though without any associated symptoms or signs of hypotony maculopathy. Mild prolonged postoperative inflammation or transient hypotony have been reported in other studies [12, 13, 15, 16, 22, 23]. However, major complications such as persistent hypotony or phthisis bulbi were not reported in the studies by Zaarour, Nguyen, and Sarrafpour. Higher rates of postoperative inflammation, hypotony, and phthisis were reported in the studies by Williams et al. and Emanuel et al. [12, 23]. Post-treatment mydriasis is another potential complication following TSCPC, which can result in clinical symptoms such as glare or other forms of visual discomfort. This phenomenon has been documented in several studies [19, 24–26], although it was not consistently reported in all investigations [8, 12, 14, 15, 23, 27]. In our study, no cases of pupillary mydriasis were observed after micropulse TSCPC. However,

this complication may have been overlooked, possibly contributing to unexplained visual loss in some cases. Another limitation of our study is that visual acuity was only assessed in patients who reported visual complaints, and no screening for (sub)clinical macular edema was conducted in asymptomatic patients. In our study, clinical macular edema with transient visual impairment was found in 3 of 165 patients. In other studies, visual loss has been described. Zaarour [15], using the same treatment parameters, found a transient visual decline in the early 1 month postoperative period, while VA in the longer term was comparable to preoperative levels and remained stable after 12 and 15 months. Other studies [12, 23, 28] have suggested that using higher energy levels or extended treatment durations during micropulse TSCPC may have a more significant impact on visual acuity (VA). However, it is important to note that VA loss in glaucoma populations is also influenced by natural fluctuations in VA, which may limit the observed effects.

We found no differences in the amount of IOP lowering after TSCPC between patients with primary and secondary glaucoma, although there were significant IOP differences between both pre- and postoperative IOP levels in these groups. This suggests that TSCPC can be a viable alternative to invasive incisional glaucoma surgery, particularly in patients with secondary glaucoma and those for whom incisional surgery may be challenging, such as individuals with scarred or compromised conjunctival tissue.

Our data revealed no significant differences in the IOP-lowering effect or complication rate of TSCPC regarding lens status. Notably, in aphakic patients, these findings underscore that TSCPC is a safe and effective alternative to incisional surgery, especially for high-risk patients who are at an increased risk of complications such as hypotony or expulsive hemorrhagic bleeding.

In the literature, the retreatment rate with micropulse TSCPC in the literature varies between 0.5% and 68.5% [29]. In our study, the retreatment rate was 38.5% over a 5-year follow-up period. This rate is lower compared to Khan et al. (53%) but higher compared to the studies by Chen (5%) and Basto et al. (19.7%). Since retreatment rates depend on specific treatment

goals within a study (e.g., IOP < 21 mmHg, IOP reduction of at least 20%, medication reduction), these rates can vary between studies. In our previous study [17], we found that 54.8% of the retreated patients had already achieved treatment success (>20% IOP lowering or less medication) after the first treatment and that retreatment in these patients was performed to gain additional IOP lowering or further reduction of medication. Extended analysis of the retreated patients in this study will be published in a separate article. Additionally, the predominance of white patients in our study may have contributed to our retreatment rate.

Limitations

This study provides valuable data on the long-term outcomes of Micropulse TSCPC. However, its findings are limited by significant loss to follow-up over the 5-year period and the lack of diversity due to a predominantly white population.

CONCLUSION

Our data show that after 5 years of follow-up, micropulse TSCPC is a safe and effective treatment for lowering IOP and decreasing the number of IOP-lowering medications. Micropulse TSCPC can also be considered a good alternative treatment option for patients after failed incisional glaucoma surgery or patients who are at high risk for incisional surgery.

ACKNOWLEDGEMENTS

We sincerely thank all the patients who participated in the study for their invaluable contributions.

