ORIGINAL RESEARCH

Estimating the Ideal Treatment Protocol and Success Predictors for Double-session Micropulse Transscleral Laser for Glaucoma Management

Leopoldo Magacho[1], Francisco E Lima[2], Marcos P Ávila[3]

Received on: 10 July 2021; *Accepted on:* 22 April 2022; *Published on:* 30 August 2022

Abstract

Aim: To identify the ideal treatment protocol and success predictors for double-session micropulse transscleral (MP3) laser for glaucoma management.

Materials and methods: Patients who underwent double-session MP3, with a minimum follow-up of 6 months, were retrospectively investigated. Logistic regression analysis was used to verify preoperative success predictors. The following comparisons were made: (1) Between eyes that obtained surgical success vs failure, (2) According to the time required for MP3, and (3) Considering only eyes that required retreatment.

Results: A total of 191 eyes from 148 patients were included. The preoperative intraocular pressure (IOP) was significantly higher than at last follow-up visit (27.3 ± 6.9 vs 14.6 ± 6.0 mm Hg, $p < 0.001$). Success was observed in 90.5% of the eyes. On logistic regression analysis with preoperative IOP and MP3 time as independent variables, only previous IOP was identified as a statistically significant factor ($p = 0.004$), with lower IOP relating to higher success. Eyes that required lower MP3 time underwent more MP3 procedures than those with higher MP3 time (1.2 ± 0.5 vs 1.1 ± 0.3, $p = 0.03$). In the 36 eyes that underwent retreatment, preoperative IOP was higher (31.6 ± 7.4 vs 26.3 ± 6.4 mm Hg, $p < 0.001$); eyes with successful IOP treatment had a higher MP3 treatment time at the first surgery than eyes with failed IOP correction (364.1 ± 68.2 vs 330.0 ± 18.0 seconds, $p = 0.02$).

Conclusion: Thus, an ideal double-session MP3 protocol should use a high laser energy at the first surgery, and a high preoperative IOP can be considered as a predictor of surgical failure.

Clinical significance: This is the first study to give special attention to the double-session MP3 protocol and success predictors.

Keywords: Glaucoma, Intraocular pressure, Laser, Micropulse trasscleral cyclophotocoagulation.

Journal of Current Glaucoma Practice (2022): 10.5005/jp-journals-10078-1375

Introduction

The micropulse transscleral laser (MP3, IRIDEX Cyclo G6 Laser System, Mountain View, California) is a new glaucoma surgical modality.[1–20] Unlike the conventional cyclodestructive surgery, the MP3 procedure does not use the laser in a continuous, localized, and disruptive mode. In fact, the MP3 laser breaks the continuous laser energy into micropulse (0.5 ms "on" time vs 1.1 ms "off" time), which allows heat dissipation between pulses. Therefore, this technique apparently does not provoke cyclophotocoagulation. However, minor damage to the ciliary body may occur.

Several studies have reported good results with MP3.[1,5,7–11,13–19] However, the technique is still based on the surgeon's expertise and, presently, there is no rigid surgical protocol. Moreover, previously published results cannot be extrapolated to different glaucoma cohorts. Certain investigators have used fixed parameters,[1,2,5,12,14,18] while others have employed the same power (2000 mW) but varied the exposure time according to the surgeon's discretion.[3,6,7,15,17,19] Lastly, other studies have even varied power[4,10,11] to achieve the best efficacy/safety relation.

Sanchez et al.[21,22] hypothesized ideal MP3 parameters based on total energy levels in Joules (J = time in seconds × power in Watts × duty cycle: 31.3%) at a midrange level, between 112 and 150 J, most likely at a point closer to 150 J. "High" energy levels (≥200 J) would have yielded greater IOP reduction if severe complications were less prevalent. This assumption was made considering a single treatment at each eye hemisphere (superior and inferior) and a constant dwell time with MP3 probe swinging. However, some authors have advocated different treatment protocols, such as varying the time per probe swing[4,11] or even using a different procedure where the probe stops at a given location for a period of 10 seconds before moving to the adjacent area ("stop-and-go").[6]

The double-session MP3 technique is a variation proposed to deliver a higher amount of MP3 laser to the treated eye to

[1]Department of Ophthalmology, Federal University of Goiás (CEROF-HC-UFG), Goiânia, Goiás, Brazil; VER Hospital de Olhos, Goiânia, Goiás, Brazil

[2,3]Department of Ophthalmology, Federal University of Goiás (CEROF-HC-UFG), Goiânia, Goiás, Brazil; CBCO—Centro Brasileiro de Cirurgia de Olhos, Goiânia, Goiás, Brazil

Corresponding Author: Leopoldo Magacho, Department of Ophthalmology, Federal University of Goiás (CEROF-HC-UFG), Goiânia, Goiás, Brazil; VER Hospital de Olhos, Goiânia, Goiás, Brazil, Phone: +556230969696, e-mail: lmagacho@hotmail.com

How to cite this article: Magacho L, Lima FE, Ávila MP. Estimating the Ideal Treatment Protocol and Success Predictors for Double-session Micropulse Transscleral Laser for Glaucoma Management. J Curr Glaucoma Pract 2022;16(2):111–116.

