• Clinical Research •

Prophylactic juxtapapillary laser photocoagulation in pediatric morning glory syndrome

Yi-Hua Zou[1], Kai-Qin She[2], Jia-Ning Ren[1], Ting-Yi Liang[1], Ping Fei[1], Yu Xu[1], Jing Li[1], Xiang Zhang[1], Jie Peng[1], Pei-Quan Zhao[1]

[1]Department of Ophthalmology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China
[2]Department of Ophthalmology, West China Hospital, Sichuan University, Chengdu 610000, Sichuan Province, China
Co-first authors: Yi-Hua Zou and Kai-Qin She
Correspondence to: Pei-Quan Zhao and Jie Peng. Department of Ophthalmology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China. zhaopeiquan@xinhuamed.com.cn; pengjie918@126.com
Received: 2021-07-23 Accepted: 2021-11-04

Abstract

● **AIM:** To determine the anatomic and visual outcomes of prophylactic juxtapapillary laser photocoagulation treatment alone in the prevention of retinal detachment (RD) in a cohort of pediatric patients diagnosed with morning glory syndrome (MGS).

● **METHODS:** A total of 24 eyes of 22 consecutive patients aged 0-15y diagnosed with MGS treated with prophylactic juxtapapillary laser photocoagulation alone were reviewed. Data including demographics, ocular examination, anatomic and visual outcomes, following treatment and complications were collected.

● **RESULTS:** Two patients had bilateral laser treatment and 20 had monocular laser treatment. The age at treatment of 13 (59.1%) patients was less than 12mo. The presenting symptoms included strabismus (6/22, 27.3%), decreased vision (2/22, 9.1%), and routine fundus screening (14/22, 63.6%). Fifteen (68.2%) patients underwent cranial magnetic resonance imaging (MRI) examinations, and 3 of those 15 (20.0%) had abnormal findings in the nervous system. Based on preoperative wide-field fundus photography and B-scan echography, all (100.0%) eyes had no obvious RD. On postoperative 1mo and 6mo and the following follow-ups, the anatomic outcomes of all eyes remained stable. The mean follow-up duration was 27.7±17.5mo. No severe complications were found. Preoperative visual acuity acquired from 2 (9.1%) patients ranged from light perception to 20/200. Postoperative acuity acquired from 11 (50.0%) patients ranged from light perception to 20/125.

● **CONCLUSION:** The preliminary anatomic and visual outcomes of prophylactic juxtapapillary laser treatment alone in pediatric MGS patients are relatively stable in a short-term follow-up. Further long-term clinical observation will be needed to confirm its efficacy and safety.

● **KEYWORDS:** prophylactic juxtapapillary laser photocoagulation; morning glory syndrome; retinal detachment
DOI:10.18240/ijo.2022.05.12

Citation: Zou YH, She KQ, Ren JN, Liang TY, Fei P, Xu Y, Li J, Zhang X, Peng J, Zhao PQ. Prophylactic juxtapapillary laser photocoagulation in pediatric morning glory syndrome. *Int J Ophthalmol* 2022;15(5):766-772

INTRODUCTION

Morning glory syndrome (MGS) is a rare congenital cavitary anomaly of the optic disc, that was first named by Kindler[1] in 1970 because of its resemblance to the morning glory flower. It is characterized by an enlarged and excavated optic disc with juxtapapillary chorioretinal pigment disturbance, radial retinal blood vessels, and a central white glial tuft. The prevalence of this condition is 3.6/100 000 in children, and the exact pathogenesis of MGS remains unknown[2].

MGS could be complicated with other ocular diseases, such as persistent fetal vasculature (PFV), cataracts, microphthalmia and retinal detachment (RD). It has been reported that approximately 1/3 of those with MGS can develop RD, and a small number of cases have spontaneous resolution[3]. The development process of RD may result from various factors, mainly abnormal communications between the subarachnoid space and subretinal space or retinal breaks, which contribute to the migration of cerebrospinal fluid or vitreous humor to the subretinal space and the traction of preretinal glial tissues[4-5].

