Clinical Research 

# Efficacy and safety of subthreshold micropulse laser in the treatment of acute central serous chorioretinopathy

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### Abstract

• **AIM**: To analyze the efficacy and safety of subthreshold micropulse laser (SML) in the treatment of acute central serous chorioretinopathy (CSC).

• **METHODS:** This is a retrospective case analysis study. Totally 58 eyes of 58 patients were enrolled, and they were divided into different groups. And 39 patients were treated with SML (SML group) and 19 patients were only observed (observation group). The follow-up period was 3mo after diagnosis. The best corrected visual acuity (BCVA), central retinal thickness (CRT), superficial retinal vascular density (SRVD), deep retinal vascular density (DRVD), the superficial and deep foveal avascular zone (FAZ) area, retinal light sensitivity (RLS), perfusion area of choroidal capillary layer (CCL), subfoveal choroidal thickness (SFCT) and fundus autofluorescence (FAF) were investigated.

• **RESULTS:** The BCVA, CRT, SRVD, DRVD, the superficial and deep FAZ area, RLS, SFCT of SML group were significantly improved at 3mo (all *P*<0.05). In the observation group, only CRT, DRVD and SFCT were improved (all *P*<0.05). Other research items in the observation group were not significantly different from baseline (all *P*>0.05). At the last follow-up, the BCVA and RLS in the SML group were better than those in the observation group, and CRT was lower, SRVD and DRVD, perfusion area of CCL were larger (all *P*<0.05). On FAF, no change of treatment spots was found after treatment. No structural laser damage was observed on optical coherence tomography (OCTA), and no choroidal neovascularization was observed.

• **CONCLUSION:** SML treatment of acute CSC can improve BCVA, RLS, and perfusion area of CCL, reduce CRT,

increase SRVD and DRVD, and is safe.

• **KEYWORDS:** central serous chorioretinopathy; subthreshold micropulse laser; optical coherence tomography angiography; microperimetry

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#### INTRODUCTION

entral serous chorioretinopathy (CSC) is a common / fundus disease characterized by serous detachment of the neural retina in the posterior pole, often accompanied with dysfunction of the choroid and retinal pigment epithelium (RPE)<sup>[1]</sup>. Patients with CSC usually manifested as visual acuity decreased, metamorphopsia, micropsia and dark vision, it's more common in young and middle-aged men<sup>[2]</sup>. The disease is usually divided into acute CSC (aCSC) and chronic CSC, but the exact time scale between the acute and chronic forms has not a consensus. Many cases of aCSC are self-limiting with spontaneous resolution of subretinal fluid (SRF) within 3-4mo, but up to 30%-50% of cases will persist and recur, then it may can cause irreversible damage to visual function<sup>[3]</sup>. It is worth noting that the short-term presence of SRF also can cause irreversible damage to photoreceptors<sup>[4]</sup>. Furthermore, persistent SRF may cause some complications, such as RPE atrophy, choroidal neovascularizations (CNV), and polypoidal choroidal vasculopathy<sup>[5]</sup>. Therefore, early and effective intervention is very necessary for aCSC.

Thus far, due to the complexity of its pathogenesis and clinical classification, there is no agreement on the treatment strategy for the disease. Traditionally, conventional laser was the only option for treating CSC. Conventional laser can close focal sites of RPE leakage, but it just can be applied to the point of angiographic leakage which is located more than 400  $\mu$ m from the fovea, moreover, vision loss, visual field defect, decreased contrast sensitivity, and CNV may occur at the treatment area, affecting the patient's visual quality<sup>[6-7]</sup>. About 10 years ago, photodynamic therapy (PDT) was introduced for the treatment of CSC, and many studies have proven

its effectiveness. However, PDT may cause choriocapillary closure, RPE alterations, and stimulate the upregulation of vascular endothelial growth factor (VEGF) and CNV<sup>[8]</sup>. More importantly, PDT treatment is expensive and unavailable in some areas. Intravitreal injections of anti-VEGF drugs have been used in the treatment of CSC, however, its effectiveness is still controversial at home and abroad, and it is an invasive treatment, which has the risk of serious complications such as intraocular hemorrhage and infection. Therefore, anti-VEGF drugs are not suitable as the first-line treatment of aCSC<sup>[9-10]</sup>. Many kinds of oral drugs are used in the aCSC, but the effect is not clear, and systemic side effects are unavoidable, further research is still required<sup>[11]</sup>. Subthreshold micropulse laser (SML) is a promising treatment modality because of its low treatment cost, repeatability, and no damage to adjacent tissues<sup>[7]</sup>. The purpose of this study was to assess the efficacy and safety of SML in the treatment of aCSC.