Source of support: Nil

Conflict of interest: None

preserve or improve efficacy with fewer retreatments while maintaining safety.[9,16] The alternation between hemispheres (superior-inferior-superior-inferior) may have theoretically resulted in heat dissipation in the "hemifield rest" and prevented the accumulation of sufficient energy in the ciliary body and surrounding structures to induce undesired damage. The first description of the technique included only patients with a total treatment time of 320 seconds (two consecutive 80-second sessions).[9] The total energy (320 × 2 × 31.3% = 200.3 J) was greater than that used in almost all published papers, with 86.5% of the eyes achieving success at 16.7 ± 3.1 months, with 1.5 ± 0.8 MP3 laser procedures performed per eye (68.5% with one, 15.7% with two, 11.2% with three, and 4.5% with four MP3 laser procedures), with few complications.[9] In an attempt to reduce MP3 retreatment, the double-session technique was maintained; however, the exposure time was increased (320–480 seconds) in new patients. Similar or even higher success rates were obtained, with an average treatment time of around 360 seconds (225.3 J).[16] In this analysis, eyes that had not undergone glaucoma surgery had fewer MP3 procedures, and no incremental side effects were observed in the whole group.[16]

Therefore, it is rational to hypothesize that the double-session MP3 procedure may have different optimal treatment protocols than the standard MP3 method. Additionally, it is important to identify success predictors and possible differences in patient characteristics in successful vs failed surgeries, including those requiring retreatment, to help guide clinicians when choosing this MP3 modality. This study was designed to fill these gaps.

Materials and Methods

One or both eyes of all patients with clinically uncontrolled glaucoma, aged 18 years or older at the time of the first MP3, who underwent double-session MP3 by two of the study authors (Leopoldo M and Francisco EL), with at least 6 months of follow-up, were retrospectively and consecutively included. The surgeries were performed at either VER Hospital de Olhos (Leopoldo M) or CBCO—Centro Brasileiro de Cirurgia de Olhos (Francisco EL) after approval by the Ethics Committee of both institutions. The study followed the tenets of the Declaration of Helsinki. Patients who underwent any other ocular surgery, including laser treatment, such as selective laser trabeculoplasty—in the 3 months before the last preoperative visit—or MP3 with any other ocular surgery (such as cataract surgery, vitrectomy, or combined with another glaucoma procedure), were excluded from the study.

All MP3 surgeries followed the double-session protocol, which consisted of two sessions ranging from 80 to 120 seconds per treatment in each hemifield, alternating between upper and lower–upper–lower (total application time: 320–480 seconds, defined at the surgeon's discretion), as described elsewhere.[9,16]

The postoperative regimen consisted of prednisolone acetate 1% eyedrops (Predfort®, Allergan Labs) once every hour until bedtime starting immediately after the surgery (topical anesthesia) or after eye patch removal. On the following day, the dosage was reduced to four (initial protocol) or five times daily (from around 1 year to date), with sequential dose reduction of one drop every 5 days until the patients were advised to discontinue using the eyedrops. This routine could be modified according to the referred eye's inflammatory reaction. Artificial tears were prescribed and instructed to be used several times a day when necessary. The use of glaucoma medications was suspended, modified, or maintained at any time during the postoperative period, according to the IOP response, at the discretion of the assistant surgeon. As a rule, the use of eyedrops with prostaglandin analog or oral acetazolamide (Diamox®) was initially suspended if used preoperatively. Only the surgeon responsible for the case measured the IOP of each patient, with the same calibrated Goldmann tonometer at each center.

Age, sex, race, refraction (spherical equivalent), best-corrected visual acuity in LogMAR, number of previous antiglaucoma surgeries, lens status (phakic, aphakic, or pseudophakic), type of glaucoma, MP3 treatment time at each procedure, vertical cup-to-disk ratio, pachymetry, and visual field indices [mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI)] of each patient were annotated. Only reliable Swedish interactive threshold algorithm standard 24-2 (Humphrey Systems, Dublin, California) visual fields were considered in the study.[23] The IOP and number of glaucoma medications used by the patients were recorded at the visit immediately prior to the surgery (maximum of 30 days before surgery). The IOP and number of glaucoma medications used by the patients, as well as any complications, were recorded during each postoperative visit. For statistical analysis, the following postoperative evaluation visits were taken into consideration: 1 ± 1, 15 ± 5, 30 ± 7, 90 ± 15, 180 ± 30, 365 ± 45 (when available) days, and the last recorded visit.

