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ORIGINAL RESEARCH

Management of Pseudophakic Malignant Glaucoma Using Modified Nd:YAG Laser Treatment Methodology Through Surgical Preset Iridectomy

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ABSTRACT

Introduction: The use of the neodymium:yttrium–aluminum-garnet (Nd:YAG) laser to treat malignant glaucoma (MG) has been described in the literature since the 1980s. However, the technique has been reported to have a short-term effect, with a notable relapse rate. In the present study, we report the efficacy and durability of a modified Nd:YAG laser treatment methodology for treatment of pseudophakic or aphakic MG.

Methods: Patients with chronic angle-closure glaucoma and deemed at high risk of developing post-operative MG received prophylactic peripheral iridectomy during their conventional operation beginning in 2017. When the diagnosis of pseudophakic or aphakic MG was confirmed, a thorough Nd:YAG laser capsulo/zonulo-hyaloido-vitreolysis (CZHV) was performed through iridectomy, along with standardized pre- and post-laser medications. This retrospective case series includes 14 eyes of 11 patients with MG who had surgical preset iridectomy and modified Nd:YAG laser CZHV between 2017 and 2022. Outcome measures included resolution and recurrence of MG and incidence of treatment complications.

Results: The mean follow-up was 27.1 ± 15.0 months (range, 12–48). Long-term resolution of MG was obtained in all included eyes at the end of the follow-up. Six eyes (42.9%) achieved long-term resolution with a single Nd:YAG laser intervention. Eight eyes (57.1%) achieved long-term resolution following two to three laser interventions, with two eyes (14.3%) experiencing recurrence. There was no complication during the follow-up. At the final visit, a significant reduction ($P = 0.0001$) in the mean intraocular pressure (IOP) was observed (13.1 ± 2.8 mmHg) compared to presentation (21.4 ± 6.3 mmHg).

Conclusion: The modified Nd:YAG laser treatment methodology is a minimally invasive option to manage pseudophakic or aphakic MG with sustained effectiveness. Reduced inflammatory reactions due to prophylactic peripheral iridectomy, rapid diagnosis, and timely treatment initiation have all contributed to the

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favorable outcomes associated with this modified treatment methodology.

Keywords: Nd:YAG laser; Malignant glaucoma; Aqueous misdirection; Iridectomy; Capsulo/zonulo-hyaloido-vitreolysis

Key Summary Points

Why carry out this study?

The theoretical effectiveness of the neodymium:yttrium-aluminum-garnet (Nd:YAG) laser for treating pseudophakic or aphakic malignant glaucoma (MG) is widely acknowledged; however, its durability in real-world practice is typically lower.

Through surgical preset iridectomy, we devised a modified Nd:YAG laser procedure that demonstrates effectiveness and durability.

What was learned from the study?

Effective long-term management of pseudophakic or aphakic MG can be accomplished with a progressive therapeutic approach involving Nd:YAG laser capsulo/zonulo-hyaloido-vitreolysis from iridectomy and appropriate medication administration.

The favorable outcomes associated with this modified treatment methodology can be attributed to the timely initiation of treatment and the reduction of inflammatory reactions facilitated by prophylactic peripheral iridectomy.

INTRODUCTION

Malignant glaucoma (MG) is a rare and potentially devastating form of secondary angle closure characterized by a diffusely shallow anterior chamber, normal to elevated intraocular pressure (IOP), and the presence of one or more patent iridotomies/iridectomies. Based on its presumed etiology, it is also known as ciliary block glaucoma, cilio-vitreo-lenticular block glaucoma, and aqueous misdirection syndrome [1, 2]. Classically, MG is reported to occur in eyes with angle-closure glaucoma following filtration surgery. However, the syndrome may also emerge after many different ocular interventions in anatomically predisposed eyes with or without glaucoma. It may occur at any point after the intervention, from the immediate period to years later [3, 4].

The first-line management after MG diagnosis should include the administration of tropical cycloplegics, topical aqueous humor suppressants, and anti-inflammatory medications. However, it has been reported to be effective in only about half of patients, with a nearly 100% relapse rate [5, 6]. A variety of office-based lasers may be used as the second-line therapy. The neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, aiming to create a direct path between the anterior chamber and posterior segment, is one of the widely acknowledged options that has been used in pseudophakic or aphakic eyes for nearly 40 years [7–11]. The efficacy of transscleral cyclophotocoagulation (TSCPC) has been discussed for the past decade. In addition to lowering aqueous production, the coagulative shrinkage of the ciliary body may subsequently disrupt the ciliary–hyaloid interface and allow misdirected aqueous flow forward again. However, TSCPC is often reserved for patients with uncorrectable low vision as a destructive intervention [2, 9]. Surgical intervention is required in MG that is refractory to non-surgical therapy. Pars plana vitrectomy (PPV) with lens extraction is a common surgical therapeutic approach. Zonulo-hyaloido-vitrectomy performed from the anterior chamber through a tunnel within the iridectomy is a safer alternative for pseudophakic MG [2, 5, 12, 13].

