Lasers in Medical Science (2025) 40:225
https://doi.org/10.1007/s10103-025-04473-0

RESEARCH

Comparative efficacy of subthreshold micropulse laser versus conventional laser therapy in central serous chorioretinopathy

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Received: 8 March 2025 / Accepted: 1 May 2025

Abstract

Subthreshold micropulse laser (SML) and conventional laser photocoagulation (CLP) have established efficacy in treating central serous chorioretinopathy (CSC), but systematic comparisons of their effectiveness, safety, and long-term outcomes remain lacking.We carried out this retrospective study. A total of 109 eyes from 109 CSC patients were included, with 53 eyes in the conventional laser group and 56 eyes in the SML group. The SML group was treated with a 577-nm wavelength laser, targeting areas of leakage and subretinal fluid (SRF). For patients without identifiable leakage points, the treatment area covered the SRF region. The conventional laser group received single-spot laser treatment with a laser spot reaction of ≤grade 1, targeting leakage points identified by early-phase fluorescein angiography (FFA). Disease duration, leakage points on FFA, best-corrected visual acuity (BCVA) during follow-up, central macular thickness (CMT), SRF resolution, and safety were analyzed. The mean follow-up duration was 6.90±2.77 months. The conventional laser group had a shorter mean disease duration compared to the SML group ($P=0.002$), and there was a significant difference in the distribution of leakage points between the two groups ($P=0.000$). At 6 months post-treatment, compared to baseline, the BCVA change was 0.24±0.28 in the CL group ($P=0.02$) and 0.19±0.18 in the SML group ($P=0.04$). There were no significant differences in BCVA between the two groups at any follow-up time point, though. CMT changes from baseline to final follow-up demonstrated a mean reduction of 228.00±181.01 μm in the CL group versus 176.97±143.39 μm in the SML group (both $P<0.001$). No significant differences were observed in mean CMT or final OCT changes between the two groups at any follow-up time point. The complete SRF resolution rates were 83.01% in the conventional laser group and 87.50% in the SML group ($P=0.59$).Both SML and CL treatments are safe and effective for CSC. CL therapy is a safe and effective option for patients with acute disease, clearly identifiable leakage points located>250 μm from the foveal center, while SML is preferable for patients with longer disease duration, unclear leakage points, or leakage points located within 250 μm of the foveal center.
Clinical trial number: Not applicable.

Keywords Central serous chorioretinopathy · Subthreshold micropulse laser · Conventional laser

Background

Central serous chorioretinopathy (CSC) represents one of the leading causes of visual impairment among middle-aged males [1]. This condition is clinically characterized by serous detachment of the neurosensory retina in the macular region, with or without associated retinal pigment epithelial (RPE) detachment. The annual incidence of CSC in male patients ranges from 5.5 to 9.9 per 10,000 individuals [2, 3]. Current therapeutic approaches for CSC primarily include observation, photodynamic therapy (PDT), conventional laser (CL) treatment, and subthreshold micropulse laser (SML) therapy [1], [4, 5]. While PDT demonstrates

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Published online: 17 May 2025

significant efficacy in promoting subretinal fluid absorption and visual function recovery, its application is limited by potential risks of choroidal ischemia and the recent challenges in obtaining photosensitizing agents due to their high cost and limited availability. CL treatment accelerates subretinal fluid absorption by sealing leakage points, offering rapid therapeutic effects. However, its use is constrained by potential complications such as retinal scarring, scotoma formation, and secondary choroidal neovascularization (CNV), making it unsuitable for certain CSC patients.

SML, initially introduced in the 1990s, selectively targets RPE cells and has been applied in the treatment of various retinal disorders [6]. Previous studies have demonstrated that SML exhibits comparable efficacy to PDT and superior outcomes to intravitreal anti-VEGF injections in promoting subretinal fluid absorption in CSC patients [7, 8]. Nevertheless, comparative studies between SML and CL in CSC treatment remain limited, with short follow-up durations and a predominant focus on visual acuity and central macular thickness (CMT) as primary outcome measures. There is a notable paucity of research addressing other CSC-related parameters such as leakage point location and RPE morphology. Therefore, we conducted this retrospective study to compare the therapeutic efficacy of SML and CL in CSC treatment and to analyze relevant factors, aiming to identify the optimal treatment strategy for CSC.