Success criteria were defined as follows: at the last visit, an IOP between 6 and 18 mm Hg and an IOP reduction of more than 20% with or without medication use, or at least a 50% reduction in the IOP or number of glaucoma medications, compared to preoperative values with no serious complications, such as loss of vision or phthisis bulbi. The need for any other glaucoma surgery, such as trabeculectomy, tube shunt implantation, or cyclodestructive procedures to lower the IOP, was considered a treatment failure in this study. Multiple MP3 surgeries were not considered as a criterion for failure. When a certain eye failed, it was excluded from the study during that follow-up period. In these cases, the IOP, number of medications, and follow-up time in months were annotated as their last values for statistical purposes.

The number of MP3 surgeries performed in each patient's eye and the interval between the first and each retreatment (if retreatments were necessary) were recorded at the end of the follow-up period. Retreatment was necessary if any eye failed to achieve the target pressure (defined by the surgeon) with maximum tolerated topical therapy after any MP3 surgery. The surgeon responsible for the case could use different MP3 exposure times at their discretion if one or more retreatments were necessary relative to the protocol followed at initial surgery. The referred eye was categorized in the subgroup of the first surgery and was not excluded from the analysis. However, only patients with double-session MP3 in all surgeries were included. The existence of any other MP3 treatment protocol, regardless of whether it was observed in the primary surgery or in any retreatment (such as a single or even triple-session MP3), was considered an exclusion criterion. For retreatments, the final MP3 treatment time was also recorded.

Statistical analyses were performed using the SPSS software version 22.0 (SPSS Inc., Chicago, Illinois, USA). The Kolmogorov–Smirnov test was used to evaluate sample normality. The paired Student's *t*-test was used to compare IOP, the number of medications taken before surgery vs during all postoperative visits, visual field indices, and eye characteristics. The Kaplan–Meier curve was used to estimate the survival analysis of the double-session MP3 procedures for the treatment of glaucoma. The Pearson correlation was used to correlate the percentage of IOP reduction and MP3 time,

while the Spearman correlation was used to verify the correlation between MP3 time and success. A linear regression analysis was used to estimate the final IOP, considering all IOP measurements until the 6th month (minimal follow-up time). A logistic regression analysis was used to verify preoperative successful predictors in the double-session MP3 procedure for glaucoma with the type of glaucoma, presence of previous glaucoma surgery, preoperative IOP, MP3 time, need for retreatment, and glaucoma severity (as measured by the MD) as independent variables. Because clinicians may rely on the preoperative IOP to determine the MP3 treatment time, a second logistic regression analysis was performed that included only these two variables as independent ones to verify how much (in percentage) the final model (success as a dependent variable) was explained by them, as estimated by the Nagelkerke R^2.

Subsequently, preoperative IOP, MD, number of previous glaucoma surgeries, number of glaucoma medications, and MP3 time were compared in the eyes that achieved treatment success vs failure. All patients were then categorized into two groups according to the MP3 exposure time in the first surgery for a third analysis: group I (GI), 320–360 seconds; group II (GII), more than 360 seconds. The last evaluation was made with all eyes that underwent multiple MP3 sessions and compared to those with treatment success vs failure. The independent Student's *t*-test was used to compare the same variables analyzed in the whole cohort but between groups at this time. The Kaplan–Meier curve was used to estimate the survival analysis in GI and GII, and the results were compared with those of a logrank (Mantel–Cox) test. The alpha error in the multiple comparisons of the IOP and number of medications was corrected using the method proposed by Cross and Chaffin.[24] For IOP comparisons, $p < 0.0062$ was considered statistically significant for the analysis considering MP3 time and $p < 0.0125$, for the eyes that had undergone retreatment; for medications, $p < 0.0083$ and $p < 0.0062$ were considered statistically significant. For all the remaining comparisons, the alpha error was set to 5% ($p < 0.05$).

Results

A total of 191 eyes from 148 patients were included, with a mean follow-up time of 14.4 ± 6.8 months. The mean age of the patients was 64.7 ± 12.8 years, and 58.1% of the patients were women. Of the patients, there were 37 phakic, 149 pseudophakic, and five aphakic eyes, with 134 Caucasians, 50 Afro-descendants, and seven Asians. Glaucoma diagnosis and surgical outcomes are presented in Table 1. Table 2 displays the visual field indices and eye characteristics. There was no change in the visual acuity (LogMAR) at the last visit (0.51 ± 0.58) compared with the preoperative values (0.47 ± 0.54, $p = 0.09$). Eighty-nine eyes had an average of 1.5 ± 0.9 previous glaucoma surgeries, while in 102 eyes, the MP3 procedure was the first glaucoma surgery. The mean duration of MP3 treatment was 364.9 ± 57.6 seconds (320–480 seconds).