Despite the widespread use of Nd:YAG laser for treatment of pseudophakic MG, there is no consensus regarding this application. Previous reports differ in terms of application site, laser parameters, and even terminology, making it challenging for other clinicians to replicate the application. In addition, it has been reported that the procedure has a short-term effect with a

high relapse rate. Approximately 70% of previously reported patients with repeat Nd:YAG laser treatment achieved long-term resolution, while the remaining 30% of cases ultimately required TSCPC or surgical interventions, resulting in increased economic burden and treatment duration [2, 5, 9, 10]. Here, we report a modified Nd:YAG laser treatment methodology for treatment of pseudophakic MG, which comprises a disruption of the peripheral lens capsule and/or zonule, anterior hyaloid, and anterior vitreous (capsulo/zonulo-hyaloido-vitreolysis, CZHV) through surgical preset iridectomy. At the end of the follow-up, all cases in the study indicated long-term resolution of MG without further interventions. To the best of our knowledge, no case series have resolved pseudophakic MG with the Nd:YAG laser approach alone.

METHODS

Subjects

This was a non-comparative retrospective case series conducted at Shenzhen Eye Hospital (Shenzhen, China). The institutional research review board and ethics committee of Shenzhen Eye Hospital approved the study protocol (Reference No. 2023KYPJ044). The study was conducted in accordance with the World Medical Association's Declaration of Helsinki. Written informed consent for participation is not required for retrospective study in accordance with national legislation and institutional requirements. However, all patients included in this study were still undergoing regular follow-ups during data collection for this study, so all patients signed written informed consent after an explanation of the nature of the study during their follow-up, prior to the data analysis. Between March 2017 and March 2022, the medical records of all eligible patients from the glaucoma service of Shenzhen Eye Hospital were evaluated. Eligible participants were those with pseudophakic/aphakic eyes with MG who had surgical preset iridectomy and underwent the modified Nd:YAG laser treatment. The diagnostic criteria for MG included a uniformly shallow or flat anterior chamber, presence of a patent iridectomy or iridotomy (Fig. 1a–e), and IOP higher than 21 mmHg or IOP elevation of more than 5 mmHg within 24 h. The diagnosis was made in the absence of other etiology, such as suprachoroidal hemorrhage or effusion (confirmed by indirect ophthalmoscopy or B-scan) and bleb leakage (confirmed by fluorescein staining under slit-lamp examination).

From the medical records, the following demographic and clinical data were collected: age, gender, eye affected, ocular diagnosis, history of previous treatment including surgeries, history of the previous episode of MG in either eye, precipitating ocular surgeries, duration between surgery and onset of MG, IOP, anterior chamber depth, lens status, location and size of the iridectomy, topical and systemic medications used (fixed combination anti-glaucoma eye drops was counted as two medications), laser procedures undertaken for MG, complications and other characteristic ocular findings. B-scan, ultrasound biomicroscopy (UBM), and anterior segment optical coherence tomography (AS-OCT) images were obtained when available.

The primary outcome measure for the present study was the resolution of MG. Resolution was defined as reformation of the central anterior chamber (Fig. 1j, k) with IOP lower than 21 mmHg without systemic anti-glaucoma drugs (on two consecutive visits at least 1 week apart). The secondary outcome measures included MG recurrence and treatment complications. Patients were followed up for at least 12 months after the last Nd:YAG laser CZHV. Only one patient was excluded due to incomplete documentation and follow-up.

Surgical Preset Iridectomy

Beginning in January 2017, patients at high risk of developing MG with pseudophakic/aphakic eyes or with planned intraoperative lens extraction received prophylactic peripheral iridectomy during their scheduled glaucoma surgeries. Patients suspected of being prone to MG met one of the following criteria: (1) chronic angle-closure glaucoma (CACG)