Materials and methods

This retrospective case series study was conducted with approval from the Ethics Committee of Peking University People's Hospital, and written informed consent was obtained from all participants. We enrolled 109 eyes of 109 patients diagnosed with CSC between January 2022 and June 2024 at the Department of Ophthalmology, Peking University People's Hospital. Diagnosis was confirmed through fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT). The cohort comprised 85 eyes from 85 male patients and 24 eyes from 24 female patients, aged 27 to 69 years (mean ± SD: 45.02 ± 10.13 years). Among these, 56 patients underwent SML treatment, while 53 received CL treatment.

All patients underwent comprehensive ophthalmic examinations, including best-corrected visual acuity (BCVA, recorded as LogMAR), intraocular pressure measurement, slit-lamp examination, indirect ophthalmoscopy, OCT (using RTVue-XR Avanti OCT, Optovue, USA, or Cirrus 5000 HD-OCT, Zeiss, Germany), color stereoscopic fundus photography, fundus autofluorescence (FAF), and FFA (using Zeiss FF450 plus or Optos 200Tx laser scanning ophthalmoscope, UK), as well as ICGA (Spectralis, Heidelberg, Germany). RPE changes were classified based on FAF findings as follows: no significant change (no RPE alterations in the treatment area compared to baseline), mild change (focal RPE roughness without distinct laser spots), and significant change (presence of clearly visible laser spots) (8). Follow-up examinations included OCT, FAF, and fundus photography at each visit. FFA was repeated at 3- and 6-months post-treatment. The outcomes at 1 month, 3 months, and 6 months post-treatment were included in the study.

Inclusion criteria were: (1) age ≥ 18 years; (2) CSC diagnosis confirmed by FFA, ICGA and OCT; (3) treatment with either SML or CL; and (4) minimum follow-up duration of 6 months. Exclusion criteria included: (1) history of any other retinal disorders, including rhegmatogenous retinal detachment, age-related macular degeneration, epiretinal membrane, high myopia fundus changes, and ocular tumors; and (2) any form of intraocular laser treatment or surgery within the preceding 3 months.

Laser treatment protocols

SML treatment was performed using the IRIDEX IQ 577 system in micropulse mode with the following parameters: wavelength 577 nm, exposure time 200 ms, duty cycle 5%, spot size 200 μm, and power 400 mW. The treatment area encompassed leakage points and regions with subretinal fluid. For patients without identifiable leakage points, the treatment covered the subretinal fluid area. CL treatment was administered using the Zeiss Visulas Trion system in single-spot scanning mode with parameters: wavelength 561 nm, exposure time 100ms, spot size 100 μm, and power 60-100mW, aiming for ≤ grade 1 laser spots. Treatment was guided by early-phase FFA leakage points, with 1–3 spots applied per leakage point. For patients presenting with definitive leakage sites located beyond 250 μm from the foveal center, CL was employed. In cases where leakage points are either undetectable or situated within the 250 μm of the macular fovea, SML was employed.

Statistical analysis

Data analysis was performed using SPSS 22.0 software. Quantitative data are presented as mean ± standard deviation, with between-group comparisons conducted using independent samples t-tests. Qualitative data were analyzed using Fisher's exact test. A p-value < 0.05 was considered statistically significant.

Table 1 Baseline characteristics of the two patient groups

	CL group	SML group	*p*
Age (years)	44.03 ± 9.92	46.00 ± 10.41	0.46
Gender (Male/Female)	46/7	39/17	0.038*
Eyes (right eye/left eye)	18/35	33/23	0.012*
Disease duration (days)	55.67 ± 65.95	150.93 ± 144.68	0.002*
Follow up time (months)	6.57 ± 1.41	7.23 ± 3.65	0.36
Baseline visual acuity	0.26 ± 0.27	0.30 ± 0.27	0.68
Baseline OCT (μ m)	427.93 ± 168.07	371.97 ± 141.35	0.17

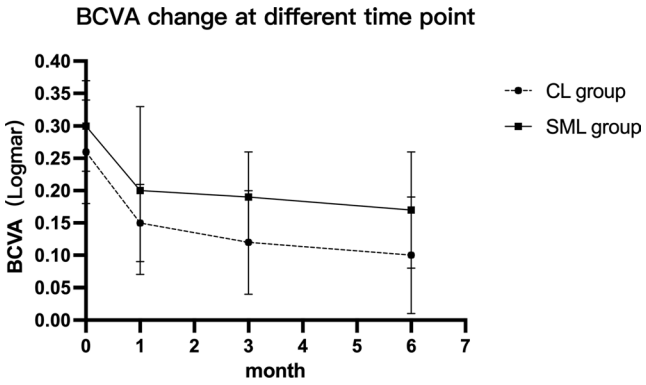

Fig. 1 Changes in visual acuity in the two treatment groups. Post-treatment visual acuity measurements demonstrated progressive improvement in both groups. However, no statistically significant differences were observed in mean visual acuity at each follow-up time point or in the final visual acuity improvement between the two groups

