




# Five-Year Outcomes of Subthreshold Yellow Micropulse Laser Treatment in Chronic Central Serous Chorioretinopathy: Could it be Any Marker of Response to Treatment?

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## ABSTRACT

**Objective:** The aim of the study was to assess the results of 577 nm subthreshold yellow micropulse laser treatment (SYMLT) in patients with chronic central serous chorioretinopathy (CSC) with a five-year follow-up. We also evaluated the effect of baseline characteristics on relapse and the SYMLT treatment responses.

**Methods:** A total of 81 eyes of 72 patients with chronic CSC were followed for at least 5 years. Patients were treated with 577-nm SYMLT in multiple sessions at a 5% duty cycle. Best-corrected visual acuity (BCVA), central macular thickness (CMT), central macular volume (CMV), total macular volume (TMV) and subfoveal choroidal thickness (SFCT) were measured by spectral-domain optical coherence tomography (SD-OCT). Other basic SD-OCT parameters were recorded.

**Results:** The mean BCVA improved from  $0.46 \pm 0.25$  Log MAR to  $0.11 \pm 0.22$  Log MAR and the mean CMT decreased from  $404.60 \pm 72.46$   $\mu\text{m}$  to  $243.50 \pm 24.97$   $\mu\text{m}$  at last visit ( $p < 0.001$ ). At the last visit, 70 eyes (86.4%) had complete subretinal fluid (SRF) resorption with SYMLT sessions, and 11 eyes (13.6%) had residual SRF. While recurrence was not observed in sixty-eight (83.9%) patients within five years, it was observed in 13 (16.1%). In multivariate analyses, there was a statistically significant correlation between recurrence and  $\text{SFCT} \geq 416.00$   $\mu\text{m}$  ( $p < 0.001$ ) and baseline  $\text{SFCT} \geq 474.00$   $\mu\text{m}$  and baseline BCVA were significantly correlated with non-response to SYMLT ( $p = 0.025$  and  $p = 0.040$ , respectively).

**Conclusion:** SYMLT has been found to be a safe and effective in long-term follow-up. Clinical characteristics and some SD-OCT parameters might be predictors of treatment response to SYMLT and its recurrence.

## INTRODUCTION

Central serous chorioretinopathy (CSC) is typically characterized by serous neurosensory retinal detachment with or without retina pigment epithelium (RPE) detachment, which is one of the most common retinal diseases in the middle-aged population.<sup>[1]</sup> The blurred vision, metamorphopsia, relative central scotoma, micropsia, or reduced contrast sensitivity may occur due to subretinal fluid (SRF) and RPE defects.<sup>[2]</sup> The CSC has two clinical features, acute and chronic forms, including duration of SRF persistence, photoreceptor damage, and RPE atrophy.

In acute CSC, SRF resolves spontaneously in at least three or four months, but persists in chronic CSC cases, leading to vision loss.<sup>[3,4]</sup>

The common hypotheses regarding the etiology of CSC are based on the presence of local and/or diffuse leakage in fundus fluorescein angiography (FA) and /or indocyanine green angiography (ICGA), which are the essential imaging systems for CSC diagnosis.<sup>[5]</sup> Although the exact etiology of this disease is still unknown, treatment methods targeting the possible hyperpermeability of choroidal vessels and RPE pump dysfunction are currently being applied.

Due to the unclear mechanism of CSC, various treatment approaches: conventional laser photocoagulation (CLP), photodynamic therapy (PDT), intravitreal anti-vascular endothelial growth factor (anti-VEGF) agent injections, and systemic anti mineralocorticoid drugs are applied.<sup>[6,7]</sup> However, all these procedures may lead to some undesirable side effects, including central or paracentral scotomas, contrast sensitivity loss, choroidal neovascularization, choroidal ischemia, RPE atrophy, endophthalmitis, and systemic side effects.<sup>[4,8,9]</sup>

Subthreshold micropulse laser treatment (SMLT), which includes a more specific classification as subvisible therapies and non-damaging therapies, has been used for various choroid-retinal diseases for the past few years with the advantages of eliminating the side effects of previous treatments.<sup>[10]</sup> The SMLT triggers a biological response with heat shock protein expression that promotes recovery and restoration of the outer blood-retinal barrier and, ultimately resorption of the SRF.<sup>[11]</sup> There are some types of SMLT categorized according to the laser system wavelength and laser settings. The researches have mainly shown short-term effects in follow-up visits with a limited number of eyes, including mainly 810 nm SMLT, 532 nm SMLT, and some 577 nm SMLT.<sup>[12-14]</sup>

In the present study, we aimed to evaluate the efficacy and safety of 577 nm subthreshold yellow micropulse laser treatment (SYMLT) in patients with chronic CSC at their five-year follow-up visit. Also, we evaluated the effect of baseline characteristics on the SYMLT treatment responses and recurrences.