In the literature, the treatment of advanced RD in MGS is challenging. Some cases are treated when total RD occurs, which requires silicone oil or long-acting gas tamponade[6]. In

addition, cases that have recurrent RD always need multiple interventions[7]. Complications of these operations are severe in the long term, such as silicone oil emulsification, keratopathy and photophobia[8]. Despite the reports of cases with successful retinal attachment after treatment[9-11], the follow-up periods in these studies were not long enough, and long-term complications were ignored. In addition, the visual acuity prognosis is very poor in these conditions since RD has occurred for a long time. Considering these findings, early prophylactic treatment is actually needed to improve the anatomical and visual prognosis.

Juxtapapillary laser treatment alone is generally used as a supplement to vitrectomy in RD of MGS. The mechanism of laser treatment is to produce adhesion, through the thermal effect, between the retinal pigment epithelium (RPE), neuroepithelium and choroid to create a barrier to prevent subretinal fluid migration[12-13]. Prophylactic juxtapapillary laser treatment is controversial in the literature for the prevention of RD in MGS, as the likely risk of visual loss is attributed to the papillomacular bundle (PMB) injury. However, more animal and human studies have demonstrated that lasers in the region of the PMB do not cause loss of visual function[14-15]. Hence, this study aimed to report the preliminary anatomic and visual outcomes of prophylactic juxtapapillary laser treatment alone in a cohort of pediatric MGS patients from a single institution.

SUBJECTS AND METHODS

Ethical Approval This study adhered to the tenets of the Declaration of Helsinki (2008) and was approved by the Ethics Committee of Xinhua Hospital affiliated with the Shanghai Jiao Tong University School of Medicine. Written information consent was acquired from the parents of all patients.

Subjects Consecutive patients with a diagnosis of MGS from April 2015 to February 2021 were enrolled. The patients underwent comprehensive ophthalmic examinations before and after treatment. All patients were examined with binocular indirect ophthalmoscopy with a +20 D lens or slit-lamp microscope by the same clinician (Zhao PQ). Wide-field fundus images were taken with RetCam III (Clarity, Pleasanton, California, USA) or Optos Optomap 200Tx (Optos, PLC, Dunfermline, Scotland, UK). A/B-scan echography (CineScan, BVI Co., France) examinations were performed to measure the axial length, maximal depth and width of excavation and to evaluate the status of the whole globe. The frequencies of the probe of the A-scan and B-scan echography were 11 MHz and 10 MHz, respectively. Intraocular pressure (IOP) was measured using a non-contact tonometer (Topcon CT-90, Tokyo, Japan) or rebound tonometer (iCare, Tiolat Oy, Helsinki, Finland) every time.

The criterion for laser treatment was diagnosis of MGS without obvious RD in those aged 0-15y. Patients with refractive media opacity, PFV, tractional or rhegmatogenous retinal detachment (RRD) or without intact data were excluded. All the patients were under general anesthesia monitored by an experienced pediatric anesthesiologist. Fundus photography and fluorescein angiography (FA) were performed according to the reported literature[16]. All patients underwent prophylactic laser treatment alone by two experienced clinicians (Xu Y and Peng J) after fundus photos were taken. This treatment was three to five rows of confluent gray-white laser spots at 360° of the retina around the edge of the optic disc through a 520 nm-wavelength, a power of 180-250 mW and a 300ms-duration laser with an indirect ophthalmoscope (Novus, Lumenis, USA). The laser spots were grid, and the intensity was moderate (Figure 1). The laser spots were given around the border of these areas, including atrophy of RPE and small folds around the optic disc (Figure 2A). The visible macular area was spared with laser carefully to protect the PMB (Figure 1).

Main Outcomes Baseline data for age, gender, laterality of MGS and symptoms at presentation were collected. Ophthalmic evaluations, including visual acuity, axial length, IOP and ocular complications, were noted one-month, six months and after every year postoperatively. Cranial magnetic resonance imaging (MRI) was also suggested for all patients. The main outcomes were the status of the retina and best corrected visual acuity (BCVA), which were evaluated during follow-ups.