The preoperative IOP was significantly higher than that recorded at the last follow-up visit (27.3 ± 6.9 vs 14.6 ± 6.0 mm Hg, $p < 0.001$; a 44.2 ± 21.0% reduction). The IOP reduction, relative to the preoperative values, was statistically significant in all evaluations during the study (Fig. 1; $p < 0.001$ for all time points). The number of topical glaucoma medications was reduced from 3.6 ± 0.6 preoperatively to 2.1 ± 1.0 at the last recorded visit ($p < 0.001$; a 42.6 ± 29.5% reduction; Fig. 2; 12.0% with no medication) and was consistently lower in all documented appointments ($p < 0.001$). Additionally, 69 patients (72 eyes) were taking an average of 774.3 ± 262.5 mg of oral acetazolamide preoperatively, compared with none at the postoperative visits ($p < 0.001$).

Three eyes developed hypotony of at least 30 days (one evolving with phthisis bulbi), all of which presented neovascular glaucoma. One eye progressed to vision loss due to glaucoma worsening, while 10 eyes had persistent flare (>2 months), and nine showed persistent mydriasis (five of which had resolved at 1-year follow-up). Five eyes had worsening cataracts (two of which had previous cataracts, as described in their medical charts), 12 eyes lost two or more lines of vision, three showed cystoid macular edema, two had corneal decompensation, two had transient corneal edema, and one had choroidal and retinal detachment, but without hypotony. Five eyes underwent trabeculectomy, and five eyes underwent endoscopic cyclophotocoagulation in an attempt to control the IOP after MP3 failure.

There was no significant correlation between MP3 time and success (r = 0.092, $p = 0.2$) or percentage of IOP reduction (r = 0.09, $p = 0.2$). Success was obtained in 90.5% of eyes with

Table 1: Glaucoma diagnosis and surgical outcomes

Glaucoma diagnosis	*"n"*	*Success*	*Failure*
Primary open-angle glaucoma	125	118	7
Chronic angle-closure glaucoma	17	17	0
After vitreoretinal surgery	11	11	0
After penetrating keratoplasty	10	9	1
Neovascular	6	4	2
Juvenile	3	3	0
After congenital cataract surgery	3	2	1
Pigmentary	3	1	2
Traumatic	3	3	0
Aphakic	2	2	0
Normal-pressure glaucoma	2	2	0
ICE syndrome	2	0	2
Uveitic	2	0	2
Congenital	1	0	1
Pseudophakic	1	1	0

ICE, iridocorneal endothelial

Table 2: Visual field indices and the eye's characteristics

Preoperative MD (dB)	–10.34 ± 6.06	$p < 0.001$
MD at the last visit (dB)	–10.91 ± 6.05	
Preoperative PSD (dB)	7.36 ± 3.36	$p = 0.05$
PSD at the last visit (dB)	7.66 ± 3.18	
Preoperative VFI (%)	70.3 ± 16.3	$p = 0.02$
VFI at the last visit (%)	68.5 ± 16.8	
Vertical C/D ratio	0.84 ± 0.15	
Spherical equivalent	–0.018 ± 2.48	
CCT (µm)	534 ± 39.1	

CCT, central corneal thickness

1.2 ± 0.5 MP3 surgeries—81.2% with one, 15.2% with two, 3.1% with three, and 0.5% with four MP3 procedures. Considering only 173 successful eyes: 86.2% had one, and 13.8% had two MP3 procedures (1.1 ± 0.3 MP3 surgeries). The first retreatment (when it occurred) was after 5.1 ± 4.0 months (75% until the 5-month follow-up), and the last MP3 procedure occurred 6.0 ± 3.8 months after the first (66.7% before 6 months after the first surgery). The Kaplan–Meier chart estimated the survival of the MP3 procedure to be 32.4 months [95% confidence interval (CI): 30.7, 34.0], limited to 36 months.

The linear regression analysis estimated the final IOP as –6.973 + (Previous IOP × 0.107) + (IOP^{15d} × 0.339) + (IOP^{3m} × 0.289) + (IOP^{6m} × 0.645). IOP at day 1 ($p = 0.3$) and at 30 days ($p = 0.9$) were not included in the final equation. The logistic regression analysis estimated that none of the tested preoperative independent variables—type of glaucoma ($p = 0.07$), previous glaucoma surgery ($p = 0.1$), preoperative IOP ($p = 0.3$), MP3 time ($p = 0.09$), need for retreatment ($p = 0.9$), and glaucoma severity ($p = 0.1$)—were predictors of surgical success in the double-session MP3 procedure for glaucoma. In the second logistic regression analysis, with preoperative IOP and MP3 time as independent variables, only previous IOP was identified as a statistically significant predictor of surgical success ($p = 0.004$), with a lower IOP responsible for a higher success (odds ratio: 0.910; 95% CI: 0.854, 0.971). This regression model with these two variables explained approximately 11.5% of the procedure success (Nagelkerke $R^2 = 0.115$).