## MATERIALS AND METHODS

In this study, 81 eyes of 72 patients who underwent SYMLT for chronic or chronic recurrent CSC between October 2014 and December 2015 were retrospectively included in this study. This study adhered to the ethical standards of the Declaration of Helsinki. It was approved by the Local Ethical Committee Review Board. Informed consent was obtained from all individual participants included in the study.

The inclusion criteria were as follows: (1) patients with symptomatic chronic or recurrent CSC for three months or more; (2) CSC with SRF involving the fovea documented by SD-OCT; (3) patients without a history of CSC treatment; (4) patients with at least five-years of follow-up and relevant data. Exclusion criteria were: (1) patients with a history of comorbid ocular conditions; (2) patients who had received other prior therapy, including oral systemic treatment, anti-VEGF treatment, CLP, PDT; (3) patients who did not receive a follow-up for five years after initiation of SYMLT, respectively.

All patients underwent detailed ophthalmologic examinations including best-corrected visual acuity (BCVA) using the Snellen chart, intraocular pressure (IOP) measurement with Goldman applanation tonometer, anterior segment examination, and dilated biomicroscopic fundus examina-

tion. BCVA was converted to logarithm units of minimum angle of resolution (logMAR) for statistical analyzes.

CSC was diagnosed in patients with a single or multiple sites of active leakage, RPE changes on FA, and a serous macular detachment of the neurosensory retina on SD-OCT (Nikon RS-3000, Japan). The leakage pattern in FA was recorded as focal or diffuse. All patients had undergone FA prior to SYMLT; and again at 12- months and the last visit to identify any side effects such as choroidal neovascularization and RPE changes. In SD-OCT measurements, central macular thickness (CMT), central macular volume (CMV), total macular volume (TMV), subretinal fluid (SRF) height and subfoveal choroidal thickness (SFCT) were evaluated and recorded before the SYMLT and in every follow-up visit. The baseline height of pigment epithelial defects, such as pigment epithelial detachment (PED) or RPE bumps, was manually measured by a single observer (H.S.K.) using SD-OCT. Elevation was defined as 0  $\mu\text{m}$  when no RPE lesion associated with the leakage site was observed. The hyperreflective dot (HRD) was counted manually within an area with a radius of 1500  $\mu\text{m}$  centered on the fovea using a horizontal raster scan.

For the treatment, the 577-nm SMLT system (Supra 577Y Subliminal Laser System; Quantel Medical, Clermont-Ferrand, France) was performed using an Area-Centralis lens (Volk Optical, Mentor, OH, USA). The SYMLT was performed in the micropulse mode using a 160- $\mu\text{m}$  spot diameter and 5% duty cycle (DC) energy for 20 ms. The micropulse laser power used in SYMLT was derived from one test burn for each eye. The power was initially increased to the minimum threshold value to cause a barely visible burn, then it was reduced 50% of this energy level so that no visible or detectable retinal changes were made. FA-guided images were used to determine the area to be treated, and the laser shots were transmitted to the active leakage area and the surrounding one-spot-size area. If the SRF did not completely resolve in 3 months after the treatment or if there was a recurrence, SYMLT was repeated. If SRF did not completely resolve (either no response or partial response), after three sessions of SYMLT, patients were referred to other treatment options such as PDT, CLP, and anti-VEGF. In the evaluation of treatment responses, no response was defined as a decrease in SRF of <50% or an increase compared to the result of previous treatment after 3 SYMLT sessions; and partial response was defined as the SRF reduction of more than 50% but not completely resolved compared to the result of previous treatment after 3 SYMLT sessions

## Statistical analyzes

Statistical analyses were performed using SPSS ver. 22.0 (SPSS Inc., Chicago, IL, USA). The distribution of the data was tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk test. Pre- and post-laser SRF height was analyzed using the paired Student's t-test. Descriptive analyses were presented using medians and interquartile range for non-normally distributed and ordinal variables.

Friedman tests were conducted to test whether there is a significant change in non-normally distributed variables and the other parameters were analyzed using the Wilcoxon signed-ranks test. Post-treatment values were compared with the baseline values using repeated-measures ANOVA (analysis of variance). Statistical significance was accepted when p-value was <0.05.