#### SUBJECTS AND METHODS

**Ethical Approval** This study was conducted following the principles of the Declaration of Helsinki. Informed consent was obtained from all subjects. This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University, the approval number is 2023-KY-0265-001.

Study Design and Participants This was a retrospective case analysis study, which included patients with aCSC who visited the First Affiliated Hospital of Zhengzhou University from August 2020 to May 2022. All patients were diagnosed by fundus fluoresceien angiography (FFA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT). The 58 eyes of 58 patients were included in the study, they were assigned into SML group (n=39) and observation group (n=19), SML group received SML therapy, and a month later, if the subretinal fluid was not completely absorbed, the treatment could be repeated, the observation group only reviewed regularly. If both eyes of the patient are affected, choose the left eye to be included in the study. The follow-up period was 3mo after diagnosis in our hospital.

Patients who were diagnosed as CSC by FFA, ICGA and OCT and whose course of disease was less than 3mo could be included in the study. Exclusion criteria were: 1) Patients had received PDT, conventional laser photocoagulation and intravitreal injection of anti-VEGF agents. 2) Suffering from hypertension, diabetes, liver and kidney dysfunction, and other systemic diseases. 3) Being treated with systemic steroids. 4) History of eye trauma or eye surgery. 5) Combined with high myopia or other fundus diseases, including CNV. 6) Allergy history of indocyanine green or fluorescein sodium.

**Data Collection** All selected patients underwent ophthalmic examination at diagnosis and 3mo after diagnosis, including best corrected visual acuity (BCVA), intraocular pressure,



**Figure 1 Software measurement diagram** A: Diagram of CRT measurement; B: Diagram of SFCT measurement. CRT: Central retinal thickness; SFCT: Subfoveal choroidal thickness.

fundus examination after mydriasis, OCT, optical coherence tomography angiography (OCTA), microperimetry, and review as needed during follow-up. All patients in SML group underwent fundus autofluorescence (FAF) before and 3mo after treatment to observe the effects of SML on RPE. FFA and ICGA be performed before treatment and then repeated as required. Check the BCVA with the international standard visual acuity chart, and convert it to a logarithm of the minimum angle of resolution (logMAR) scale for analysis. Central retinal thickness (CRT) and subfoveal choroidal thickness (SFCT) are automatically measured by OCT (SVision VG200) built-in software. CRT is defined as the height from the internal limiting membrane to Bruce's membrane (Figure 1).

**Treatments** SML treatments are carried out by the same experienced ophthalmologist. All patients were fully dilated with tropicamide phenylephrine eye drops, then the topical anesthesia was performed with obucaine eye drops. The IQ 577 laser therapeutic instrument of Iridex Company in the United States is used and set to the micropulse mode, the laser parameter was set to 5% duty cycle, the spot diameter was 200  $\mu$ m, the exposure time was 200ms, the treatment energy is 400 mW, and the 7×7 matrix mode without spacing between two spots is adopted, the photocoagulation range covers the entire edema area. After SML therapy, pranoprofen eye drops were given for analgesia and anti-inflammatory. Recheck one month after treatment, if there is still SRF, the treatment can be repeated.

**Statistical Analysis** Statistical analysis was performed using SPSS 26.0. All quantitative data were tested for normality using Shapiro-Wilk test. The variables in accordance with the normal distribution were expressed as mean±standard deviation (SD), and the differences between groups were analyzed by *t*-test. Variables that did not meet the normal distribution were expressed as median [interquartile range (IQR)], and the Rank-Sum test was used to analyze the difference between groups. The intra group differences were analyzed by paired *t*-test or paired Rank-sum test. For categorical variables, the data difference between the two groups was analyzed by the Chi-