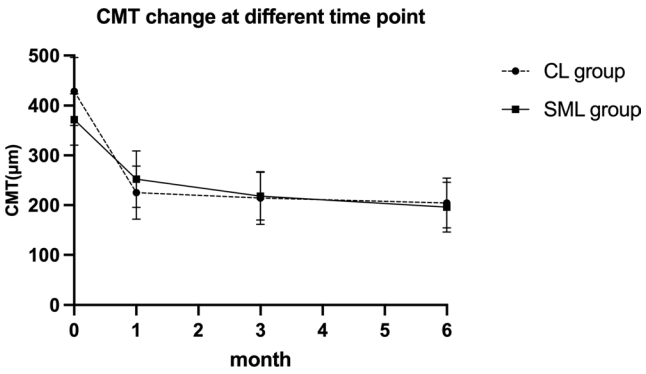

Fig. 2 OCT changes in two groups of patients. OCT measurements demonstrated progressive reduction of central macular thickness (CMT) in both groups during the 6-month longitudinal assessment. Intergroup comparisons showed no significant differences CMT outcomes at all follow-up time point or in the final CMT change

Results

Baseline characteristics of the two patient groups are presented in Table 1. The mean follow-up duration was 6.90 ± 2.77 months. The CL group exhibited a significantly shorter disease duration compared to the SML group ($P < 0.05$), while no significant differences were observed in other baseline parameters between the two groups.

At baseline, 100% of patients in the CL group exhibited definitive FFA leakage points, all located beyond a 250 μm radius from the foveal center. In the SML group, 21 cases (37.50%) demonstrated leakage points outside the 250 μm radius, 5 cases (8.93%) showed leakage points within the 250 μm radius, and 30 cases (53.57%) presented no definitive leakage points on FFA. A statistically significant difference was observed in leakage point distribution between the two groups ($P = 0.000$).

Post-treatment visual acuity measurements demonstrated progressive improvement in both groups, with the CL group achieving mean values of 0.80 ± 0.35, 0.85 ± 0.34, and 0.88 ± 0.34 at 1-, 3-, and 6-month follow-ups respectively, compared to 0.70 ± 0.28, 0.72 ± 0.29, and 0.76 ± 0.31 in the SML group during the corresponding observation periods. At the final follow-up, both groups demonstrated significant improvement in visual acuity. Compared to baseline, the BCVA change was 0.24 ± 0.28 in the CL group ($P = 0.02$) and 0.19 ± 0.18 in the SML group ($P = 0.04$). However, no statistically significant differences were observed in mean visual acuity at each follow-up time point ($p = 0.23$, 0.12 and 0.16 at 1-, 3-, and 6-month follow-ups respectively,) or in the final visual acuity improvement between the two groups ($P = 0.37$)(Fig 1).

OCT measurements demonstrated progressive reduction of central macular thickness (CMT) in both groups during the 6-month longitudinal assessment. The CL group exhibited mean CMT values of 225.00 ± 83.53 μm, 214.40 ± 82.79 μm, and 204.50 ± 72.10 μm at 1-, 3-, and 6-month post-treatment evaluations, respectively. Corresponding measurements in the SML group were 252.33 ± 95.71 μm, 218.00 ± 83.49 μm, and 195.97 ± 62.96 μm. Intragroup analysis revealed statistically significant CMT improvement from baseline to final follow-up in both cohorts ($P < 0.001$, paired t-test). Notably, intergroup comparisons showed no significant differences CMT outcomes at all follow-up time point ($P = 0.24$, 0.87, and 0.63 at 1, 3, and 6 months respectively). CMT changes from baseline to final follow-up demonstrated a mean reduction of 228.00 ± 181.01 μm in the CL group versus 176.97 ± 143.39 μm in the SML group, though this difference did not reach statistical significance ($P = 0.23$, ANCOVA adjusted for baseline values)(Fig 2). Complete resolution of subretinal fluid was achieved in 83.01% of patients in the CL group and 87.50% of patients in the SML group, with no significant difference between the two groups ($P = 0.59$) (Typical cases seeing Figs. ,, 3 and 4).