## RESULTS

In total, 81 eyes of 72 patients with a mean age of 42.04±12.98 years (range: 22–72 years) were included. There were 47 men and 25 women. The mean duration of CSC before SYMLT was 8.04±4.51 months (range: 3–21 months). The mean follow-up period was 66.54±3.66 months (range: 60–73 months). The mean session of SYMLT was found to be 1.43±0.79 times. The mean spot num-

**Table 1.** Demographic and clinical findings of study groups

	Study Group (n=72, eyes=81)
Mean age (years)	42.04±12.98 (R: 22–72)
Gender (male)	45 (62.5%)
SRE (D)	+0.67±0.34
IOP (mm Hg)	15.8±3.2
Mean duration of symptoms (months)	9.34±4.51 (R: 3–21)
Mean follow-up time (months)	66.54±3.66 (R: 60–73)
Smoking (no)	56 (77.7%)
Systemic disorders	
Hypertension	4 (5.5%)
Autoimmune diseases	5 (6.9%)
Type of leakage on FA	
Focal	67 (82.7%)
Diffuse	15 (17.3%)
Mean SRFH (µm)	163.58±33.71 (R: 114–227)
Presence of PED	
Yes	16
No	66
Mean PED height µm	2.85±8.05 (0–34)
Presence of RPE pumps	
Yes	15
No	67
Presence of HRD	
Yes	19
No	62

Data are presented as mean±standard deviation. D: Diopter; FA: Fluorescein angiography; HRD: Hyperreflective; Dot; IOP: Intraocular pressure; PED: Pigment epithelial detachment; RPE: Retina pigment epithelium; R: Range; SRE: Spheric refractive equivalent; SRFH: Subretinal fluid height.

**Table 2.** Changes of BCVA and SD-OCT parameters during the study

	Baseline visit	3 <sup>rd</sup> -mo visit	6 <sup>th</sup> -mo visit	12 <sup>th</sup> -mo visit	2 <sup>nd</sup> -year visit	3 <sup>rd</sup> -year visit	4 <sup>th</sup> -year visit	5 <sup>th</sup> -year visit	p-value
BCVA (L)	0.45±0.25	0.13±0.23	0.10±0.20	0.11±0.24	0.11±0.21	0.09±0.19	0.09±0.20	0.09±0.20	<0.001
CMT (µm)	404.60±72.46	265.32±46.24	252.73±33.65	249.14±26.28	246.82±28.98	245.37±26.00	244.96±25.44	243.50±24.97	<0.001
CMV (mm <sup>3</sup> )	0.31±0.048	0.21±0.031	0.20±0.028	0.20±0.025	0.19±0.024	0.19±0.022	0.19±0.022	0.18±0.074	<0.001
TMV (mm <sup>3</sup> )	9.83±0.503	8.82±0.253	8.80±0.288	8.75±0.218	8.73±0.219	8.72±0.227	8.71±0.226	8.69±0.239	<0.001
SFCT (µm)	375.78±60.27	353.15±45.37	350.59±45.52	348.42±46.36	344.48±40.63	342.68±42.40	340.37±42.54	340.18±44.10	0.008

Data are presented as mean±standard deviation. BCVA: Best corrected visual acuity; CMT: Central macular thickness; CMV: Central macular volume; L: Log MAR; SFCT: Subfoveal choroidal thickness; TMV: Total macular volume.

ber was  $440.14 \pm 171.08$  (range: 200–850), with a mean laser power of  $417.24 \pm 90.25$  mW (range: 260–600 mW). The basic demographic and clinical data were shown in Table 1.

The mean BCVA was  $0.46 \pm 0.25$  Log MAR at the initial visit, and it improved to  $0.11 \pm 0.22$  Log MAR at the five-year visit ( $p < 0.001$ ). The mean baseline CMT was  $404.60 \pm 72.46$   $\mu\text{m}$ , and decreased to  $243.50 \pm 24.97$   $\mu\text{m}$  at the final visit ( $p < 0.001$ ). Table 2 shows the changes of BCVA and other SD-OCT parameters during the study. At the end of the 5<sup>th</sup> year, complete SRF resorption was observed in 70 eyes (86.4%) with SYMLT sessions and 11 eyes (13.6%) had SRF despite the reduction in SRF. Of the 70 eyes, 11 were referred for additional treatments (PDT, CLP and anti-VEGF injections), and six eyes (7.5%) had complete SRF resorption with other additional treatment, and five eyes (6.1%) still had residual SRF. The mean SRFH was  $163.58 \pm 33.71$

$\mu\text{m}$  at the beginning and  $16.62 \pm 4.20$   $\mu\text{m}$  at the end of the 5<sup>th</sup> year. Of the 81 eyes, 68 (83.9%) had no recurrence within the five years, while 13 of them (16.1%) had recurrences. The six eyes with recurrent CSC had complete SRF resorption, and seven of these had no response to repeated SYMLT and were referred for additional treatment.