Authorship. All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Ronald M.P.C. de Crom (data acquisition and manuscript writing), Stefani Kujovic-Aleksov (manuscript editing), Carroll A.B. Webers (manuscript editing), Tos T.J.M. Berendschot (statistical analysis and manuscript editing), Henny J.M. Beckers (manuscript editing).

Funding. No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Ronald M.P.C. de Crom has received speaker honorarium from IRIDEX Corporation. Stefani Kujovic-Aleksov, Carroll A.B. Webers, Tos T.J.M. Berendschot, and Henny J.M. Beckers declare that they have no competing interests.

Ethical Approval. This study was conducted according to guidelines of the Declaration of Helsinki and its later amendments or comparable ethical standards and was approved by the institutional ethics committee (METC) operating at the Maastricht University Medical Centre + in Maastricht, The Netherlands, No METC 2020-2404 (24-12-2020). All patients gave informed consent prior to undergoing treatment.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material.

If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. Weinreb RN, Khaw PT. Primary open-angle glaucoma. *Lancet*. 2004;363(9422):1711–20.
2. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA*. 2014;311(18):1901–11.
3. Chen MF, Kim CH, Coleman AL. Cyclodestructive procedures for refractory glaucoma. *Cochrane Database Syst Rev*. 2019;3:CD012223.
4. Dastiridou AI, Katsanos A, Denis P, Francis BA, Mikropoulos DG, Teus MA, Konstas AG. Cyclodestructive procedures in glaucoma: a review of current and emerging options. *Adv Ther*. 2018;35(12):2103–27.
5. Kosoko O, Gaasterland DE, Pollack IP, Enger CL. Long-term outcome of initial ciliary ablation with contact diode laser transscleral cyclophotocoagulation for severe glaucoma. The diode laser ciliary ablation study group. *Ophthalmology*. 1996;103(8):1294–302.
6. Bloom PA, Tsai JC, Sharma K, Miller MH, Rice NS, Hitchings RA, Khaw PT. “Cyclodiode”. Trans-scleral diode laser cyclophotocoagulation in the treatment of advanced refractory glaucoma. *Ophthalmology*. 1997;104(9):1508–19 (discussion 19–20).
7. Ramli N, Htoon HM, Ho CL, Aung T, Perera S. Risk factors for hypotony after transscleral diode cyclophotocoagulation. *J Glaucoma*. 2012;21(3):169–73.
8. Tan AM, Chockalingam M, Aquino MC, Lim ZI, See JL, Chew PT. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. *Clin Exp Ophthalmol*. 2010;38(3):266–72.
9. Chansangpet S, Taechajongjintana N, Ratana-wongphaibul K, Itthipanichpong R, Manassakorn A, Tantisevi V, et al. Ciliochoroidal effusion and its association with the outcomes of micropulse transscleral laser therapy in glaucoma patients: a pilot study. *Sci Rep*. 2022;12(1):16403.