Other observational indicators

The CL group achieved complete SRF resolution at a mean duration of 2.36 ± 1.85 months, while the SML group demonstrated similar resolution kinetics with a mean absorption

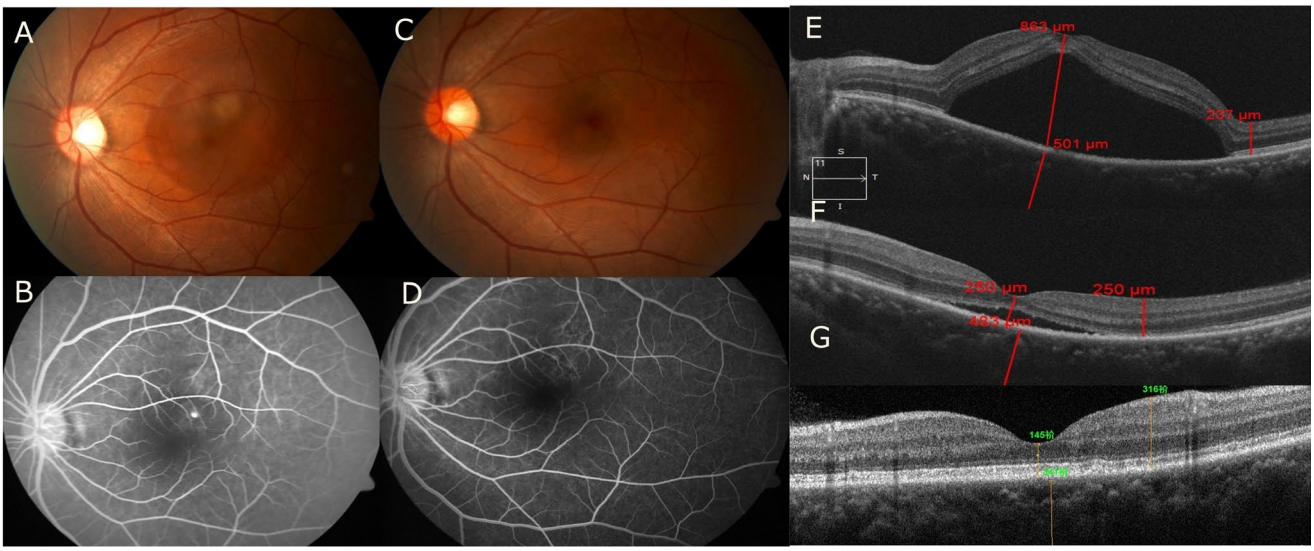

Fig. 3 Case Report 1. A 38-year-old male presented with metamorphopsia in the left eye for 10 days. BCVA was 0.52 (Logmar). Fundus examination revealed serous elevation in the posterior pole of the left retina (**A**). FFA demonstrated a leakage point beyond the 250 µm radius from the foveal center (**B**). OCT showed neurosensory detachment with a CMT of 863 µm (**E**). The patient underwent 2-spot CL treatment with 100mw energy. At 1-month follow-up, visual acuity improved to 0.1, with minimal residual subretinal fluid on OCT (CMT 250 µm, **F**). Three-month follow-up revealed complete resolution of posterior pole retinal elevation (**C**), absence of leakage points on FFA (**D**), and complete absorption of subretinal fluid on OCT (CMT 145 µm, **G**)