In the current study, we evaluated the correlation between baseline findings and recurrence. In the univariate analysis, there was a statistically significant correlation between the recurrence, and each of the duration of symptoms, baseline BCVA, initial SFCT  $\geq 416.00$   $\mu\text{m}$ , diffuse leakage pattern of FA, presence of PED and RPE pumps. In multivariate analyses, there was a statistically significant correlation between recurrence and SFCT  $\geq 416.00$   $\mu\text{m}$ . Table 3 shows the correlation analyses between the baseline findings and recurrence. Receiver operating characteristics (ROC) analysis revealed that a CMT  $\geq 416.00$   $\mu\text{m}$  predict-

**Table 3.** The univariate and multivariate correlation between recurrence and clinical parameters

	OD	CI 95%	p-value	OD	CI 95%	p-value
Baseline BCVA (L)	69.83	3.98–202.63	0.005	11.50	0.90–147.67	0.32
SFCT $\geq 416$ $\mu\text{m}$	60.00	9.63–373.66	<0.001	30.46	4.23–218.97	0.001
Leakage type on FA (diffuse)	13.16	3.01–57.35	0.001	5.96	0.67–52.33	0.10
SRFH	0.961	0.93–0.98	0.006			
Baseline TMV	0.118	0.18–0.786	0.027			
Presence of PED	4.77	1.25–18.25	0.022			
Presence of RPE pumps	4.70	1.03–21.34	0.045			
Duration of symptoms	1.22	1.048–1.421	0.011			
Age	1.066	0.99–1.13	0.054			
Baseline CMT	0.98	0.98–1.00	0.21			
Baseline CMV	0.026	0.99–30.56	0.60			

Data are presented as mean  $\pm$  standard deviation. BCVA: Best corrected visual acuity; CI: Confidence interval; CMT: Central macular thickness; CMV: Central macular volume; FA: Fluorescein angiography; HRD: Hyperreflective dot; L: Log MAR; OD: Odds ratio; PED: Pigment epithelial detachment; RPE: Retina pigment epithelium; SRFH: Subretinal fluid height; TMV: Total macular volume.

**Table 4.** The univariate and multivariate correlation between treatment response and clinical parameters

	OD	CI 95%	p-value	OD	CI 95%	p-value
Baseline BCVA	659	19.98–217.64	<0.001	5223.34	1.45–1.87	0.040
Baseline SFCT $\geq 474$ $\mu\text{m}$	340	28.17–410.30	<0.001	2186.43	3.50–1362.89	0.025
Presence of PED	10.50	2.56–42.91	<0.001	10.33	0.42–25.17	0.40
Age	1.071	1.010–1.135	0.022			
Duration of symptoms	1.262	1.102–1.463	0.001			
Baseline CMT	0.973	0.95–0.99	0.009			
Baseline CMV	0.016	00–7.41	0.082			
Baseline TMV	0.111	0.018–0.68	0.018			
SRFH	0.90	0.84–0.97	0.005			
Leakage type on FA (diffuse)	0.48	0.89–1.45	0.087			
Presence of RPE pumps	4.30	1.19–15.63	0.026			
Presence of HRD	5.66	1.52–21.10	0.010			

Data are presented as mean  $\pm$  standard deviation. BCVA: Best corrected visual acuity; CI: Confidence interval; CMT: Central macular thickness; CMV: Central macular volume; FA: Fluorescein angiography; HRD: Hyperreflective dot; L: Log MAR; OD: Odds ratio; PED: Pigment epithelial detachment; RPE: Retina pigment epithelium; SRFH: Subretinal fluid height; TMV: Total macular volume.

ed the recurrence with 83% sensitivity of 83%, and 92.6% specificity (AUC: 0.824,  $p < 0.001$ , CI 95%: 0.842–0.996).

The correlation analyses between treatment non-response (incomplete SRF resorption with SYMLT) and baseline findings are shown in Table 4. In univariate analyses, there was a statistically significant correlation between non-response to SYMLT and each of the age, duration of symptoms, baseline BCVA, baseline SFCT  $\geq 474.00 \mu\text{m}$ , baseline CMT, SRFH, diffuse leakage pattern, presence of PED, presence of RPE pumps and HRD presence. In multivariate analyses, baseline SFCT  $\geq 474.00 \mu\text{m}$  and BCVA were significantly correlated with SYMLT non-response ( $p = 0.025$  and  $p = 0.040$ , respectively). The ROC analysis revealed that CMT  $\geq 474.00 \mu\text{m}$  predicted the non-response to SYMLT with 83% sensitivity, and 85.6% specificity (AUC: 0.815,  $p < 0.001$ , CI 95%: 0.951–1.000).