Statistical Analysis Statistical analyses were performed using IBM SPSS Statistics, version 22.0 software (Armonk, NY: IBM Corp). Paired *t*-tests and Mann-Whitney *U* tests were used to compare the differences in several parameters between two subgroups of patients who were younger than 12 months old at the time of treatment and the others. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

A total of 24 eyes from 22 patients were included in this study. Two (9.1%) patients underwent bilateral treatments. At the time of treatment, 13 (59.1%) patients were younger than 12 months old. The baseline data of the patients are listed in Table 1. The median age at treatment was 10.5mo (interquartile range: 7.5-19.5mo), and the mean follow-up duration was 27.7±17.5mo. Symptoms at presentation included strabismus in 6 (27.3%), decreased vision in 2 (9.1%) and routine fundus screening in 14 (63.6%) patients (Table 1). At the preoperative, postoperative one-month and postoperative six-month follow-ups, the mean ocular axial length and IOP are listed in Table 1. There was an increasing trend of the axial length with age, but no significantly shortened axial length or elevated IOP was found. Fifteen (68.2%) patients underwent cranial MRI examinations. Three of the 15 (20.0%)

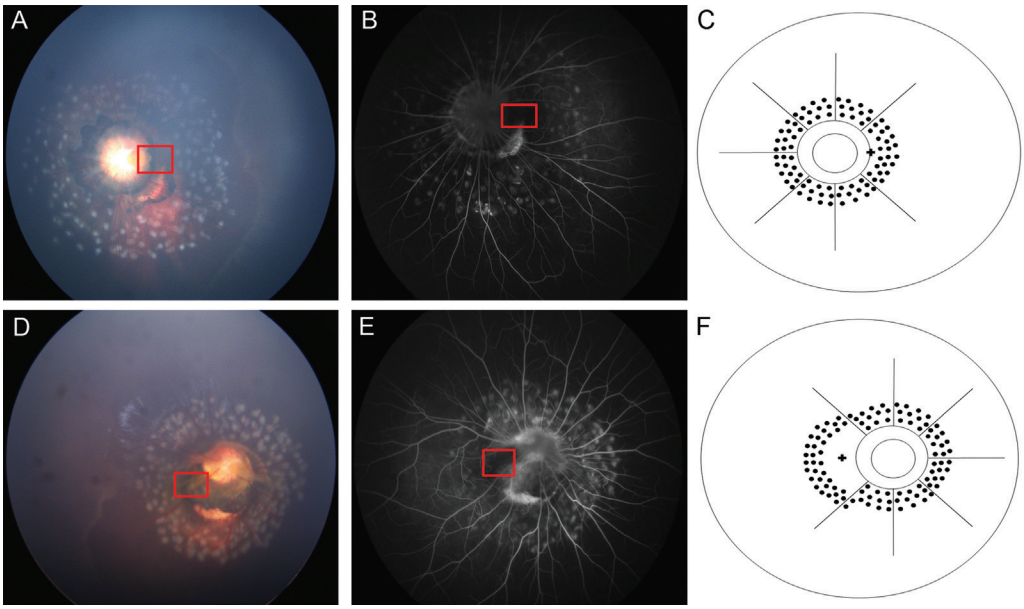

Figure 1 Laser delivery according to locations of the foveal area A, B: RetCam III and FA images. Case 15, 24 months old, left eye with a diagnosis of MGS. D, E: RetCam III and FA images. Case 8, 43 months old, right eye with a diagnosis of MGS. The foveal areas (red rectangles) were located at the edge of the excavations. Confluent grid laser spots were delivered around the optic disc with the fovea spared. C, F: The diagrammatic sketches. Black dots: Laser spots; Black cross symbol: The fovea.

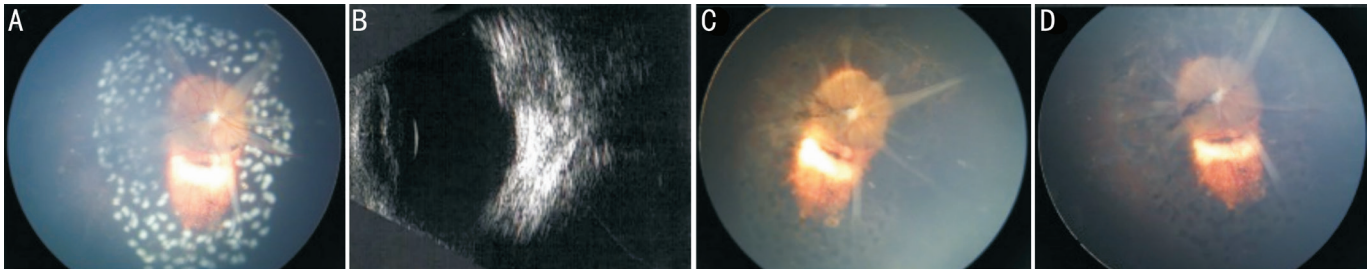

Figure 2 Representative images of Case 21 with small retinal folds around the disc A: Grid gray-white laser spots were delivered around the optic disc at 26 months of age. The small retinal folds around the optic disc and the patchy area of atrophic retinal pigment epithelium were spared. B: The corresponding preoperative echography showed no retinal detachment was found. C, D: The fundus photos showed that the response of laser spots was good and that the retina was flat at the postoperative one-month and six-month follow-ups.