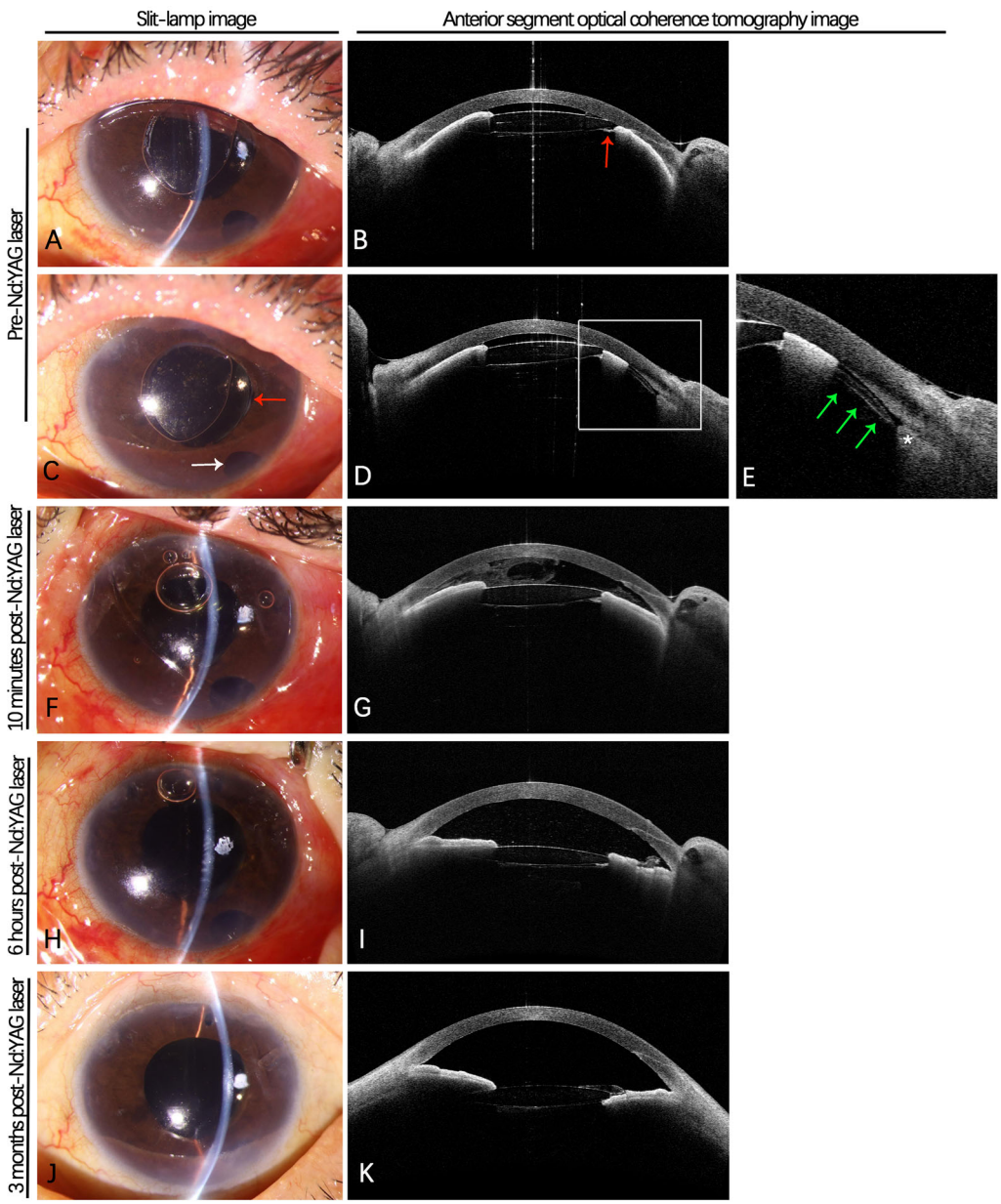

Fig. 1 Representative pre- and post-Nd:YAG laser slit-lamp and AS-OCT images. **a–c** The patient presented after glaucoma filtration surgery with total iridocorneal touch, a shallow anterior chamber, and elevated intraocular pressure, not responding to initial medical treatment. White arrow shows patent and sufficiently sized surgical preset iridectomy. Red arrow shows the gap between the dilated iris pupillary margin and intraocular lens optic, where the Nd:YAG laser was first applied. **d** AS-OCT image captured across the iridectomy (the boxed area). **e** Magnification of the boxed area showing anterior rotated ciliary body (white asterisks). Green arrows showing the lens capsule-zonule-anterior hyaloid complex, where the subsequent Nd:YAG laser focused on. **f**, **g** Ten minutes after one successful Nd:YAG laser treatment, the anterior chamber immediately deepened, and loose vitreous was observed in the anterior chamber. **h**, **i** Six hours after one successful Nd:YAG laser treatment, the anterior chamber further deepened and the anterior chamber angles widened. Hyperreflective particles were uniformly distributed in the anterior chamber. **j**, **k** Three months after the last Nd:YAG laser treatment, the anterior chamber depth returned to normal and remained constant. *Nd:YAG* neodymium:yttrium-aluminum-garnet, *AS-OCT* anterior segment optical coherence tomography

scheduled for trabeculectomy or combined cataract extraction and trabeculectomy; (2) patients with CACG with previous MG history in either eye. The iris tissue excised had to be at least 2.5 mm × 2 mm in size to generate a sufficiently sized patent iridectomy. Briefly, superior peripheral iridectomy was performed in eyes that underwent trabeculectomy or combined cataract extraction and trabeculectomy; in other operative eyes where a peripheral iridectomy is not typically performed, an inferior peripheral iridectomy was performed through scleral tunnel incision (Fig. 1c).

Modified Nd:YAG Laser Capsulo/Zonulo-Hyaloido-Vitreolysis Technique

Once the MG diagnosis was confirmed, a protocol-based, stepwise treatment plan was followed (Fig. 2). All patients received rapid medical care as their first-line management. This included topical cycloplegic (1% atropine sulfate) 3–4 times daily, osmotic agent (intravenous 20% mannitol in a dose of 1g/kg) 1–2 times daily, topical corticosteroids 4–6 times daily, and topical aqueous humor suppressant(s). Subconjunctival corticosteroids (dexamethasone 2–3 mg daily) and systemic acetazolamide (oral acetazolamide 250 mg twice daily) were administered at the discretion of the treating specialists.

If the condition did not improve (central anterior chamber did not reform) 24 h after medical treatment, pseudophakic/aphakic eyes with prophylactic peripheral iridectomy were treated with Nd:YAG laser CZHV. One of the two senior glaucoma consultants carried out all laser interventions. When conditions permitted, the Nd:YAG laser was performed exclusively through the surgical preset iridectomy, with a power setting started at 2 mJ. The peripheral lens capsule and/or zonule were the initial focus points. Once the lens capsule and/or zonule had been completely perforated under direct observation of the treating specialists, the focus point was shifted posteriorly to penetrate the anterior hyaloid and disrupt the anterior vitreous. When a free passage was successfully established, the anterior chamber immediately deepened, and loose vitreous was occasionally observed in the anterior chamber, herniating through the iridectomy (Fig. 1f, g). The laser power ranged from 2 mJ to 5 mJ, and the number of laser shots varied based on whether the passage was well formed.