Eyes with successful surgery had borderline lower preoperative IOP (26.8 ± 6.3 vs 32.0 ± 10.3 mm Hg, $p = 0.05$) and fewer previous glaucoma surgeries (0.6 ± 0.8 vs 1.4 ± 1.6, $p = 0.06$), with similar previous numbers of glaucoma topical medication (3.6 ± 0.7 vs 3.5 ± 0.5, $p = 0.7$), MD (–10.6 ± 6.8 vs –12.3 ± 6.4 dB, $p = 0.4$), and MP3 time (366.8 ± 58.5 vs 346.6 ± 45.5 seconds, $p = 0.09$), than the eyes with MP3 failure.

A total of 136 eyes had an MP3 exposure time ranging between 320 and 360 seconds (GI: 331.4 ± 18.1 seconds), compared to 55 eyes with an exposure time of more than 360 seconds (GII: 447.6 ± 32.9 seconds, $p < 0.001$). Previous IOP (26.7 ± 7.1 vs 28.9 ± 6.3 mm Hg, $p = 0.04$), final IOP (14.8 ± 6.3 vs 14.1 ± 5.3, $p = 0.4$), and all measured IOPs (Fig. 1) were similar between the two groups. The number of topical glaucoma medications was also similar preoperatively (GI: 3.6 ± 0.6 vs GII: 3.6 ± 0.7, $p = 0.8$) and at the last recorded visit (2.1 ± 1.1 vs 2.0 ± 0.9, $p = 0.6$, Fig. 2). However, GI had more MP3 procedures (1.2 ± 0.5: 78.7% with one, 16.2% with two, 4.4% with three, and 0.7% with four MP3 procedures) than GII (1.1 ± 0.3: 87.3% with one and 12.7% with two MP3 procedures, $p = 0.03$). Success was observed in 88.2% of eyes in GI and 96.3% in GII. The Kaplan–Meier chart estimated the survival of the MP3 procedure as 32.0 months in GI (95% CI: 30.1, 33.9) and 23.2 months in GII (95% CI: 22.2, 24.2), which were limited to 36 months in GI and 24 months in GII (Fig. 3, $p = 0.3$).