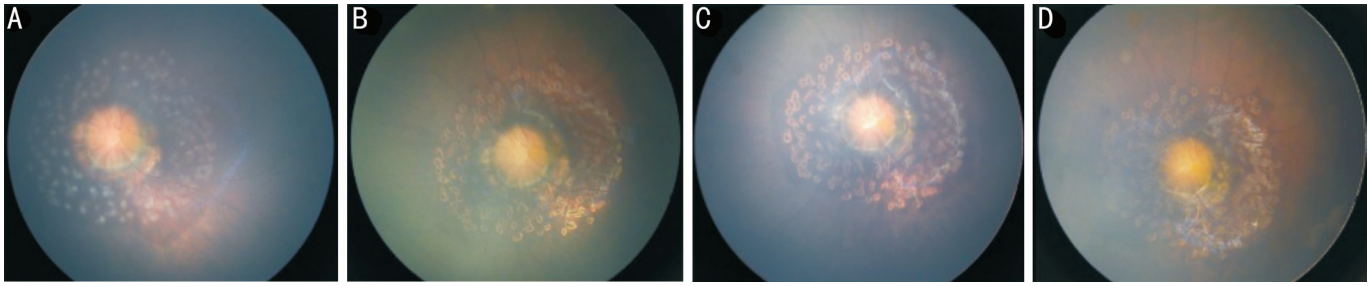

Figure 3 Representative images of Case 6 A: Grid gray-white laser spots were delivered around the optic disc at five months of age; B-D: Fundus photos at one-month, six-month postoperatively and at the final follow-up after 23mo. The response of laser spots was good, and the retina in the posterior pole was flat.

patients had various abnormal findings in the central nervous system, including one moyamoya, one encephalocele, and one intracranial arteriostenosis.

On fundus photography and B-scan echography at the preoperative and postoperative one-month, postoperative six-month and following follow-ups, the anatomic outcomes of all eyes remained stable (Figures 2 and 3). None of them developed obvious RD during the entire follow-up course. Preoperative BCVA acquired from 2 (9.1%) patients ranged from light perception to 20/200. Postoperative acuity acquired from 11 (50.0%) patients ranged from light perception to 20/125 (Table 2). Patient noncompliance limited this examination for others. No visual losses were reported from any patients or their parents.

Table 1 Baseline data of all included patients diagnosed with MGS

Parameters	Total	<12 months old at the time of treatment (*n*=13)	Others (*n*=9)	*P* between the two subgroups
Laterality, *n* (%)				/
Unilateral	20 (90.9)	11 (84.6)	9(100)	
Right	7 (35.0)	3 (27.3)	4 (44.4)	
Left	13 (65.0)	8 (72.7)	5 (55.6)	
Bilateral	2 (9.1)	2 (15.4)	0	
Gender, *n* (%)				/
Male	11 (50.0)	6 (46.2)	5 (55.6)	
Female	11 (50.0)	7 (53.8)	4 (44.4)	
Symptom at presentation, *n* (%)				/
Strabismus	6 (27.3)	3 (23.1)	3 (33.3)	
Decreased vision	2 (9.1)	1 (7.7)	1 (11.1)	
Fundus screening	14 (63.6)	9 (69.2)	5 (55.6)	
Age at presentation, mo	6.0 (3.0-17.3)	4.0 (3.0-6.0)	21.0 (9.0-25.5)	0.00[b]
Age at treatment, mo	10.5 (7.5-19.5)	8.0 (5.5-10.0)	24.0 (16.5-27.5)	0.00[b]
Follow-up duration, mo	27.7±17.5	26.0±18.5	30.2±16.6	0.71[a]
Ocular axial length, mm				
Preop.	19.1±1.5	18.7±1.4	19.6±1.6	0.23[a]
Postop. 1mo	20.0±1.5	19.7±1.5	20.3±1.5	0.51[a]
Postop. 6mo	20.6±1.7	20.3±1.5	21.1±1.8	0.33[a]
Intraocular pressure, mm Hg				
Preop.	7.3±3.8	7.0±3.2	7.8±4.8	0.69[a]
Postop. 1mo	8.3±2.4	8.0±2.1	8.6±2.8	0.71[a]
Postop. 6mo	9.4±1.6	9.0±1.7	9.8±1.5	0.43[a]

Parametric data were presented as mean±SD (standard deviation), and nonparametric data were presented as median (interquartile range). [a]Paired *t*-test; [b]Mann-Whitney *U* test.