In eyes where exclusive Nd:YAG laser CZHV through iridectomy was not achievable due to total iridocorneal touch (Fig. 1a–c), the Nd:YAG laser was first applied through the dilated pupil. The initial laser focus point should be determined strategically, ideally situated between the dilated iris pupillary margin and the intraocular lens optic, targeting the lens capsule and adjacent anterior hyaloid (Fig. 1b, c). The initial power setting was started at 1 mJ. After one successful application of the transpupillary Nd:YAG laser capsulotomy and hyaloidotomy, which immediately deepened the anterior chamber and reversed the iridocorneal touch, additional Nd:YAG laser CZHV was accomplished through the surgical preset iridectomy as described above. In this intervention, the laser power varied from 1 mJ to 5 mJ, and the number of laser shots varied depending on whether the passages were well established in the two laser applications.

The post-laser medications were topical cycloplegics (1% atropine sulfate) 3–4 times daily, topical corticosteroids 4–6 times daily, and topical aqueous humor suppressant(s). Within the first week, subconjunctival corticosteroids (dexamethasone 2–3 mg daily) and an osmotic agent (intravenous 20% mannitol in a dose of 1g/kg 1–2 times daily) were administered at the discretion of the treating specialists. Over a period of 3 months, topical cycloplegics, topical corticosteroids, and aqueous humor suppressant(s) were gradually tapered. However, indefinite topical cycloplegic therapy may be required to prevent recurrence. Following the laser intervention, follow-up visits were scheduled for day 1, day 2, day 3, week 1, week 2, month 1, and at varied intervals until the final visit.

Treatment for Recurrent Anterior Chamber Shallowing and Recurrent MG

During the follow-up, if the anterior chamber shallowed again with fibrotic recondensation of

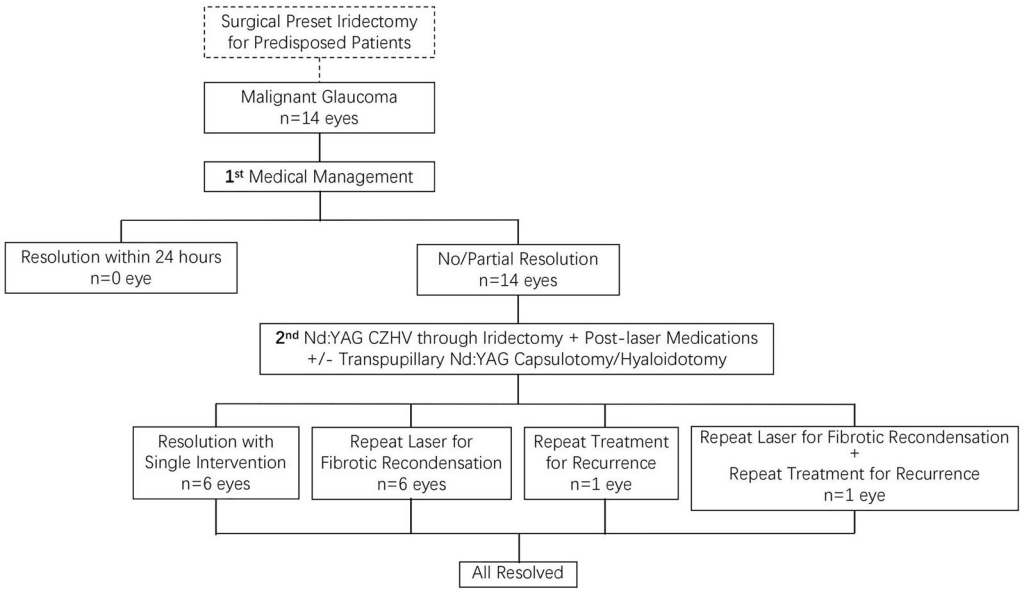

Fig. 2 Treatment algorithm and outcomes of treatment for malignant glaucoma. *Nd:YAG* neodymium:yttrium-aluminum-garnet, *CZHV* capsulo/zonulo-hyaloido-vitreolysis

the anterior hyaloid behind the peripheral iridectomy directly visualized or suspected, the Nd:YAG laser CZHV via iridectomy was applied again on the same day, independent of the IOP levels. The previous post-laser medications were followed if the situation occurred within 3 months of the first laser intervention. Instead, at the discretion of the treating specialists, topical corticosteroids and topical cycloplegics were administered again and reduced over 1 month.

If recurrent MG was identified, the complete modified Nd:YAG laser treatment protocol (pre-laser medications ± transpupillary Nd:YAG laser capsulotomy and hyaloidotomy + Nd:YAG laser CZHV + post-laser medications) was immediately applied again, irrespective of the interval between MG recurrence and the last laser intervention. In case MG was not improved after repeated medical and modified Nd:YAG laser treatments, zonulo-hyaloido-vitrectomy performed from the anterior chamber was planned as a surgical intervention. However, all cases demonstrated resolution of MG with no need for further surgical intervention in the current series.

Statistical Analysis

All data were analyzed using SPSS version 21.0 software (IBM Corp., New York, NY, USA). Continuous and categorical variables were presented as mean ± standard deviation and proportion (%). The normality of data distribution was evaluated using the Shapiro–Wilk normality test. Normally distributed variables were compared by the two-sample *t* test. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Fourteen eyes of 11 patients underwent this novel treatment and were included in the final analysis. Table 1 shows the demographic information of the included patients. There were six female and five male patients. All patients were initially diagnosed with CACG, with one eye having retinitis pigmentosa and the other having vascular glaucoma secondary to branch retinal vein occlusion. Various surgeries were performed as initial treatment, but all eyes were managed with prophylactic peripheral iridectomy. Among these included eyes, 13 (92.9%)

Table 1 Demographic and clinical features of the included patients (n = 11 patients/14 eyes)