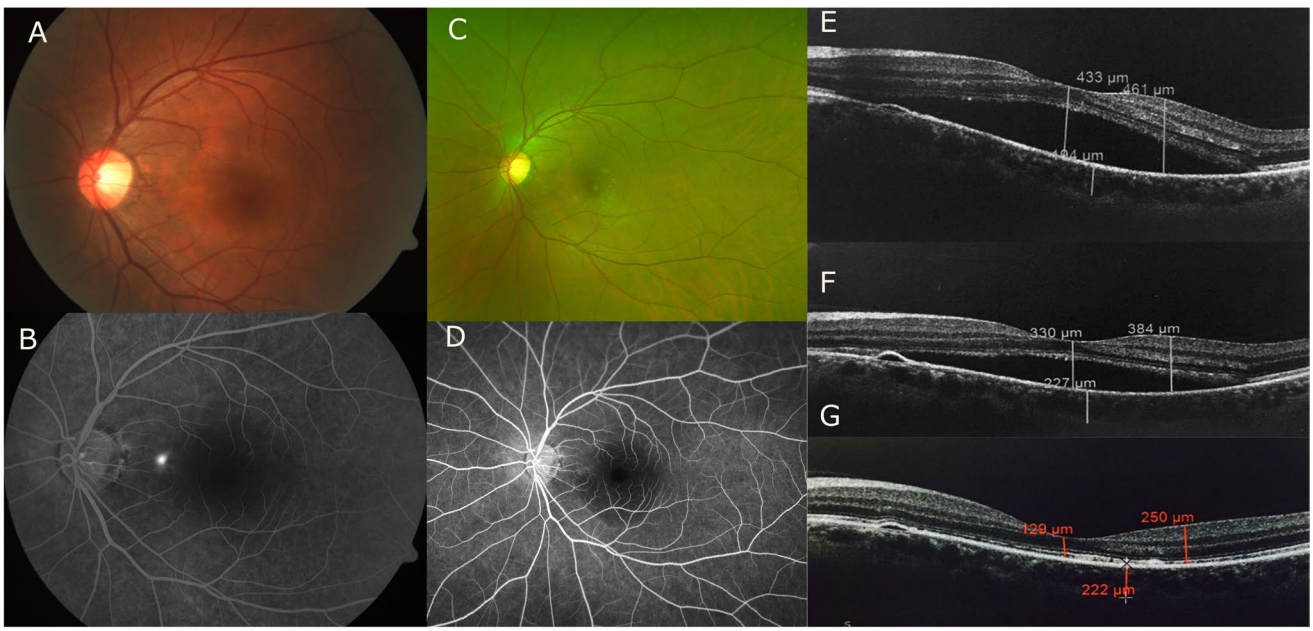

Fig. 4 Case Report 2 A 39-year-old female presented with decreased vision in the left eye for 1 month. BCVA was 0.30. Fundus examination showed serous elevation in the posterior pole of the left retina (**A**). FFA revealed a leakage point beyond the 250 µm radius from the foveal center (**B**). OCT demonstrated neurosensory detachment with localized RPE detachment and a CMT of 433 µm (**E**). The patient received SML treatment. At 1-month follow-up, visual acuity improved to 0.6, with minimal residual subretinal fluid on OCT (CMT 330 µm, **F**). Three-month follow-up showed complete resolution of posterior pole retinal elevation (**C**) with visual acuity of 0.1. FFA revealed complete resolution of leakage points (**D**), and OCT demonstrated complete absorption of subretinal fluid (CMT 129 µm, **G**)

time of 2.69 ± 1.72 months. There was no statistically significant intergroup difference in SRF clearance rates ($p = 0.265$). In the CL group, recurrence occurred in 5 cases, and another 5 cases exhibited persistent subretinal fluid at the 3-month follow-up, resulting in 8 cases receiving additional CL treatment (all with leakage points), and 2 cases receiving SML treatment. The SML group showed recurrence in 2 cases and persistent subretinal fluid in 5 cases at 3-month follow-up,

with 7 patients receiving additional SML treatment. No significant differences were observed in recurrence rates or retreatment rates between the two groups.

Safety results

Regarding RPE alterations observed through FAF: in the CL group, 5 cases (9.43%) demonstrated significant changes at laser spot locations, 39 cases (73.58%) showed mild changes, and 9 cases (16.99%) exhibited no significant changes. In the SML group, no new significant RPE alterations were observed in the laser-irradiated areas compared to pretreatment status.

Discussion

This retrospective study compared the therapeutic efficacy of CL and SML in patients with central serous chorioretinopathy (CSC). The findings revealed that patients receiving CL treatment had a shorter average disease duration, with identifiable leakage points located outside the foveal avascular zone. In contrast, SML-treated patients exhibited longer disease duration, and some cases presented without definitive leakage points. Both laser modalities demonstrated comparable outcomes in visual acuity improvement, subretinal fluid absorption rate and duration, and changes in CMT. This study provides new evidence supporting the therapeutic effectiveness of both CL and SML in CSC management.

The pathological process of CSC primarily involves choroidal capillary impairment leading to choroidal hyperpermeability and subsequent RPE dysfunction [9, 10]. CSC management requires addressing systemic risk factors while emphasizing ocular treatment. Due to incomplete understanding of CSC's pathological mechanisms, the optimal treatment approach remains controversial. Ocular interventions include observation, PDT, CL, and SML therapy. Although CSC is considered a self-limiting condition, approximately 50% of patients fail to achieve spontaneous resolution, 20–30% experience single or multiple recurrences, and 5% progress to chronic CSC with permanent visual impairment [11]. Current evidence supports half-dose PDT as the gold standard for CSC treatment. However, its application is limited in China due to drug unavailability and high costs. In the absence of PDT, CL and subthreshold SML have been increasingly utilized, necessitating comparative studies to evaluate their efficacy and application differences.