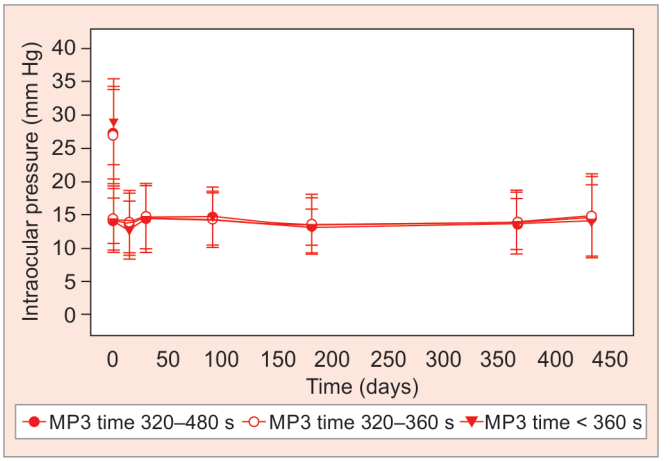

Fig. 1: IOP behavior during the study

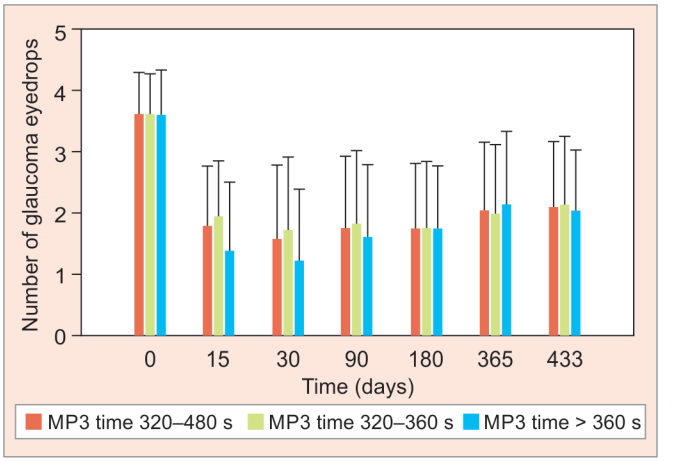

Fig. 2: Number of glaucoma eyedrops at each evaluation

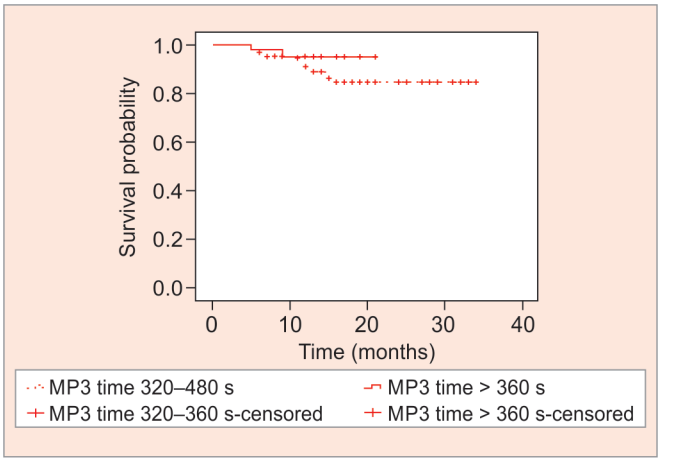

Fig. 3: Kaplan–Meier survival curves according to MP3 time

A total of 36 eyes underwent multiple MP3 surgeries (retreatment was necessary), 24 of which achieved treatment success. Preoperative IOP was higher in these eyes than in those without retreatment (31.6 ± 7.4 vs 26.3 ± 6.4 mm Hg, $p < 0.001$). However, no difference was found in the number of preoperative medications administered (3.5 ± 0.7 vs 3.7 vs 0.4, $p = 0.1$) or MD

(–10.5 ± 7.0 vs –11.9 ± 5.2 dB, $p = 0.4$). Considering only these 36 eyes, eyes with treatment success (GI) had a similar number of previous glaucoma surgeries (1.1 ± 0.8) when compared to eyes with treatment failure (GII, 1.0 ± 1.6, $p = 0.8$), preoperative IOP (30.8 ± 5.6 vs 33.2 ± 10.1 mm Hg, $p = 0.3$), number of topical glaucoma medications (3.7 ± 0.4 vs 3.5 ± 0.5, $p = 0.2$), and MD (–11.4 ± 3.8 vs –12.31 ± 6.4 dB, $p = 0.4$). GI had a higher MP3 treatment time at the first surgery (364.1 ± 68.2 vs 330.0 ± 18.0 seconds, $p = 0.02$), but lower total MP3 time, considering all retreatments (792.1 ± 167.1 vs 1091.6 ± 310.0 seconds, $p = 0.007$), and fewer MP3 procedures (2.0 ± 0.0 vs 2.6 ± 0.6, $p = 0.005$) with a greater percentage of IOP reduction at the last visit (53.6 ± 16.3 vs 0.96 ± 34.6%, $p < 0.001$).

Discussion

Previous published MP3 papers focused on demonstrating the efficacy and safety of the procedure.[1–19] While this information is critical, it is very important to find indicators of success to help specialists improve the surgical outcomes of glaucoma when choosing this surgical modality.

In the present study, patients younger than 18 years of age were excluded from the analysis. Lee et al.[5] reported significantly lower success rates in pediatric patients with glaucoma at 12 months than in adults (22.22 vs 72.22%), using the same MP3 protocol in both groups. Our preceding analysis (unpublished data) yielded similar results. Therefore, young age is a previously known predictor of treatment failure and, therefore, a potential bias if included in the multivariate logistic regression. In this cohort, patient ages ranged from 21 to 92 years.

The double-session MP3 technique is a safe and effective glaucoma surgical option.[9,16] In this larger cohort with a longer follow-up duration, success was achieved in 90.5% of eyes, with a 44.2 ± 21.0% IOP reduction at the last follow-up visit, with a mean of 1.2 ± 0.5 MP3 surgeries performed. The average MP3 time (364.9 ± 57.6 seconds) was higher than almost all previously published papers,[1–15,17–19] and similar to that reported in our previous study,[16] in which comparable results were achieved, especially in patients without previous glaucoma surgery. Despite the higher MP3 treatment time, no increase in complications number nor severity was observed.

The linear regression analysis demonstrated that neither the IOP at postoperative 1 day nor that at postoperative 30 days were significant determinants of the final IOP; this information is consistent with clinical observations. The IOP on postoperative day 1 sometimes does not decrease, and it may take more time for IOP to decrease after surgery. In contrast, patients still experience the effects of previous glaucoma medications; thus, a low IOP can also be measured at this time point. Around 30 days postoperatively, there is frequently a small increase in IOP, which necessitates the addition of glaucoma medication. In fact, only 12% of the eyes were medication-free at the last postoperative visit. While this situation may be considered a limitation for some clinicians, we believe this is an important safety indicator for the procedure because even with higher exposure time, the double-session MP3 rarely evolves to hypotony. On the contrary, glaucoma medication is usually needed to achieve the target IOP. Finally, IOP at postoperative days 15, 90, and 180 may be considered good predictors of the final IOP and important markers of procedure success. Because not all patients were followed up for more than 6 months, the remaining visits were not included in this analysis.