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Table 1 Comparison of demographic and baseline characteristics between the two groups				
Items	SML group (n=39)	Observation group (n=19)	Statistical value	e P
Gender (male/female)	30/9	15/4	χ <sup>2</sup> =0.003	0.955
Age (y)	46±8	45±8	<i>t</i> =0.230	0.819
Course of disease (d)	42±16	41±17	<i>t</i> =0.352	0.726
BCVA (logMAR)	0.34±0.17	0.33±0.15	<i>t</i> =0.056	0.955
RLS (dB)	19.6 (18.3-22.2)	19.4 (17.7-22.4)	<i>Z</i> =-0.613	0.540
CRT (µm)	477±129	497±128	<i>t</i> =-0.561	0.557
SRVD (%)	45.73 (44.05-45.98)	45.73 (44.68-46.33)	<i>Z</i> =-0.381	0.703
DRVD (%)	47.89 (46.79-49.14)	47.50 (46.75-48.74)	<i>Z</i> =-0.555	0.579
Superficial FAZ (mm <sup>2</sup> )	0.429 (0.388-0.501)	0.429 (0.388-0.449)	<i>Z</i> =-0.083	0.934
Deep FAZ (mm <sup>2</sup> )	0.441 (0.364-0.505)	0.442 (0.385-0.478)	<i>Z</i> =-0.008	0.993
Perfusion area of CCL (mm <sup>2</sup> )	22.798±1.298	22.605±1.234	<i>t</i> =0.539	0.592
SFCT (µm)	464±137	493±143	<i>t</i> =-0.757	0.452

IQR: Interquartile range; SML: Subthreshold micropulse laser; BCVA: Best corrected visual acuity; RLS: Retinal light sensitivity; CRT: Central retinal thickness; SRVD: Superficial retinal vascular density; DRVD: Deep retinal vascular density; FAZ: Foveal avascular zone; CCL: Choroidal capillary layer; SFCT: Subfoveal choroidal thickness.

Ible 2 Changes of research items in the observation group during follow-up mean±SD/IQE				
Items	Baseline	Last follow-up	Statistical value	Р
BCVA (logMAR)	0.33±0.15	0.27±0.19	<i>t</i> =1.277	0.218
RLS (dB)	19.4 (17.7-22.4)	20.1 (18.1-22.2)	<i>Z</i> =-0.685	0.494
CRT (µm)	497±128	413±146	<i>t</i> =2.504	0.022
SRVD (%)	45.73 (44.68-46.33)	45.60 (44.34-47.63)	<i>Z</i> =-0.644	0.520
DRVD (%)	47.50 (46.75-48.74)	49.86 (46.95-50.44)	<i>Z</i> =-2.173	0.030
Superficial FAZ (mm <sup>2</sup> )	0.429 (0.388-0.449)	0.436 (0.383-0.473)	<i>Z</i> =-0.946	0.344
Deep FAZ (mm <sup>2</sup> )	0.442 (0.385-0.478)	0.465 (0.383-0.477)	<i>Z</i> =-1.349	0.177
Perfusion area of CCL (mm <sup>2</sup> )	22.606±1.234	22.800±1.452	<i>t</i> =-0.989	0.336
SFCT (µm)	493±143	453±143	<i>t</i> =3.205	0.005

IQR: Interquartile range; BCVA: Best corrected visual acuity; RLS: Retinal light sensitivity; CRT: Central retinal thickness; SRVD: Superficial retinal vascular density; DRVD: Deep retinal vascular density; FAZ: Foveal avascular zone; CCL: Choroidal capillary layer; SFCT: Subfoveal choroidal thickness.

square test. *P* values less than 0.05 were considered statistically significant.

#### RESULTS

**Patient Demographics and Baseline Characteristics** Fifty-eight patients were included in this study, the mean age of the patients was  $46\pm8$  (range: 32-64)y, the average course of disease was  $42\pm16$  (range: 16-78)d, and there were 45 males and 13 females. They were divided into SML group (n=39) and observation group (n=19), there was no significant difference in age, gender, course of disease and baseline characteristics of the research items between the two groups (all P>0.05; Table 1).

**Changes in Research Items of the Observation Group** Compared with the baseline data, the last follow-up of patients in the observation group showed that CRT decreased, deep retinal vascular density (DRVD) increased, and SFCT decreased, the differences were statistically significant (all P<0.05; Table 2). But, there was no significant difference in BCVA, retinal light sensitivity (RLS), superficial retinal vascular density (SRVD), superficial and deep foveal avascular zone (FAZ) area, and perfusion area of choroidal capillary layer (CCL) (all P>0.05; Table 2).

**Changes in Research Items of the Subthreshold Micropulse Laser Group** In the SML group, compared with before treatment, BCVA, RLS, SRVD, DRVD and perfusion area of CCL were increased, CRT and SFCT were significantly reduced, the area of superficial and deep FAZ were reduced 3mo after treatment, the differences were statistically significant (all P<0.05; Table 3, Figure 2).