CL has been extensively applied in various retinal disorders. In CSC patients, CL specifically targets leakage points identified on FFA, aiming to seal the blood-retinal barrier and achieve subretinal fluid resolution [12]. Compared to observation, CL significantly reduces the duration of subretinal fluid [13, 14]. In our study, CL-treated patients demonstrated significant visual improvement post-treatment, potentially attributable to rapid subretinal fluid absorption. However, CL application is restricted by leakage point location due to potential complications including scotomas, blind spots, and secondary CNV [15]. All CL-treated patients in this study had confirmed leakage points outside the 250 μm foveal zone. Notably, our protocol utilized lower laser energy with subthreshold or grade 1 laser reactions, smaller treatment areas, and fewer laser spots, resulting in reduced RPE damage compared to conventional CL protocols, as evidenced by FAF findings.

Compared to CL, SML induces minimal damage to RPE and outer retinal layers. At appropriate doses, SML selectively targets RPE while preserving photoreceptor layers, avoiding visible tissue damage [16]. Initially introduced in 1997 for macular edema secondary to retinal vein occlusion and diabetic retinopathy [17, 18], SML was first applied to CSC treatment by Chen et al. in 2008[19]. Some researchers suggest that SML-generated heat is insufficient to cause protein denaturation [20], while others propose that SML may enhance heat shock protein expression, thereby restoring RPE function [21]. Our SML-treated cohort also demonstrated significant subretinal fluid absorption and visual improvement, though optimal energy parameters require further investigation.

Comparative studies between these two laser modalities remain limited [22]. Lijun Zhou et al. conducted a prospective study in acute CSC patients, finding both methods equally effective in anatomical and functional recovery, though CL showed faster onset. [22]. Our study revealed no significant differences in subretinal fluid absorption time, final visual acuity, or OCT improvements between groups. This finding may be partially explained by the inherent limitations of retrospective design, particularly the significant difference in disease duration between groups. However, this result also suggests SML's efficacy in chronic CSC cases. As disease duration increases, the prevalence of typical leakage points decreases, making SML a preferable option for such patients. Besides disease duration differences, our study groups also differed in leakage point characteristics and locations. The SML group received treatment covering leakage points and/or extensive subretinal fluid areas, with post-treatment FAF showing no significant RPE changes compared to baseline. This observation may reflect that RPE alterations in these patients primarily resulted from chronic CSC progression rather than SML intervention.

The retrospective nature of this study introduces baseline characteristic bias, representing a significant limitation. However, these baseline differences highlight the

importance of selecting appropriate laser modalities based on specific CSC clinical features. Therefore, low-energy CL appears safe and effective for acute cases with identifiable leakage points beyond 250 μm from the foveal center, while SML may be preferable for chronic cases with indefinite or foveal leakage points.

In conclusion, this retrospective analysis demonstrates that both CL and SML are safe and effective for CSC treatment, with modality selection dependent on specific clinical characteristics. Future prospective clinical studies are warranted to further compare these two treatment strategies.

Acknowledgements The authors would like to thank Professor Xiaoxin Li of Peking University People's Hospital for helpful discussions on topics related to this work.

Author contributions Huijun Qi was responsible for designing the protocol, writing the protocol and report, conducting the search, treating the patients, extracting, analyzing data and writing the manuscript. Yaoyao Sun was responsible for conducting the research, treating the patients, analyzing data and writing the manuscript. Mingwei Zhao and Heng Miao were responsible for conducting the research, treating the patients and writing the manuscript.

Funding This work was supported by the National Natural Science Foundation of China (No. 82301211) and Beijing Natural Science Foundation (J230028). Sources of material are not available commercially.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval All patients provided written informed consent to participate in accordance with the Helsinki Declaration guidelines. Informed consents have been obtained to publish the images in an online open-access publication. The Medical Ethics Committee of Peking University People's Hospital approved this study (2016PHA008). All methods were carried out in accordance with relevant guidelines and regulations of retinal vein occlusion. All experimental protocols were approved by Committee of Clinical Drug Trials, Peking University People's Hospital. Informed consent was obtained from all patients and/or their legal guardian(s).

Competing interests The authors declare no competing interests.

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