Interestingly, the logistic regression analysis failed to estimate preoperative successful predictors in the double-session MP3 for patients with glaucoma. Yelenskiy et al.[7] identified three independent predictors of success: diagnosis, previous glaucoma surgery, and other concurrent procedures (some eyes had phacoemulsification and/or another glaucoma surgery along with MP3). Despite the absence of statistical significance, in the present study, type of glaucoma ($p = 0.07$) and previous glaucoma surgery ($p = 0.1$) were independent variables with better results in this regard. However, previous double-session MP3 results have already indicated similar success rates between eyes with or without previous glaucoma surgery, despite the need for fewer MP3 procedures in the last group for comparable results.[16]

When only preoperative IOP and MP3 were considered in the logistic regression analysis, only lower preoperative IOP was identified as an independent success predictor ($p = 0.004$). This model was built because clinicians may rely on preoperative IOP to determine the MP3 time for each surgery. However, only around 11.5% of MP3 success can be explained by this model. Nevertheless, higher preoperative IOP may be considered as a failure predictor since a higher previous IOP was found in eyes requiring retreatment. Preoperative IOP was not statistically different between successful or failure eyes (26.8 ± 6.3 vs 32.0 ± 10.3 mm Hg, $p = 0.05$). However, a mean IOP difference of >5 mm Hg should be considered of important clinical significance.

There was no correlation between MP3 time and success ($r = 0.092$, $p = 0.2$) or percentage of IOP reduction ($r = 0.09$, $p = 0.2$). It seems that an increase in MP3 exposure does not necessarily reflect a proportional improvement in surgical outcomes. Apparently, there is a floor effect in the MP3 efficacy related to the exposure time: lower than a certain number may achieve similar success rates, but at the expense of a larger number of surgeries, as shown before,[9,16] and here, when results were compared based on MP3 exposure time (320–360 vs above 360 seconds). In contrast, there is also a ceiling effect, where an additional hypotensive ocular effect would not be observed, which would explain the absence of correlation and statistical significance of the MP3 exposure time as a predictor of surgical success.

Higher MP3 time at the first double-session MP3 was also an important success predictor in eyes where retreatment was necessary (364.1 ± 68.2 vs 330.0 ± 18.0 seconds, $p = 0.02$). Moreover, no eye with more than two surgeries was able to achieve success (2.0 ± 0.0 vs 2.6 ± 0.6, $p = 0.005$); these are critical and new information. Two conclusions can arise from the following results: clinicians should use a higher laser exposure time in the double-session MP3 first surgery, and if failure is observed after the second (when necessary), a different glaucoma surgical modality should be considered rather than a third MP3 surgery. In fact, the mean MP3 time of 360 seconds identified herein was observed because the initial double-session protocol consisted of a fixed time of 320 seconds. The latest surgeries usually employed an MP3 time higher than 360 seconds, as noticed by the lower mean follow-up time in the GII (23.2 vs 32.0 months), in an attempt to achieve better efficacy and less retreatment. Thus, in contrast to previously published studies that suggest lower energy as the ideal MP3 protocol (however, analyzing only single session MP3 surgeries),[21,22] it is possible that total energy of approximately 250–260 J (400–420 seconds x 2 J × 31.3%) would be the optimal double-session MP3 protocol.

The retrospective nature of the study, the absence of a rigid protocol to determine the MP3 application time in each case, and

the reliance only on surgeon discretion are the main limitations of this study. Nonetheless, these results should not be extrapolated to MP3 surgeries with only one swing per eye hemisphere. Thus, prospective randomized controlled trials with different double-session MP3 protocols, in comparison with the standard MP3 technique, are needed to confirm the results presented here.

Conclusion

The probable ideal double-session MP3 protocol for the surgical treatment of glaucoma includes higher energy at the first surgery, while higher preoperative IOP is a failure predictor. Therefore, the ideal patient should not have too high preoperative IOP.

Clinical Significance

This is the first study to give special attention to the double-session MP3 protocol and success predictors.