Comparison of Research Items Between Two Groups at the Last Follow-up At 3mo, BCVA and RLS in SML group were better than those in the observation group, and CRT was lower, SRVD, DRVD and perfusion area of CCL were larger, differences were statistically significant (all P<0.05; Table 4). However, there was no significant difference in the superficial and deep FAZ area and SFCT compared with the observation group (all P>0.05; Table 4).

**Safety** On FAF, all SML-treated patients showed different degrees and types of fluorescence reduction or enhancement before treatment, and no change of treatment spots was found



Figure 2 A 46 years old male patient's fundus examination before and after SML treatment A: FFA and ICGA at the time of diagnosis; B: OCT before treatment (B1) and 3mo after treatment (B2); C: SRVD before treatment (C1) and 3mo after treatment (C2); D: DRVD before treatment (D1) and 3mo after treatment (D2); E: Superficial FAZ area before treatment (E1) and 3mo after treatment (E2); F: Deep FAZ area before treatment (F1) and 3mo after treatment (F2); G: Perfusion area of CCL before treatment (G1) and 3mo after treatment (G2); H: RLS before treatment (H1) and 3mo after treatment (H2). SML: Subthreshold micropulse laser; FFA: Fluoresceien angiography; ICGA: Indocyanine green angiography; OCT: Optical coherence tomography; SRVD: Superficial retinal vascular density; DRVD: Deep retinal vascular density; FAZ: Foveal avascular zone; CCL: Choroidal capillary layer; SFCT: Subfoveal choroidal thickness; RLS: Retinal light sensitivity.

Items	Baseline	Last follow-up	Statistical value	Р
BCVA (logMAR)	0.30 (0.22-0.40)	0.10 (0.05-0.15)	<i>Z</i> =-5.747	<0.01
RLS (dB)	19.6 (18.3-22.2)	24.9 (22.1-26.9)	Z=-6.085	<0.01
CRT (µm)	504 (389-564)	184 (174-214)	Z=-6.085	<0.01
SRVD (%)	45.73 (44.05-45.98)	47.63 (45.76-48.19)	Z=-4.804	<0.01
DRVD (%)	47.89 (46.79-49.14)	51.44 (49.99-53.02)	Z=-5.444	<0.01
Superficial FAZ (mm <sup>2</sup> )	0.429 (0.388-0.501)	0.411 (0.362-0.465)	Z=-4.488	<0.01
Deep FAZ (mm²)	0.441 (0.364-0.505)	0.415 (0.362-0.497)	Z=-4.683	<0.01
Perfusion area of CCL (mm <sup>2</sup> )	22.979 (21.769-23.732)	24.576 (23.965-25.010)	<i>Z</i> =-0.685	<0.01
SFCT (µm)	420 (358-527)	365 (305-475)	<i>Z</i> =-5.353	< 0.01

IQR: Interquartile range; SML: Subthreshold micropulse laser; BCVA: Best corrected visual acuity; RLS: Retinal light sensitivity; CRT: Central retinal thickness; SRVD: Superficial retinal vascular density; DRVD: Deep retinal vascular density; FAZ: Foveal avascular zone; CCL: Choroidal capillary layer; SFCT: Subfoveal choroidal thickness.

Table 4 Comparison of research items between two groups of patients at 3mo after diagnosis         mean±SD/IQR					
Items	SML group ( <i>n</i> =39)	Observation group (n=19)	Statistical value	Р	
BCVA (logMAR)	0.10 (0.05-0.15)	0.30 (0.10-0.40)	<i>Z</i> =-3.517	<0.01	
RLS (dB)	24.48±2.58	20.56±2.86	<i>t</i> =5.239	<0.01	
CRT (μm)	184 (174-214)	475 (249-518)	<i>Z</i> =-5.154	<0.01	
SRVD (%)	47.63 (45.76-48.19)	45.60 (44.34-47.63)	Z=-2.212	0.027	
DRVD (%)	51.44 (49.99-53.02)	49.86 (46.95-50.44)	Z=-3.239	0.001	
Superficial FAZ (mm <sup>2</sup> )	0.411 (0.362-0.465)	0.436 (0.383-0.473)	<i>Z</i> =-0.837	0.403	
Deep FAZ (mm²)	0.415 (0.362-0.497)	0.465 (0.383-0.477)	<i>Z</i> =-1.234	0.217	
Perfusion area of CCL (mm <sup>2</sup> )	24.576 (23.965-25.010)	22.652 (21.922-22.652)	Z=-3.919	< 0.01	
SFCT (μm)	365 (305-475)	438 (353-510)	<i>Z</i> =-1.624	0.104	

IQR: Interquartile range; SML: Subthreshold micropulse laser; BCVA: Best corrected visual acuity; RLS: Retinal light sensitivity; CRT: Central retinal thickness; SRVD: Superficial retinal vascular density; DRVD: Deep retinal vascular density; FAZ: Foveal avascular zone; CCL: Choroidal capillary layer; SFCT: Subfoveal choroidal thickness.