## DISCUSSION

The aim of this study was to evaluate the long-term (five years) efficacy and safety of SYMLT in patients with chronic CSC. The major findings of our study are as follow: (1) 86.4% of patients had complete resolution of SRF with no detectable side effects; (2) %83.9 of patients had no recurrence after the first SYMLT and 16.1% of patients had at least one recurrence; (3) higher SFCT values were found to be correlated with SYMLT non-response and recurrence.

It is well known that the majority of acute CSC cases progress to complete SRF resorption with good final visual acuity, therefore, the first-line treatment is observed. But 5% of chronic CSC may cause severe vision loss.<sup>[15]</sup> The chronicity of the SRF is significantly associated with the final anatomical and functional outcome of CSC patients. The long duration of SRF leads to separation of the outer retinal layer from the RPE and choroid, followed by photoreceptor death, resulting in permanent visual impairment.<sup>[16]</sup> Therefore, a treatment modality that resorbs the SRF and does not damage the outer retinal layers would be a very suitable option in the treatment of these patients. Although many treatment methods have been used, there is still no definitively safe and effective gold standard treatment option.

Recently, subthreshold laser systems have been introduced to eliminate the risks of conventional laser systems, with the potential to reduce retinal thickness in diabetic macular edema, branch retinal vein occlusion and chronic CSC.<sup>[17]</sup> As is known, the subthreshold laser is clearly safe for patients, but its exact mechanism of action remains unclear. Some of the evidence has shown that tissue response involves the expression of heat shock proteins (HSP), including HSP70.<sup>[11]</sup> Heat shock proteins act as chaperones for correcting misfolded proteins, thereby potentially rejuvenating RPE cells, restoring their cellular function, and reducing apoptosis and inflammation. So, subthreshold lasers induce a biological response that promotes the recovery and restoration of the outer blood-retinal barrier,

and ultimately resorption of SRF. Although many studies reveal the short-term safety and efficacy of these lasers in chronic CSC treatment, long-term studies with large patient populations are limited. To the best of our knowledge, this study reports the longest follow-up results of SYMLT for the treatment of chronic CSC with the largest study population. The laser systems in clinical use could be listed as 577 nm, 810 nm diode, and 532 nm subthreshold laser systems. The 577-nm yellow light spectrum is well absorbed by both oxyhemoglobin and melanin, but it is also not absorbed by xanthophylls, which provides safer treatment close to the central macular region.<sup>[18]</sup> This leads to concentration of energy in a smaller volume, allowing in turn a reduction in power and shortening of the pulse duration.<sup>[19]</sup> Various studies are using 810-nm diode SMLT in CSC, but the average laser power in these studies was higher than the average laser power used in our study.<sup>[12,20]</sup> This may emphasize that the 577 nm yellow laser is better absorbed by the RPE and hemoglobin, thus target effects are achieved at lower power than 810-nm diode SMLT modalities. However, no study has reported complications attributed to treatment, except for two studies that reported some SMLT-attributed pigmentary changes in the RPE, but used 810-nm diode SMLT in only a few cases<sup>[20,21]</sup> Two more recent studies evaluated the short-term efficacy of 532 nm SMLT in patients with chronic CSC. Although the results of these two studies are contradictory, we can state that the efficiency and visual gains of 532 nm SMLT in chronic CSC are very low compared to our results.<sup>[14,22]</sup> Kim et al.<sup>[23]</sup> reviewed three-year follow-up results of 27 patients with chronic CSC who had SYMLT, and they revealed that 22 of 27 patients (81.5%) had complete SRF resolution with SYMLT. Similarly, the rate of complete resolution of SRF in our study was 86.4% at the end of the five-year period.

The PDT with verteporfin has been found effective for resorption of SRF in chronic CSC in several studies.<sup>[11,23,24]</sup> The mechanism of PDT is the reduction of choroidal leakage by choroidal vascular remodeling due to transient choroidal hypoperfusion. However, conventional PDT has some undesirable side effects in patients with CSC, including RPE changes and atrophy, permanent choroidal ischemia, and secondary choroidal neovascularization.<sup>[24,25]</sup> Therefore, modified PDT protocols have been defined to reduce these effects. However, since PDT is an invasive procedure and it is applied with medications that may cause anaphylactic reactions, it may cause systemic side effects. Lai et al.<sup>[26]</sup> evaluated the effect of half-dose PDT with a mean follow-up time of 74.1 months, and found that PDT treatment improved visual acuity and decreased the recurrence compared to untreated eyes. At the end of that study, CSC recurrence was observed in 20% of eyes and persistent SRF was detected in 6.7% of eyes. Özmert et al.<sup>[27]</sup> compared the efficacy and safety of SYMLT and PDT in patients with CSC and revealed that SYMLT seems to be as effective as PDT in the treatment of CSC without any side effect and results in the resorption of SRF without causing visible retinal scarring. In our study, we

found 16.1% recurrence incidence and 91.3% of eyes with complete SRF resolution with SYMLT. In long term, SYMLT has comparable and not inferior results in the treatment of chronic CSC.