Age (years)	50.6 ± 11.3 (range, 31–65)
Male/female	5:6
Initial diagnosis	
CACG	14
BRVO + NVG	1
RP	1
Aphakic/pseudophakic	1:13
IOP at presentation (mmHg)	21.4 ± 6.3 (range, 13–35)
IOP at final follow-up (mmHg)	13.1 ± 2.8 (range, 8–18)
No. of anti-glaucoma medications at final follow-up	0.9 ± 1.1 (range, 0–3)
Follow-up (months)	27.1 ± 15.0 (range, 12–48)
Axial length (mm)	22.6 ± 1.2 (range, 21.1–25.2)

CACG chronic angle closure glaucoma, *RP* retinitis pigmentosa, *BRVO* branch retinal vein occlusion, *NVG* neovascular glaucoma, *IOP* intraocular pressure

eyes developed MG in the first post-operative month, while only one (7.1%) eye developed MG in the third post-operative month. The mean age at MG onset was 50.6 ± 11.3 years (range, 31–65 years). Thirteen eyes were pseudophakic, and one was aphakic at MG diagnosis. All pseudophakic eyes were implanted with a posterior chamber intraocular lens. The mean axial length was 22.6 ± 1.2 mm (range, 21.1–25.2 mm).

At the end of the follow-up, all included eyes had achieved long-term resolution of MG. As first-line management, all eyes diagnosed with MG received medical care immediately. However, none of the eyes demonstrated improvement (reformation of the central anterior chamber) after 24 h of medical treatment alone. The modified Nd:YAG laser treatment was performed through surgical preset iridectomy and was initially effective (central anterior chamber reformed) in all eyes. Six of 14 eyes (42.9%) achieved long-term resolution with a single Nd:YAG laser intervention. Six eyes (42.9%) had anterior chamber shallowed again secondary to fibrotic recondensation and received repeat Nd:YAG laser CZHV; one eye (7.1%) demonstrated a recurrence and underwent one repeat modified Nd:YAG laser treatment; one eye (7.1%) had both fibrotic recondensation in early post-laser stage and a recurrence 1 month after the second Nd:YAG laser CZHV, thus underwent one repeat modified Nd:YAG laser treatment as the third intervention. All eight eyes achieved long-term resolution with the second and third laser interventions (Fig. 2).

The mean follow-up was 27.1 ± 15.0 months (range, 12–48). A statistically significant decrease (P = 0.0001) was observed between the mean IOP at the final visit (13.1 ± 2.8 mmHg, range 8–18 mmHg) and the mean IOP at presentation (21.4 ± 6.3 mmHg, range 13–35 mmHg). At the final visit, the mean number of topical aqueous humor suppressants was 0.9 ± 1.1 (range, 0–3). One eye continued to receive topical cycloplegics even after the resolution of MG. No major complications were observed during or after the modified Nd:YAG laser treatment. Figure 1 depicts a representative case from the present series. Table 2 lists the clinical information and treatment outcomes of all the cases in this series.

DISCUSSION

One and a half centuries have passed since von Graefe first described MG [1]. Our understanding of this uncommon syndrome has grown dramatically, but its treatment outcomes remain unsatisfactory. At the outset, some patients with MG may be diagnosed in a delayed fashion, resulting in delayed provision of optimal treatment [3]. Grzybowski et al. suggested that the term "chronic fluid misdirection syndrome" better describes the nature of MG, as anterior chamber shallowing and aqueous misdirection can be observed several days before elevation in IOP occurs [2]. Our observation appears to be in line with this

Table 2 Data chart of all cases in the series

Patient no.	Case no.	Age (years)	Gender	Initial diagnosis	Eye	Axial length (mm)	Previous surgical history	Previous MG history	Surgical procedure before MG onset	Lens status at MG onset	Location of peripheral iridectomy
1	1	31	F	CACG	OD	21.90	Tr	+	P/I+AGVI + SPI	Pseudophakia	Inferior
2	2	40	M	CACG	OD	23.06	P/I	−	Tr (SPI)	Pseudophakia	Superior
3	3	62	M	CACG	OS	22.57	P + Tr (SPI)	−	AGVI	Aphakia	Superior
4	4	42	M	CACG	OS	22.27	LPI; P/I + CTRI	+	AGVI + SPI	Pseudophakia	Inferior
5	5	53	F	CACG	OD	21.37	LPI; P/I + VSL	+	Tr (SPI)	Pseudophakia	Superior
	6*	55	F	CACG	OS	21.38	LPI; Tr; P/I + VSL	+	AGVI + SPI	Pseudophakia	Inferior
6	7	46	M	CACG; RP	OS	23.42	−	−	Tr + P/I (SPI)	Pseudophakia	Superior
7	8	63	M	CACG; BRVO + NVG	OD	23.21	−	+	P/I + AGVI + SPI	Pseudophakia	Inferior
8	9	61	M	CACG	OS	22.05	LPI	−	Tr + P/I (SPI)	Pseudophakia	Superior
9	10	65	F	CACG	OD	21.40	Tr	+	P/I + VSL + SPI	Pseudophakia	Inferior
	11	65	F	CACG	OS	21.08	Tr + P/I	+	AGVI + SPI	Pseudophakia	Inferior
10	12	41	F	CACG	OD	22.69	P/I + VSL + ECP	−	Tr (SPI)	Pseudophakia	Superior
11	13	42	F	CACG	OD	25.18	-	−	Tr + P/I + CTRI (SPI)	Pseudophakia	Superior
	14	42	F	CACG	OS	24.29	-	−	Tr + P/I + CTRI (SPI)	Pseudophakia	Superior