**Figure 3 A 46 years old male patient's FAF** A: FAF before treatment; B: FAF 3mo after treatment. FAF: Fundus autofluorescence.

after treatment (Figure 3). No structural laser damage was observed on OCT and OCTA, and no CNV was found. **DISCUSSION** 

## CSC is an idiopathic chorioretinopathy with predominantly macular involvement, characterized by localized serous detachment of the neuroepithelial layer and RPE layer<sup>[7]</sup>. The exact pathophysiological mechanism of CSC remains unknown. The most widely accepted explanation currently includes two factors: high permeability of choroidal vessels and RPE dysfunction<sup>[3]</sup>. The hypothesis of choroidal dysfunction holds that the hyperpermeability of choroidal vessels and the focal hypoperfusion of choroidal capillaries lead to ischemia and hypoxia of adjacent retinal tissues, thereby impairing the structure and function of RPE layer, and exudates enter the subretinal neuroepithelial layer<sup>[12-13]</sup>. However, the theory of RPE dysfunction believes that VEGF secreted by RPE can maintain the normal structure and homeostasis of choroidal capillaries, long-term diseases and chronic RPE atrophy lead to the increase of choroidal capillary hydrostatic pressure and the decrease of RPE barrier function, resulting in the accumulation of SRF<sup>[14]</sup>. For many years, aCSC has been considered a selflimiting disease, most of which can recover without any damage within 3-4mo after onset<sup>[1]</sup>, so many scholars advocate observing the changes of the disease. However, research by Gawecki et al<sup>[15]</sup> shows that the presence of SRF in the course of CSC, even in its acute and fast-resolving form, can lead to functional and morphological alterations of the retina. Uzlu *et al*<sup>[16]</sup> found the longer the course of the disease, the</sup>more severe the damage to the retinal structure and function, when the symptoms persist for more than 4mo, even if the anatomical structure is restored, the patient's visual function will be irreversibly damaged. Therefore, early, effective and safe treatment of aCSC is very necessary.

SML is a kind of short and high-frequency repetitive pulse laser with the characteristics of short exposure time, low energy and high density<sup>[17]</sup>. It is different from the traditional continuous laser and can minimize the related thermal damage. The key part of SML treatment is RPE, it activates the function of RPE, heats the RPE complex through a dense spot of light, induces HSP70 expression, inhibits apoptosis and down-regulates inflammatory factors. At the same time, light stimulates sublethal RPE cells to produce pigment epitheliaderived factors and VEGF inhibitors, restores pump function and outer barrier, and finally reduces choroidal permeability to achieve therapeutic effect<sup>[18-19]</sup>. SML can use either the 577 nm or the 810 nm wavelength, the 577 nm micropulse laser can minimize the absorption of yellow light by lutein in the inner and outer plexiform layer of the macula, so it is relatively safe for the treatment of macular fovea and its vicinity<sup>[20]</sup>. Gawecki et al<sup>[21]</sup> confirmed that SML can effectively promote the absorption of SRF without changing the structural morphology of retina. In this study, no change of treatment spots was found after SML treatment, and no laser scar or structural damage was found on OCT and OCTA. This indicates that SML therapy for aCSC is safe in the short term and can be applied to the macular region and its adjacent tissues, which has more advantages than traditional laser and PDT, this is consistent with the previous safety research results of micropulse laser<sup>[18,22]</sup>.