The effect of clinical parameters on the duration of acute central serous chorioretinopathy episodes has been evaluated in many previous studies. Daruich et al.<sup>[28]</sup> found that older age,  $\geq 500 \mu\text{m}$  SFCT, and  $\geq 50 \mu\text{m}$  RPE change at leakage sites are independent factors for longer-lasting episodes of acute central serous chorioretinopathy. Another study revealed that the longer duration of symptoms, female gender and basic SD-OCT factors like HRDs and retinal RPE bumps were associated with longer SRF resolution time. Also, there are few studies evaluating the correlation between response to treatment modalities and clinical characteristics. Borrelli et al.<sup>[29]</sup> reported that thicker SFCT, narrower SRF, less PED, and less HRD were independently predictive for complete SRF resolution with oral eplerenone treatment in patients with CSC. Rijssen et al.<sup>[30]</sup> revealed that the ellipsoid zone continuity on SD-OCT was positively correlated with good visual acuity in patients treated with PDT, but the authors did not evaluate the correlation between treatment response and clinical findings. In the current study, we found that higher SFCT and worse baseline BCVA was correlated with the non-response to SYMLT. Also, higher SFCT was found to be correlated with recurrence. These findings might be related to the mechanism of SYMLT and/or our treatment titrations. In this study, we applied the SYMLT with 5% DC for preventing laser damages due to over energy. In this issue, there is currently no consensus reached on SYMLT settings by the majority of retinal practitioners. Unlike our study, Kim et al.<sup>[23]</sup> emphasized that 15% DC is important in treatment titration. However, it may also be reasonable to increase the DC titration to 15% in patients who do not respond to treatment and who are at risk of recurrence, and to give the patient a chance for re-treatment. In addition, the lack of response in patients with possible high choroidal hyperpermeability may be related to the lack of sufficient regulation of RPE dysfunction by HSP upregulation due to the SYMLT principle of action.

The limitations of the study can be listed as follows. Firstly, the study design was retrospective. We only performed SYMLT for the same duration (20-ms) and the same DC rate (5%), so it may be more valuable in future studies to compare treatment results with different titration settings. Finally, we evaluated the retinal and choroidal structures with SD-OCT but newer OCT modalities, such as swept-source OCT or OCT angiography devices, may provide more detailed information about patients' response to treatment or the causes of relapse.

In conclusion, we assessed the clinical outcomes of patients with chronic CSC treated with SYMLT with this study. We would like to emphasize that this treatment modality is effective and safe in treating chronic CSC patients throughout the five years follow-up. Particularly, this study highlights the clinical characteristics and presence of SD-

OCT parameters as predictors of treatment response to SYMLT. In further studies, these SD-OCT variables could potentially be used as a tool to identify CSC patients who would benefit mainly from SYMLT modalities or to refer the patient to other treatment modalities.

#### Ethics Committee Approval

This study approved by the Fatih Sultan Mehmet Training and Research Hospital Clinical Research Ethics Committee (Date: 12.03.2015, Decision No: 2015/5).

#### Informed Consent

Retrospective study.

#### Peer-review

Internally peer-reviewed.

#### Authorship Contributions

Concept: H.S.S.K., A.A., Y.O.; Design: H.S.S.K., A.A., Y.O.; Supervision: A.A., Y.O.; Materials: H.S.S.K., A.P., A.S.; Data: H.S.S.K., A.P., A.S.; Analysis: H.S.S.K., A.P., A.S.; Literature search: A.A., Y.O.; Writing: H.S.S.K.; Critical revision: A.A., Y.O.

#### Conflict of Interest

None declared.