10. Johnstone MA, Song S, Padilla S, Wen K, Xin C, Wen JC, et al. Microscope real-time video (MRTV), high-resolution OCT (HR-OCT) & histopathology (HP) to assess how transcleral micropulse laser (TML) affects the sclera, ciliary body (CB), muscle (CM), secretory epithelium (CBSE), suprachoroidal space (SCS) & aqueous outflow system. *Investig Ophthalmol Vis Sci*. 2019;60:2825.
11. Aquino MC, Barton K, Tan AM, Sng C, Li X, Loon SC, Chew PT. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. *Clin Exp Ophthalmol*. 2015;43(1):40–6.
12. Emanuel ME, Grover DS, Fellman RL, Godfrey DG, Smith O, Butler MR, et al. Micropulse cyclophotocoagulation: initial results in refractory glaucoma. *J Glaucoma*. 2017;26(8):726–9.
13. Kuchar S, Moster MR, Reamer CB, Waisbourd M. Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. *Lasers Med Sci*. 2016;31(2):393–6.
14. Yelenskiy A, Gillette TB, Arosemena A, Stern AG, Garris WJ, Young CT, et al. Patient outcomes following micropulse transscleral cyclophotocoagulation: intermediate-term results. *J Glaucoma*. 2018;27(10):920–5.
15. Zaarour K, Abdelmassih Y, Arej N, Cherfan G, Tomey KF, Khoueir Z. Outcomes of micropulse transscleral cyclophotocoagulation in uncontrolled glaucoma patients. *J Glaucoma*. 2019;28(3):270–5.
16. Nguyen AT, Maslin J, Noecker RJ. Early results of micropulse transscleral cyclophotocoagulation for the treatment of glaucoma. *Eur J Ophthalmol*. 2019;30(4):700–5.
17. de Crom R, Slangen C, Kujovic-Aleksov S, Webers CAB, Berendschot T, Beckers HJM. micropulse trans-scleral cyclophotocoagulation in patients with glaucoma: 1- and 2-year treatment outcomes. *J Glaucoma*. 2020;29(9):794–8.
18. Khan HM, Law G, Docherty G, Gooi P. Safety and efficacy of micropulse transscleral cyclophotocoagulation: 2-year follow-up in a tertiary Canadian centre. *Can J Ophthalmol*. 2024;59(1):19–23.
19. Chen HS, Yeh PH, Yeh CT, Su WW, Lee YS, Chuang LH, et al. Micropulse transscleral cyclophotocoagulation in a Taiwanese population: 2-year clinical outcomes and prognostic factors. *Graefes Arch Clin Exp Ophthalmol*. 2022;260(4):1265–73.
20. Basto RC, Almeida J, Roque JN, Henriques SP, Goncalves AS, Vaz FT, et al. Clinical outcomes of micropulse transscleral cyclophotocoagulation: 2 years of experience in Portuguese eyes. *J Curr Glaucoma Pract*. 2023;17(1):30–6.
21. Sarrafpour S, Saleh D, Ayoub S, Radcliffe NM. Micropulse transscleral cyclophotocoagulation: A look at long-term effectiveness and outcomes. *Ophthalmol Glaucoma*. 2019;2:167–71.
22. Varikuti VNV, Shah P, Rai O, Chaves AC, Miranda A, Lim BA, et al. Outcomes of micropulse trans-scleral cyclophotocoagulation in eyes with good central vision. *J Glaucoma*. 2019;28(10):901–5.
23. Williams AL, Moster MR, Rahmatnejad K, Resende AF, Horan T, Reynolds M, et al. Clinical efficacy and safety profile of micropulse transscleral cyclophotocoagulation in refractory glaucoma. *J Glaucoma*. 2018;27(5):445–9.
24. Magacho L, Lima FE, Avila MP. Double-session micropulse transscleral laser (CYCLO G6) for the treatment of glaucoma. *Lasers Med Sci*. 2019;35(7):1469–75.
25. Masis MNA, Gonzalez MM. Pupillary mydriasis and recovery after transscleral micropulse cyclophotocoagulation. In: *The 27th annual AGS meeting*, New York; 2018.
26. Radhakrishnan SWJ, Tran B. Outcomes of micropulse cyclophotocoagulation—a multicenter review. In: *The 26th annual AGS meeting*, Colorado, CA; 2017.
27. Yu SW, Ma A, Wong JK. Micropulse laser for the treatment of glaucoma: a literature review. *Surv Ophthalmol*. 2019;64(4):486–97.
28. Egbert PR, Fiadoyor S, Budenz DL, Dadzie P, Byrd S. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. *Arch Ophthalmol*. 2001;119(3):345–50.
29. Grippo TM, Toteberg-Harms M, Giovingo M, Francis BA, de Crom R, Jerkins B, et al. Evidence-based consensus guidelines series for micropulse transscleral laser therapy—surgical technique, post-operative care. Expected outcomes and retreatment/enhancements. *Clin Ophthalmol*. 2023;17:71–83.