OCTA is a new ocular examination technology developed in recent years, and it has attracted the attention of ophthalmologists as soon as it was born because of its advantages in the examination of fundus blood vessels. With the clinical application of OCTA, its application in retinal and choroidal vascular diseases is more and more widespread. It can clearly display the characteristics of retinal and choroidal vascular morphology, so it has strong application value in the research of retinal and choroidal vascular diseases<sup>[23]</sup>. In a study comparing the density of superficial retinal microvessels in patients with aCSC and controls, Yu et al<sup>[24]</sup> found that the density was reduced in patients with aCSC. Podkowinski et al<sup>[25]</sup> showed that deep retinal capillary density and vascular perfusion in the SRF region were decreased in aCSC, and these changes may lead to chronic changes in the microvascular system and potential morphological changes. Previous studies have shown that changes in vascular density and FAZ are related to the course and prognosis of some retinal diseases<sup>[26]</sup>. Reich *et al*<sup>[27]</sup> showed that patients with aCSC had reduced</sup>blood flow in the CCL. Therefore, this study observed SRVD, DRVD, superficial and deep FAZ area, the perfusion area of CCL before and after SML treatment to evaluate its therapeutic effect. After SML treatment, we can find that SRVD, DRVD and the perfusion area of CCL of patients has increased, and the area of superficial and deep FAZ has decreased, while in the observation group, only DRVD has increased. At 3mo, we found in the comparison of two groups, the changes of SRVD, DRVD and perfusion area of CCL of SML group were better than those of the observation group. Under physiological conditions, the choroidal capillaries provide oxygen and metabolic exchange to the outer retina, including

the RPE and photoreceptors. The retinal circulation provides about 15% of the metabolic activity of the inner segment of the photoreceptors<sup>[28]</sup>. Therefore, both retinal and choroidal circulation provide nutrients for photoreceptors to maintain their normal metabolism. Our study demonstrated that SML could effectively improve retinal and choroidal blood circulation. This suggests that SML is effective in treating aCSC. The change in DRVD in the observation group shows that aCSC can heal itself to a certain extent. At the same time, we can see that the SFCT in the observation group also decreased compared to baseline at the last follow-up, and there is no significant difference between the observation group and the SML group. RPE has significant paracrine influence on the retina, and likely choroid, while there is little to none in the choroid itself, repair of RPE and improvement of the choroid may have occurred in both the SML group and the observation group. At the same time, we cannot ignore that choroidal thickness is affected by many factors, such as age, axial length, intraocular pressure, and may fluctuate at different time points within a day. The area of superficial and deep FAZ decreased after SML treatment, but the difference was not statistically significant compared with the observation group. This may be because SRF mainly exists in the fovea of the macula, and the absorption of SRF here is the slowest, which has the greatest impact on the structure and function of the fovea. In addition, the capillary damage or morphological changes of FAZ caused by ischemia and hypoxia in the macular area require a longer time to repair, however, the observation time of this study is shorter, the recovery of the superficial and deep FAZ may take longer.

In recent years, microperimetry has been widely used in fundus diseases. It combines fundus morphology examination with retinal function examination to detect visual field changes caused by macular disease and evaluate visual function<sup>[29]</sup>. CSC is a fundus disease mainly affecting the macular area. In the past, central vision was used to evaluate the function of the macular area, but the central vision only reflected the function of the fovea, and there was a lack of corresponding detection methods for the parafovea and perifovea. MP-3 microperimetry can measure RLS in a larger range, and is not affected by eye movement and fixation stability. In this study, compared with before treatment, BCVA, CRT and RLS in SML group were significantly improved 3mo after treatment, and were significantly higher than those in the observation group, however, in the observation group, only CRT was reduced, BCVA and RLS at the last follow-up were not significantly different from baseline. This shows that SML can effectively protect and even improve the visual function of the lesion area while promoting the absorption of SRF in patients with aCSC. The improvement in visual function may be due to the absorption of SRF, which improves the physiological environment of retinal cells, restores the physiological function of retinal cells and intercellular synaptic connections, and improves the function of visual signal transduction pathways. Işık<sup>[22]</sup> observed the efficacy of SML in the treatment of chronic CSC and found that SML promoted the absorption of SRF and provided significant anatomical and functional improvements, which is consistent with the results of this study. However, in our study, we used microperimetry to evaluate the therapeutic effect of SML more objectively, and used OCTA to quantitatively analyze the blood flow changes of the retina and choroid and the changes of FAZ area. This made the changes of retina and choroid before and after SML treatment more intuitive to show in front of us, and provided us with a deeper understanding of the pathophysiological mechanism of CSC.