Table 2 continued

Patient no.	Case no.	Vitreous hernia	Fibrotic recondensation	Recurrence	IOP at presentation (mmHg)	IOP at final follow-up (mmHg)	No. of aqueous humor suppressants at final follow-up	Cycloplegics at final follow-up	Follow-up (months)
1	1	+	−	+, 1st month post-treatment	14	14	0	−	48
2	2	+	+, 2nd day post-treatment	−	19	12	1	−	48
3	3	−	−	−	27	17	0	−	45
4	4	−	−	−	15	14	0	−	40
5	5	+	+, 2nd day post-treatment	+, 1st month post-treatment	17	15	1	−	40
	6*	+	+, 3rd day post-treatment	−	22	8	0	+	15
6	7	+	+, 2nd day post-treatment	−	25	15	3	−	36
7	8	−	+, 3rd day post-treatment	−	20	12	2	−	24
8	9	+	+, 2nd day post-treatment	−	24	14	0	−	24
9	10	−	−	−	28	12	1	−	12
	11	−	−	−	13	11	0	−	12
10	12	+	+, 2nd day post-treatment	−	35	18	3	−	12

Table 2 continued

Patient no.	Case no.	Vitreous hernia	Fibrotic recondensation	Recurrence	IOP at presentation (mmHg)	IOP at final follow-up (mmHg)	No. of aqueous humor suppressants at final follow-up	Cycloplegics at final follow-up	Follow-up (months)
11	13	+	−	−	24	9	1	−	12
	14	+	−	−	16	12	1	−	12

*Case presented in Fig. 1

MG malignant glaucoma, *IOP* intraocular pressure, *CACG* chronic angle closure glaucoma, *RP* retinitis pigmentosa, *BRVO* branch retinal vein occlusion, *NVG* neovascular glaucoma, *Tr* trabeculectomy, *P/I* phacoemulsification and intraocular lens implantation, *P* phacoemulsification, *SPI* surgical preset iridectomy, *LPI* laser peripheral iridotomy, *CTRI* capsular tension ring implantation, *VSL* visco-synechiolysis, *AGVI* Ahmed glaucoma valve implantation, *ECP* endoscopic cyclophotocoagulation, *OD* right eye, *OS* left eye

suggestion. In the present study, all patients had shallowed anterior chambers at presentation, but only half of the cases (7/14) presented with IOP of 22 mmHg or higher. The IOP may even be low in the early stages of MG development. Tomey et al. proposed that post-operative wound leakage may be a causative factor for MG following cataract surgery. A similar situation may also occur in filtration surgeries, where increased aqueous outflow induces the initial forward movement of the lens–iris diaphragm and triggers the cycle of aqueous misdirection [14]. Rather than an early symptom, IOP elevation in MG is the consequence of an already initiated vicious cycle, although in certain cases IOP does elevate with some rapidity. Therefore, the universal diagnostic criteria for ocular hypertension, IOP of 22 mmHg or above, may not be ideal to serve as a diagnostic criterion for MG and may lead to delayed diagnosis and postponed treatment. In the present study, for uniformity across observation and consistency in practice, IOP as a diagnostic criterion for MG was defined as higher than 21 mmHg or elevation of more than 5 mmHg within 24 h. Yet in a more proactive stance, we suggest once other etiologies have been excluded, MG diagnosis should be considered regardless of the IOP level. A diagnostic strategy for post-operative shallow anterior chamber following cataract and glaucoma filtration surgeries is depicted in Fig. 3.

There is clearly an anatomical predisposition for MG. Previous studies have identified hyperopia, chronic angle closure, plateau iris configuration, and anteriorly rotated ciliary processes as risk factors for the development of MG [5, 15, 16]. However, the exact mechanism underlying MG remains uncertain. Quigley et al. suggested that choroidal expansion is the precipitating event that increases vitreous pressure and induces the initial compensatory outflow of aqueous from the anterior chamber [17]. Shaffer and Hoskins proposed misdirection of aqueous, wherein aqueous is misdirected posteriorly either into or around the vitreous causing increased transvitreal pressure and decreased anterior hyaloid conductivity [18]. Chandler et al. indicated that zonular laxity combined with higher vitreous pressure causes the lens to move forward [19]. Whatever the