## REFERENCES

- Haimovici R, Koh S, Gagnon DR, Lehrfeld T, Wellik S; Central Serous Chorioretinopathy Case-Control Study Group. Risk factors for central serous chorioretinopathy: a case-control study. *Ophthalmology* 2004;111:244–9. [\[CrossRef\]](#)
- Loo RH, Scott IU, Flynn HW Jr, Gass JD, Murray TG, Lewis ML, et al. Factors associated with reduced visual acuity during long-term follow-up of patients with idiopathic central serous chorioretinopathy. *Retina* 2002;22:19–24. [\[CrossRef\]](#)
- Bujarborua D. Long-term follow-up of idiopathic central serous chorioretinopathy without laser. *Acta Ophthalmol Scand* 2001;79:417–21. [\[CrossRef\]](#)
- Sartini F, Figus M, Nardi M, Casini G, Posarelli C. Non-resolving, recurrent and chronic central serous chorioretinopathy: available treatment options. *Eye (Lond)* 2019;33:1035–43. [\[CrossRef\]](#)
- Wong KH, Lau KP, Chhablani J, Tao Y, Li Q, Wong IY. Central serous chorioretinopathy: what we have learnt so far. *Acta Ophthalmol* 2016;94:321–5. [\[CrossRef\]](#)
- Hanumunthadu D, Tan ACS, Singh SR, Sahu NK, Chhablani J. Management of chronic central serous chorioretinopathy. *Indian J Ophthalmol* 2018;66:1704–14. [\[CrossRef\]](#)
- Nicolò M, Desideri LF, Vagge A, Traverso CE. Current pharmacological treatment options for central serous chorioretinopathy: a review. *Pharmaceuticals (Basel)* 2020;13:264. [\[CrossRef\]](#)
- Ober MD, Yannuzzi LA, Do DV, Spaide RF, Bressler NM, Jampol LM, et al. Photodynamic therapy for focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy. *Ophthalmology* 2005;112:2088–94. [\[CrossRef\]](#)
- Yannuzzi LA, Slakter JS, Gross NE, Spaide RF, Costa DL, Huang SJ, et al. Indocyanine green angiography-guided photodynamic therapy for treatment of chronic central serous chorioretinopathy: a pilot study. 2003. *Retina* 2012;32 Suppl 1:288–98. [\[CrossRef\]](#)
- Dorin G. Evolution of retinal laser therapy: minimum intensity photocoagulation (MIP). Can the laser heal the retina without harming it? *Semin Ophthalmol* 2004;19:62–8. [\[CrossRef\]](#)

11. Sramek C, Mackanos M, Spittler R, Leung LS, Nomoto H, Contag CH, et al. Non-damaging retinal phototherapy: dynamic range of heat shock protein expression. *Invest Ophthalmol Vis Sci* 2011;52:1780–7. [CrossRef]
12. Malik KJ, Sampat KM, Mansouri A, Steiner JN, Glaser BM. Low-intensity/high-density subthreshold microPulse diode laser for chronic central serous chorioretinopathy. *Retina* 2015;35:532–6. [CrossRef]
13. 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;255:2299–306.
14. Sousa K, Calvão-Santos G, João M, Gomes N, Falcão M. 532-nm subthreshold micropulse laser for the treatment of chronic central serous retinopathy. *Clin Ophthalmol* 2020;14:525–31. [CrossRef]
15. Baran NV, Gürlü VP, Esgin H. Long-term macular function in eyes with central serous chorioretinopathy. *Clin Exp Ophthalmol* 2005;33:369–72. [CrossRef]
16. Mrejen S, Sarraf D, Mukkamala SK, Freund KB. Multimodal imaging of pigment epithelial detachment: a guide to evaluation. *Retina* 2013;33:1735–62. [CrossRef]
17. Wood EH, Karth PA, Sanislo SR, Moshfeghi DM, Palanker DV. Nondamaging retinal laser therapy for treatment of central serous chorioretinopathy: What is the evidence? *Retina* 2017;37:1021–33.
18. Mainster MA. Decreasing retinal photocoagulation damage: principles and techniques. *Semin Ophthalmol* 1999;14:200–9. [CrossRef]
19. Mainster MA. Wavelength selection in macular photocoagulation. *Tissue optics, thermal effects, and laser systems. Ophthalmology* 1986;93:952–8. [CrossRef]
20. Lanzetta P, Furlan F, Morgante L, Veritti D, Bandello F. Nonvisible subthreshold micropulse diode laser (810 nm) treatment of central serous chorioretinopathy. A pilot study. *Eur J Ophthalmol* 2008;18:934–40. [CrossRef]
21. Gawęcki M. Increase in central retinal edema after subthreshold diode micropulse laser treatment of chronic central serous chorioretinopathy. *Case Rep Ophthalmol Med* 2015;2015:813414. [CrossRef]
22. Ambiya V, Kumar A. Role of 532 nm transfoveal subthreshold micropulse laser in non-resolving central serous chorioretinopathy with subfoveal leaks. *Ther Adv Ophthalmol* 2020;12:2515841420945107.
23. Kim YJ, Kim SY, Ha S, Moon D, Seong S, Kwon OW, et al. Short-duration multiple-session subthreshold micropulse yellow laser (577 nm) for chronic central serous chorioretinopathy: results at 3 years. *Eye (Lond)* 2019;33:819–25. [CrossRef]
24. Klais CM, Ober MD, Freund KB, Ginsburg LH, Luckie A, Mauguet-Fayssse M, et al. Choroidal infarction following photodynamic therapy with verteporfin. *Arch Ophthalmol* 2005;123:1149–53. [CrossRef]
25. Colucciello M. Choroidal neovascularization complicating photodynamic therapy for central serous retinopathy. *Retina* 2006;26:239–42. [CrossRef]
26. Lai TY, Wong RL, Chan WM. Long-term outcome of half-dose verteporfin photodynamic therapy for the treatment of central serous chorioretinopathy (An American Ophthalmological Society Thesis). *Trans Am Ophthalmol Soc* 2015;113:T8.
27. Özmert E, Demirel S, Yanık Ö, Batioğlu F. Low-fluence photodynamic therapy versus subthreshold micropulse yellow wavelength laser in the treatment of chronic central serous chorioretinopathy. *J Ophthalmol* 2016;2016:3513794. [CrossRef]
28. Daruich A, Matet A, Marchionno L, De Azevedo JD, Ambresin A, Mantel I, et al. Acute central serous chorioretinopathy: factors influencing episode duration. *Retina* 2017;37:1905–15. [CrossRef]
29. Borrelli E, Zuccaro B, Zucchiatti I, Parravano M, Querques L, Costanzo E, et al. Optical coherence tomography parameters as predictors of treatment response to eplerenone in central serous chorioretinopathy. *J Clin Med* 2019;8:1271. [CrossRef]
30. van Rijssen TJ, Mohabati D, Dijkman G, Theelen T, de Jong EK, van Dijk EHC, et al. Correlation between redefined optical coherence tomography parameters and best-corrected visual acuity in non-resolving central serous chorioretinopathy treated with half-dose photodynamic therapy. *PLoS One* 2018;13:e0202549. [CrossRef]