In this study, SML showed good efficacy and safety in the treatment of aCSC. In fact, at present, SML has been used in a variety of fundus diseases, including diabetic macular edema and retinal vein occlusion secondary macular edema<sup>[30-31]</sup>. In recent years, some scholars have proposed to use SML for panretinal photocoagulation to treat diabetic retinopathy, and SML has also been reported to be used in the treatment of retinitis pigmentosa and secondary macular edema after cataract surgery<sup>[32-33]</sup>. In the research of these diseases, SML also shows great potential, but more clinical studies are still needed to confirm. This study still has some limitations. First, the follow-up time is short, and the long-term effect of SML treatment cannot be observed. Second, the sample size is small and there may be bias. In addition, we manually measured the FAZ area of the superficial and deep retina, which may affect the accuracy of the measurement.

In summary, we believe that 577 nm SML treatment can make the SRF rapidly absorbed, ameliorate visual function, improve retinal and choroid blood flow. Moreover, it will not produce laser spot on the retina, is safe and effective. SML is beneficial to shorten the course of disease and improve the prognosis, and has unique advantages in clinic due to its low price, few complications and repeatable treatment characteristics. It is believed that SML will be used in the treatment of many eye diseases in the future. It will have a broader application prospect.

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#### REFERENCES

- 1 Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, Jaisser F, Behar-Cohen F. Central serous chorioretinopathy: recent findings and new physiopathology hypothesis. *Prog Retin Eye Res* 2015;48:82-118.
- 2 Ross A, Ross AH, Mohamed Q. Review and update of central serous chorioretinopathy. *Curr Opin Ophthalmol* 2011;22(3):166-173.

- 3 Kaye R, Chandra S, Sheth J, Boon CJF, Sivaprasad S, Lotery A. Central serous chorioretinopathy: an update on risk factors, pathophysiology and imaging modalities. *Prog Retin Eye Res* 2020;79:100865.
- 4 Behnia M, Khabazkhoob M, Aliakbari S, Abadi AE, Hashemi H, Pourvahidi P. Improvement in visual acuity and contrast sensitivity in patients with central serous chorioretinopathy after macular subthreshold laser therapy. *Retina* 2013;33(2):324-328.
- 5 Shiragami C, Takasago Y, Osaka R, Kobayashi M, Ono A, Yamashita A, Hirooka K. Clinical features of central serous chorioretinopathy with type 1 choroidal neovascularization. *Am J Ophthalmol* 2018;193:80-86.
- 6 Semeraro F, Morescalchi F, Russo A, Gambicorti E, Pilotto A, Parmeggiani F, Bartollino S, Costagliola C. Central serous chorioretinopathy: pathogenesis and management. *Clin Ophthalmol* 2019;13:2341-2352.
- 7 Hanumunthadu D, Tan ACS, Singh SR, Sahu NK, Chhablani J. Management of chronic central serous chorioretinopathy. *Indian J Ophthalmol* 2018;66(12):1704-1714.
- 8 Pauleikhoff L, Agostini H, Lange C. Central serous chorioretinopathy. *Ophthalmologe* 2021;118(9):967-980.
- 9 Mao JB, Zhang CY, Liu CY, Zhang Y, Lin JJ, Xu ZK, Chen YQ, Fan YY, Zhao SX, Shen LJ. Comprehensive evaluation of intravitreal conbercept versus half-dose photodynamic therapy for chronic central serous chorioretinopathy. *Int J Ophthalmol* 2021;14(5):719-724.
- 10 Jung BJ, Lee K, Park JH, Lee JH. Chorioretinal response to intravitreal aflibercept injection in acute central serous chorioretinopathy. *Int J Ophthalmol* 2019;12(12):1865-1871.
- 11 van Rijssen TJ, van Dijk EHC, Yzer S, *et al.* Central serous chorioretinopathy: towards an evidence-based treatment guideline. *Prog Retin Eye Res* 2019;73:100770.
- 12 Donald J, Gass M. Pathogenesis of disciform detachment of the neuroepithelium. *Am J Ophthalmol* 1967;63(3):Suppl:1-139.
- 13 Matet A, Daruich A, Hardy S, Behar-Cohen F. Patterns of choriocapillaris flow signal voids in central serous chorioretinopathy. *Retina* 2019;39(11):2178-2188.
- 14 Bhutto I, Lutty G. Understanding age-related macular degeneration (AMD): relationships between the photoreceptor/retinal pigment epithelium/Bruch's membrane/choriocapillaris complex. *Mol Aspects Med* 2012;33(4):295-317.
- 15 Gawęcki M, Jaszczuk A, Grzybowski A. Short term presence of subretinal fluid in central serous chorioretinopathy affects retinal thickness and function. J Clin Med 2020;9(11):3429.
- 16 Uzlu D, Erdöl H, Kola M, Özbay AD. The efficacy of subthreshold micropulse yellow laser (577 nm) in chronic central serous chorioretinopathy. *Lasers Med Sci* 2021;36(5):981-988.
- 17 Inagaki K, Hamada M, Ohkoshi K. Minimally invasive laser treatment combined with intravitreal injection of anti-vascular endothelial growth factor for diabetic macular oedema. *Sci Rep* 2019;9(1):7585.
- 18 Gawęcki M. Micropulse laser treatment of retinal diseases. J Clin Med 2019;8(2):242.
- 19 Arora S, Sridharan P, Arora T, Chhabra M, Ghosh B. Subthreshold