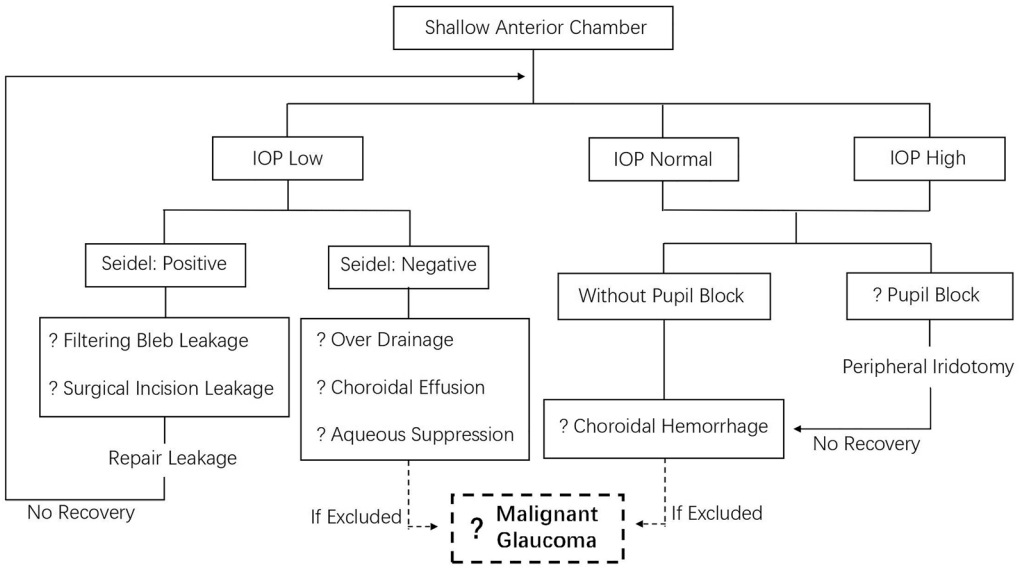

Fig. 3 Diagnostic algorithm for post-operative shallow anterior chamber. *IOP* intraocular pressure

supposition, a disturbed interaction between the lens, ciliary body, and anterior hyaloid, resulting in anterior displacement of the lens–iris diaphragm and higher hydraulic resistance of the vitreous, has received widespread acceptance as a key pathogenic pathway. As fluid accumulates in the posterior segment, the aqueous in the anterior chamber is continually lost via the trabecular meshwork. Eventually, the angle closes, establishing a vicious cycle in which the higher the pressure in the posterior segment, the more tightly the lens–iris diaphragm is held forward [2–4, 17–19].

To break the cycle of aqueous misdirection and re-equalize the transvitreal pressure, many authors have emphasized the importance of complete penetration of the lens capsule-zonule-anterior hyaloid complex rather than simply debulking the vitreous [2, 9, 20, 21]. Lai et al. reported a post-trabeculectomy pseudophakic MG in a vitrectomized eye resistant to vitreous tapping with peripheral iridectomy and intracameral injection of room air. Finally, the recurrent MG was treated with Nd:YAG laser zonulectomy and hyaloidectomy via peripheral iridectomy [22]. This case is not unprecedented. Many cases of MG have been reported in eyes with a history of PPV, and an intact capsule-zonule-anterior hyaloid complex was a shared characteristic among them [23, 24]. Debrouwere et al. emphasized that while using PPV as a therapeutic approach for MG, the efficacy of total vitrectomy was limited in 66% of their patients unless a zonulectomy was incorporated into the procedure [5]. Other studies have similarly determined that the chance of persistent or recurrent MG is higher in phakic eyes than in pseudophakic eyes, owing to the difficulties in complete removal of the anterior hyaloid and zonular fibers without damaging the lens [2, 20]. In previous MG case series, only vitrectomy combined with adequate disruption of the tissues (iris, lens capsule, zonule, anterior hyaloid, and the lens if phakic) separating the posterior and anterior chambers has been described to be 100% effective without relapse throughout the follow-up period [5, 21].

Despite its effectiveness in controlling MG, PPV has inherent risks and requires vitreoretinal surgical expertise. In recent years, the efficacy of zonulo-hyaloido-vitrectomy performed via peripheral iridectomy from the anterior chamber has been investigated for treatment of pseudophakic or aphakic MG. Studies yielded positive results, confirming that total vitrectomy is unnecessary, provided that an unobstructed passage between the posterior and anterior chambers is constructed and

maintained [12, 13, 25, 26]. In a broader sense, these findings reaffirm a theoretical standpoint that the Nd:YAG laser is well suited for treating pseudophakic or aphakic MG since it is fully capable of "cutting" and disrupting relevant anatomic structures. Indeed, most cases in previous reports (exceeding 80%) indicated a successful initial reduction in IOP and restoration of the anterior chamber after Nd:YAG laser treatment [11]. The fundamental issue with the Nd:YAG laser treatment modality lies in its durability. About 30% of cases experienced repeated relapse, with 2–4 repeat laser treatments still declared ineffective, necessitating further surgical interventions [11].

In the present series, we described a modified Nd:YAG laser treatment methodology for treatment of pseudophakic or aphakic MG. Notably, all cases demonstrated satisfactory long-term resolution within the follow-up period. Compared with existing reports, we believe the present treatment methodology is advantageous for the following reasons. The first and most significant distinction was the location where the Nd:YAG laser was applied. The Nd:YAG laser was applied in most previous studies through a newly produced or pre-existing iridotomy [7–11]. The width limitation of the laser cut iridotomy posed a risk of blockage and dispersion of the subsequent laser beam energy. It also hindered direct visualization of the succeeding laser focal point. In cases of newly formed laser iridotomy, there is a possibility that the post-iridotomy iris pigment release and anterior chamber inflammation may add further insult to the trabecular and lead to the failure of MG control [27]. In our study, the Nd:YAG laser treatment was applied through a surgical preset iridectomy. Surgical iridectomy could ensure a broad base iris channel, facilitating the prompt diagnostic exclusion of pupil block and allowing for less energy consumption with direct visualization of the subsequent laser CZHV. Some of the previous studies also reported Nd:YAG laser disruption solely through the dilated pupil [11]. As a gap is usually present in the central anterior chamber, even in cases with total peripheral iridocorneal touch, transpupillary Nd:YAG laser capsulotomy and hyaloidotomy were considered as viable initial treatment options. However, in our experience, the transpupillary laser alone was associated with frequent short-term relapse. Only transpupillary Nd:YAG laser capsulotomy and hyaloidotomy in conjunction with a thorough Nd:YAG laser CZHV through iridectomy could ensure long-term resolution. This observation is consistent with previous findings that using posterior chamber intraocular lenses, particularly in the presence of synechiae between the lens capsule and implant, may impede the flow of aqueous from the vitreous into the anterior chamber [3].