Table 2 BCVA results in this study

Case	Age (mo)	BCVA	Case	Age (mo)	BCVA
1	77	20/125	12	43	LP
3	59	HM	15	47	CF
7	64	CF	16	40	LP
8	43	CF	20	64	LP
9	89	20/200 (pre-)/20/160 (post-)	21	31	LP (pre-)/CF (post-)
11	39	20/250			

BCVA: Best corrected visual acuity; HM: Hand motion; CF: Counting fingers; LP: Light perception.

No obvious ocular or systemic complications were reported during the entire follow-up course. No hemorrhage, retinal holes, cataracts or keratitis were found in any patients. No evidence of the spontaneous resolution of RD, such as new subretinal proliferation, was noted. One patient had transient conjunctivitis after treatment and recovered by using topical antibiotics. Due to the poor visual acuity and young age of most patients, visual field examinations were not performed.

DISCUSSION

MGS is a rare congenital cavitary anomaly of the optic disc. There was a unilateral tendency and no significant difference in occurrence between genders[2], which is in agreement with the data in this study. Abnormal findings in the nervous system suggest the importance of cranial examinations for MGS patients in this study, which has also been reported in previous studies[17-18]. The median age at presentation was six months old (range: 3.0-17.3mo) in this cohort, suggesting that early fundus screening is worthwhile for early diagnosis and management.

It has been reported that approximately 80% of MGS could be complicated with other ocular diseases, such as PFV, cataracts, microphthalmia and RD[19]. As one of the most severe complications of MGS, RD has been reported to occur in 30%-38% of MGS patients[9]. Haik *et al*[3] reported that the natural

course of MGS with RD occurred in 11 of 32 eyes during a mean follow-up of 10.3y. Of the 11 eyes, four had spontaneous reattachment, and two of them exhibited redetachment. Evidence of the spontaneous resolution of RD in MGS, such as new subretinal proliferation, was not observed during the follow-up period, which suggested that RD did not occur in all the patients in this study.

In the literature, the treatment of advanced RD in MGS is challenging. Harris *et al*[7] reported an MGS case with near total RD and a tiny retinal break treated with one vitrectomy and two fluid-gas exchanges. The retina remained attached for 14mo after the final surgery. Jo *et al*[10] reported an MGS case with a retinal hole and RD treated with vitrectomy and long-acting gas tamponade. The retina was redetached one month later, and silicone oil tamponade was then used. The retina retained attached for five years after the removal of the silicone oil. Recurrent RD and multiple interventions, such as in these cases, are intolerant for some patients. Sakamoto *et al*[20] reported two MGS cases with total RD and contractile movements treated with vitrectomy, and the retina failed to be reattached in both cases, suggesting the considerable difficulty of the treatment of these conditions. Sen *et al*[6] reported nine MGS cases with RD treated with vitrectomy. Silicone oil tamponade was used in 7/9 eyes, and the rate of retinal reattachment was 66%. However, the long-term complications of the surgeries were unclear. Visual improvement is quite limited in these patients.