diode micropulse laser versus observation in acute central serous chorioretinopathy. *Clin Exp Optom* 2019;102(1):79-85.

- 20 Scholz P, Altay L, Fauser S. A review of subthreshold micropulse laser for treatment of macular disorders. *Adv Ther* 2017;34(7):1528-1555.
- 21 Gawęcki M, Jaszczuk-Maciejewska A, Jurska-Jaśko A, Grzybowski A. Functional and morphological outcome in patients with chronic central serous chorioretinopathy treated by subthreshold micropulse laser. *Graefes Arch Clin Exp Ophthalmol* 2017;255(12):2299-2306.
- 22 Işık MU. Efficacy of the subthreshold micropulse yellow wavelength laser photostimulation in the treatment of chronic central serous chorioretinopathy. *Int J Ophthalmol* 2020;13(9):1404-1410.
- 23 Yun C, Huh J, Ahn SM, Lee B, Kim JT, Hwang SY, Kim SW, Oh J. Choriocapillaris flow features and choroidal vasculature in the fellow eyes of patients with acute central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol* 2019;257(1):57-70.
- 24 Yu L, Shao Y, Chai Y, Ye LH, Yang QC, Ye L, Yuan Q, Jiang N, Yi JL. Retinal microvasculature alteration in central serous chorioretinopathy. *Mol Med Rep* 2018;17(2):2335-2340.
- 25 Podkowinski D, Foessl B, de Sisternes L, Beka S, Mursch-Edlmayr AS, Strauss RW, Bolz M. Early alterations in retinal microvasculature on swept-source optical coherence tomography angiography in acute central serous chorioretinopathy. *Sci Rep* 2021;11(1):3129.
- 26 Mao JB, Lin JJ, Zhu L, Liu CY, Yu XT, Zhang CY, Chen YQ, Zhang Y, Shen LJ. Quantitative assessment of retinal capillary vessel density and foveal avascular zone area in central serous chorioretinopathy using OCTA. *Ophthalmologica* 2020;243(5):370-378.
- 27 Reich M, Böhringer D, Cakir B, Bucher F, Daniel M, Lang S, Lagrèze W, Agostini H, Lange C. Longitudinal analysis of the choriocapillaris using optical coherence tomography angiography reveals subretinal fluid as a substantial confounder in patients with acute central serous chorioretinopathy. *Ophthalmol Ther* 2019;8(4):599-610.
- 28 Scarinci F, Jampol LM, Linsenmeier RA, Fawzi AA. Association of diabetic macular nonperfusion with outer retinal disruption on optical coherence tomography. *JAMA Ophthalmol* 2015;133(9):1036-1044.
- 29 Molina-Martín A, Pérez-Cambrodí RJ, Piñero DP. Current clinical application of microperimetry: a review. *Semin Ophthalmol* 2018; 33(5):620-628.
- 30 Citirik M. The impact of central foveal thickness on the efficacy of subthreshold micropulse yellow laser photocoagulation in diabetic macular edema. *Lasers Med Sci* 2019;34(5):907-912.
- 31 Li ZJ. Optical coherence tomography angiography assessment of 577 nm laser effect on severe non-proliferative diabetic retinopathy with diabetic macular edema. *Int J Ophthalmol* 2020;13(8):1257-1265.
- 32 Luttrull JK. Improved retinal and visual function following panmacular subthreshold diode micropulse laser for retinitis pigmentosa. *Eye* (*Lond*) 2018;32(6):1099-1110.
- 33 Verdina T, Ferrari C, Valerio E, Brombin A, Lazzerini A, Mastropasqua R, Cavallini GM. Subthreshold micropulse yellow laser for the management of refractory cystoid macular edema consequent to complicated cataract surgery. *Eur J Ophthalmol* 2021;31(5):NP93-NP98.