Orcid

Leopoldo Magacho https://orcid.org/0000-0003-2633-9806

References

1. Tan AM, Chockalingam M, Aquino MC, et al. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clin Exp Ophthalmol 2010;38(3):266–272. DOI: 10.1111/j.1442-9071.2010.02238.x
2. Aquino MCD, Barton K, Tan AMWT, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. Clin Exp Ophthalmol 2015;43(1):40–46. DOI: 10.1111/ceo.12360
3. Kuchar S, Moster MR, Reamer CB, et al. Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. Lasers Med Sci 2016;31(2):393–396. DOI: 10.1007/s10103-015-1856-9
4. Emanuel ME, Grover DS, Fellman RL, et al. Micropulse cyclophotocoagulation: initial results in refractory glaucoma. J Glaucoma 2017;26(8):726–729. DOI: 10.1097/IJG.0000000000000715
5. Lee JH, Shi Y, Amoozgar B, et al. Outcome of micropulse laser transscleral cyclophotocoagulation on pediatric versus adult glaucoma patients. J Glaucoma 2017;26(10):936–939. DOI: 10.1097/IJG.0000000000000757
6. Williams AL, Moster MR, Rahmatnejad K, et al. Clinical efficacy and safety profile of micropulse transscleral cyclophotocoagulation in refractory glaucoma. J Glaucoma 2018;27(5):445–449. DOI: 10.1097/ijg.0000000000000934
7. Yelenskiy A, Gillette TB, Arosemena A, et al. Patient outcomes following micropulse transscleral cyclophotocoagulation: intermediate term results. J Glaucoma 2018;27(10):920–925. DOI: 10.1097/IJG.0000000000001023
8. Jammal AA, Costa DC, Vasconcellos JPC, et al. Prospective evaluation of micropulse transscleral diode cyclophotocoagulation in refractory glaucoma: 1 year results. Arq Bras Oftalmol 2019;82(5):381–388. DOI: 10.5935/0004-2749.20190076
9. Magacho L, Lima FE, Avila MP. Double-session micropulse transscleral laser (CYCLO G6) for the treatment of glaucoma. Lasers Med Sci 2020;35(7):1469–1475. DOI: 10.1007/s10103-019-02922-1
10. Nguyen AT, Maslin J, Noecker RJ. Early results of micropulse transscleral cyclophotocoagulation for the treatment of glaucoma. Eur J Ophthalmol 2020;30(4):700–705. DOI: 10.1177/1120672119839303
11. Sarrafpour S, Saleh D, Ayoub, S, et al. Micropulse transscleral cyclophotocoagulation: a look at long-term effectiveness and outcomes. Ophthalmol Glaucoma 2019;2(3):167–171. DOI: 10.1016/j.ogla.2019.02.002
12. Souissi S, Baudouin C, Labbé A, et al. Micropulse transscleral cyclophotocoagulation using a standard protocol in patients with refractory glaucoma naive of cyclodestruction. Eur J Ophthalmol 2021;31(1):112–119. DOI: 10.1177/1120672119877586
13. Varikuti VNV, Shah P, Rai O, et al. Outcomes of micropulse transscleral cyclophotocoagulation in eyes with good central vision. J Glaucoma 2019;28(10):901–905. DOI: 10.1097/IJG.0000000000001339
14. Zaarour K, Abdelmassih Y, Arej N, et al. Outcomes of micropulse transscleral cyclophotocoagulation in uncontrolled glaucoma patients. J Glaucoma 2019;28(3):270–275. DOI: 10.1097/IJG.0000000000001174
15. de Crom RMPC, Slangen CGMM, Kujovic-Aleksov S, et al. Micropulse transscleral cyclophotocoagulation in patients with glaucoma: 1- and 2-year treatment outcomes. J Glaucoma 2020;29(9):794–798. DOI: 10.1097/IJG.0000000000001552
16. Magacho L, Lima FE, Avila MP. Double-session micropulse transscleral laser (CYCLO G6) as a primary surgical procedure for glaucoma. J Glaucoma 2020;29(3):205–210. DOI: 10.1097/IJG.0000000000001426
17. Preda MA, Karancsi OL, Munteanu M, et al. Clinical outcomes of micropulse transscleral cyclophotocoagulation in refractory glaucoma-18 months follow-up. Lasers Med Sci 2020;35(7):1487–1491. DOI: 10.1007/s10103-019-02934-x
18. Tekeli O, Köse HC. Outcomes of micropulse transscleral cyclophotocoagulation in primary open-angle glaucoma, pseudoexfoliation glaucoma, and secondary glaucoma. Eur J Ophthalmol 2021;31(3):1113–1121. DOI: 10.1177/1120672120914231
19. Vig N, Ameen S, Bloom P, et al. Micropulse transscleral cyclophotocoagulation: initial results using a reduced energy protocol in refractory glaucoma. Graefes Arch Clin Exp Ophthalmol 2020;258(5):1073–1079. DOI: 10.1007/s00417-020-04611-0
20. Garcia GA, Nguyen CV, Yelenskiy A, et al. Micropulse transscleral diode laser cyclophotocoagulation in refractory glaucoma: short-term efficacy, safety, and impact of surgical history on outcomes. Ophthalmol Glaucoma 2019;2(6):402–412. DOI: 10.1016/j.ogla.2019.08.009
21. Sanchez FG, Peirano-Bonomi JC, Grippo TM. Micropulse transscleral cyclophotocoagulation: a hypothesis for the ideal parameters. Med Hypothesis Discov Innov Ophthalmol 2018; 7(3):94–100. PMID: 30386797; PMCID: PMC6205680.
22. Sanchez FG, Peirano-Bonomi JC, Barbosa BN, et al. Update on micropulse transscleral cyclophotocoagulation. J Glaucoma 2020;29(7):598–603. DOI: 10.1097/IJG.0000000000001539
23. Hodapp E, Parrish RK II, Anderson DR. Clinical Decisions in Glaucoma. St. Louis, Missouri, USA; 1993.
24. Cross EM, Chaffin WW. Use of the binomial theorem in interpreting results of multiple tests of significance. Edu Psychol Meas 1982;42(1):25–34. DOI: 10.1177/0013164482421003