Considering these findings, early prophylactic treatment is truly needed to improve the anatomical and visual prognosis. In the above studies, laser photocoagulation around the optic disc is generally used as a supplement to vitrectomy. However, there remains some ambiguity about the safety of lasers in the region of the PMB. Early animal and human studies suggested that there was no obvious detriment to applying a laser in the region of the PMB[21-22]. Recently, more human studies have demonstrated that laser-associated retinal damage is limited to the outer retinal layers. The immediate morphological changes of the inner retina suggested that the RPE prevents damage to the inner retina by absorbing most of the energy of the laser[23-24]. More recently, Bloch and da Cruz[14] reported the safety of juxtapapillary laser photocoagulation in the region of the PMB for optic disc pit maculopathy. No anatomical or perimetric findings consistent with nerve fiber layer damage in the region of laser treatment were reported in any of the patients, suggesting that lasers in the region of the PMB would not cause loss of visual function. On the other hand, it is controversial to treat the fovea directly with the laser for patients with good vision. Fovea-sparing laser treatment has been applied for diabetic macular edema[25]. As the macula in MGS often develops abnormally or is displaced toward the edge of the excavation, it is important to distinguish the probable site of the fovea, which truly requires some effort. Normal macula is usually yellowish on fundus photography, with a clear foveal reflection and a clear foveal avascular zone (FAZ) on fundus FA[16]. Therefore, despite the limitation of exactly anchoring the fovea in pediatric MGS patients, the probable whole area of the macula was dignified and spared to protect the fovea and the PMB. Pre- and postoperative visual acuities of two patients who were observed to be unaffected also supported the safety of scrupulous juxtapapillary laser photocoagulation in these patients.

For the rationale of laser treatment, retinal laser photocoagulation results in permanent chorioretinal scars as a barrier for preventing subretinal fluid migration[12]. The scars could be well achieved before an accumulation of intraretinal fluid. Retinal laser photocoagulation has been utilized widely in most retinal vascular diseases, particularly diabetic macular edema and retinal vein occlusions[26]. Although the pathogenesis of these diseases is different from RD in MGS, lasers in both conditions might decrease retinal edema by stimulating RPE cell to reabsorb subretinal fluid[27]. In addition, retinal laser photocoagulation has also been extensively used in the treatment of retinal breaks, which can reduce progression to RD. For asymptomatic retinal breaks, prophylactic laser retinopexy is needed in some cases to prevent RD[28]. In addition, prophylactic laser treatment proved useful in the prevention of RD associated with congenital chorioretinal coloboma[29-30]. Uhumwangho and Jalali[29] showed that RRD developed in 2.9% of laser-treated eyes in contrast to 24.1% of untreated eyes, suggesting that prophylactic laser treatment around the coloboma had a protective effect for the prevention of RRD. For RD in MGS, prophylactic laser treatment around the optic disc may play a role by impeding the migration of subretinal fluid, which may originate from the retinal holes or abnormal communications among various compartments within the excavation to prevent the progression of RD. The data of this study provided the preliminary anatomical and visual outcomes of prophylactic juxtapapillary laser treatment for a cohort of pediatric MGS patients. The results showed that the retinas of all the patients remained flat during a mean follow-up duration of 27.2mo.

It should be mentioned that echography is an important method of examination for MGS. B-scan echography of all MGS eyes in this study showed excavation of the posterior pole, and no RD band was found during the entire follow-up period. Cennamo *et al*[31] reported that spectral-domain optical coherence tomography could sometimes show RD when echography could not, suggesting that echography may miss the diagnosis of RD sometimes compared to optical coherence tomography. In this study, it was indefinite whether

mild subretinal fluid or intraretinal fluid existed in some cases. Despite the good RPE response of the laser in all patients, the progression of serous RD may be observed in a longer time, and the efficacy of laser adhesion as a barrier may be reduced gradually, which needs to be followed up for a longer time.

Several limitations in this study should be considered. First, the number of patients was small and had unavoidable selection bias. Second, this was a retrospective study, and some examinations, such as optical coherence tomography, visual field examinations and electroretinograms (ERGs), were unavailable due to patient noncompliance. Third, this study lacked a control group without laser treatment. Despite these limitations, this study provides the preliminary anatomic and visual outcomes of prophylactic juxtapapillary laser treatment alone for pediatric MGS patients in a short-term follow-up. Further long-term clinical observation will be needed to confirm its safety.

In conclusion, this study showed the preliminary anatomic and visual outcomes of prophylactic juxtapapillary laser treatment alone in pediatric MGS patients, which were relatively stable in a short-term follow-up. No severe ocular or systemic complications were reported in any patients. Further long-term clinical observation will be needed to confirm its safety.

ACKNOWLEDGEMENTS

Foundations: Supported by the Shanghai Sailing Program (No.20YF1429700); the Clinical Research Plan of SHDC (No. SHDC2020CR5014-002).

Conflicts of Interest: Zou YH, None; **She KQ,** None; **Ren JN,** None; **Liang TY,** None; **Fei P,** None; **Xu Y,** None; **Li J,** None; **Zhang X,** None; **Peng J,** None; **Zhao PQ,** None.

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