## Kronik Santral Seröz Koryoretinopatinin Eşik Altı Sarı Mikropulse Lazer Tedavisi Beş Yıllık Sonuçları: Tedaviye Cevapta Belirteçler Olabilir mi?

**Amaç:** Bu çalışmanın amacı, kronik santral seröz koryoretinopatili (SSKR) hastaların 577 nm eşik altı sarı mikropuls lazer tedavisi (ESMLT) sonuçlarını beş yıllık takip ile değerlendirmektir. Ayrıca, başlangıç klinik özelliklerinin nüks ve ESMLT tedavi yanıtları üzerindeki etkisini değerlendirildi.

**Gereç ve Yöntem:** Kronik SSKR'li 72 hastanın 81 gözü en az beş yıl takip edildi. Hastalar 577-nm ESMLT tedavi edildi. En iyi düzeltilmiş görme keskinliği (EİDGK), santral maküla kalınlığı (SMK), merkezi maküla hacmi (MMH), toplam maküla hacmi (TMH) ve subfoveal koroid kalınlığı (SFCK) spektral domain optik koherens tomografi (SD-OKT) ile ölçüldü.

**Bulgular:** Ortalama EİDGK  $0.46 \pm 0.25$  Log MAR'dan  $0.11 \pm 0.22$  Log MAR'a yükseldi ve ortalama SMK  $404.60 \pm 72.46$   $\mu\text{m}$ 'den  $243.50 \pm 24.97$   $\mu\text{m}$ 'ye düştü ( $p < 0.001$ ). Son vizitte 70 gözde (%86.4) ESMLT seansları ile tam subretinal sıvı (SRS) rezorpsiyonu ve 11 gözde (%13.6) rezidüel SRS vardı. Beş yıl takipte 68 gözde (%83.9) nüks görülmezken, 13'ünde (%16.1) nüks görüldü. Çok değişkenli analizlerde, nüks ile SFCT  $\geq 416.00$   $\mu\text{m}$  ( $p < 0.001$ ) arasında istatistiksel olarak anlamlı bir korelasyon vardı ve başlangıç SFCT  $\geq 474.00$   $\mu\text{m}$  ve başlangıç EİDGK ile ESMLT'ye yanıt vermeme ile anlamlı korelasyon saptandı (sırasıyla  $p = 0.025$  ve  $p = 0.040$ ).

**Sonuç:** ESMLT'nin uzun süreli izlemde güvenli ve etkili olduğu bulunmuştur. Klinik özellikler ve bazı SD-OKT parametreleri, ESMLT'ye verilen tedavi yanıtının ve nüksün belirleyicileri olabilir.

**Anahtar Sözcükler:** Eşik altı sarı mikropulse lazer; kronik santral seröz koryoretinopati; spektral domain optik koherans tomografi; subfoveal koroidal kalınlık.