Another major difference was the timing of treatment initiation. In the first instance, as discussed above, the stringent adoption of an IOP threshold of 21 mmHg as diagnostic criteria in some studies may have been associated with a proportion of delayed diagnosis, resulting in a delay in initiating first-line medical therapy. Furthermore, previous studies reported 1–4-day intervals between MG diagnosis (medical therapy initiation) and Nd:YAG laser application [7–11]. Medical therapy is an important component of overall MG management. Nevertheless, it is evident that medical therapy cannot resolve the fundamental issue underlying the transvitreal pressure imbalance, raising the question of the appropriateness of a 4-day waiting time before Nd:YAG laser implementation. In our stepwise approach, the first Nd:YAG laser CZHV was applied 24 h after the medical therapy and was initially effective in all cases in reforming the anterior chamber. Although there is still disagreement over whether immediate intervention can result in enhanced rates of MG resolution, several reports have confirmed that prompt intervention may shorten recovery durations for MG with a greater probability of improvement in visual acuity and IOP [28, 29]. Indeed, timely reformation of the anterior chamber may help prevent peripheral anterior synechiae formation from persistently shallow anterior chamber and limit the extent of trabecular damage, facilitating better control of IOP and ultimately improving visual acuity.

Interestingly, as shown in Table 2, three eyes implanted with a capsular tension ring (CTR) all achieved long-term resolution with a single Nd:YAG laser intervention. The literature has not established the relationship between CTR

implantation and MG occurrence or resolution. However, zonular laxity is one of the proposed mechanisms for MG [19]. It is plausible that the utilization of CTR, a procedure widely acknowledged for its efficacy in localizing zonular weakness may also contribute to the MG reversal.

In this series, herniation of loose vitreous through iridectomy was observed in nearly half of the cases immediately following the Nd:YAG laser CZHV. Consistent with a previous study, no corneal endothelial damage or other complications were documented during the follow-up visits due to this herniation [7]. In cases where AS-OCT or UBM images were available, it was noted that the vitreous herniation completely liquefied by the end of the first month. As a matter of fact, age was also one of the factors that contributed to the successful long-term control of MG in this series. The vitreous becomes more liquefied with age, and in the present study, 92.9% [13 of 14 eyes] of cases were older than 40 years. The liquefied vitreous reduces the technical difficulty in establishing an unobstructed passage between the posterior and anterior chambers. A prior study suggested that applying Nd:YAG laser treatment in the inferior region may allow the aqueous to flow more freely into the anterior chamber due to the higher density of the aqueous compared to the vitreous [10]. However, in the current series, vitreous herniation was observed from both inferior and superior iridectomy. Furthermore, no discernible correlation existed between the resolution and recurrence of MG and the specific site of the iridectomy. In our experience, one advantage of adopting Nd:YAG laser treatment via inferior iridectomy is that Asian patients often have a relatively small palpebral fissure height. Consequently, laser treatment in the inferior region becomes more convenient since it eliminates the need to manipulate the upper eyelids manually.

The present study has several limitations. First, it is important to acknowledge that this study is retrospective and has a relatively small sample size. Second, the inclusion criteria for our study were limited to patients with pseudophakic/aphakic MG who had previously been diagnosed with CACG and underwent prophylactic peripheral iridectomy. Because the inclusion criteria were somewhat stringent and all included patients were elderly Chinese, the generalizability of this modified Nd:YAG technique to a larger and younger population will need to be evaluated in future studies. Third, MG is a rare disease, making it challenging to collect a cohort of patients within a specific timeframe. Therefore, the duration of this study was lengthy. Although all Nd:YAG laser treatments were performed exclusively by two experienced glaucoma consultants to assure consistency, the patients had variable follow-up periods. Five patients had only 12 months of follow-up, suggesting the potential that MG might recur after this rather short follow-up period. The rarity of the disease also restricts the inclusion of a comparison group, which may bias the results. Finally, the absence of universally accepted criteria delineating treatment efficacy and relapse of MG might hinder the ability to compare results with other investigations.

CONCLUSION

In conclusion, the modified Nd:YAG laser treatment methodology has demonstrated long-term efficacy in managing pseudophakic or aphakic MG. Factors contributing to the positive outcomes associated with this modified methodology were prophylactic peripheral iridectomy, rapid diagnosis, and timely initiation of Nd:YAG laser treatment. It has the advantages of being a minimally invasive procedure that can be performed simply in an outpatient setting, thus with quicker recovery and higher patient acceptance. Although challenging, it should be emphasized to patients that the term MG no longer signifies a dismal condition and that the prognosis is often favorable with modern treatment modalities.

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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. Mingmin Yang, Xiaohua Pan, Zijie Chen, Xiaoli Shen, Zhen Yu, Yufei Tao, Shan Li, Xiang Mo, Xuyang Liu and Ning Fan declare that they have no competing interests.

Ethical Approval. The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments. The ethics committee of Shenzhen Eye Hospital reviewed and approved this retrospective study (Reference No. 2023KYPJ044). Written informed consent for participation is not required for retrospective study in accordance with national legislation and institutional requirements. However, all patients included in this study were still undergoing regular follow-ups during data collection of this study, therefore all patients signed written informed consent after explanation of the nature of this study during their follow-up, prior to the data analysis.

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