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Correlation of retinal changes with choroidal changes in acute and recurrent central serous chorioretinopathy assessed by swept-source optical coherence tomography

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Abstract

Purpose: To evaluate affected choroidal regions and corresponding retinal changes in acute and recurrent central serous chorioretinopathy using swept-source optical coherence tomography.

Methods: The foveal and subfoveal choroidal thicknesses were measured with swept-source optical coherence tomography. The retina was divided into five zones on the swept-source optical coherence tomography image based on baseline choroidal thickness being <100, 100–199, 200–299, 300–399 and ⩾400 µm. The retinal and choroidal thicknesses in the same five regions were evaluated during follow-up. The measurements were then compared between baseline (when central serous chorioretinopathy was active) and follow-up (after complete resolution of disease).

Results: At baseline, in the acute group, the mean outer retinal layer thickness was significantly higher in areas with thicker choroid and lower in areas with thinner choroid. No such change was noticed in the recurrent group. In the acute group, the overall retinal thickness from baseline to follow-up decreased from 269.84 to 251.9 µm, ganglion cell layer thickness decreased from 107.14 to 101.28 µm, retinal nerve fibre layer thickness decreased from 56.96 to 49.33 µm, and no significant difference was noted in choroidal thickness. In the recurrent group, choroidal thickness significantly increased from 254.58 to 262.55 µm and ganglion cell layer decreased from 103.43 to 94.01 µm. No significant difference was noted in overall retina and retinal nerve fibre layer. Reduction in choroidal and retinal layer thicknesses was better in eyes which underwent laser treatment than the observation group.

Conclusion: Swept-source optical coherence tomography might serve as an important non-invasive tool for both evaluating the extent of pathology and to predict the recurrence rate.

Keywords: acute and recurrent, central serous chorioretinapathy, choroidal and retinal thicknesses, laser treatment, swept-source optical coherence tomography

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Introduction

The purpose of this study was to analyse the diagnosis of central serous chorioretinopathy (CSCR) and its treatment mainly on multimodal imaging. The spectral-domain optical coherence tomography (OCT) is the prime modality in imaging CSCR. The non-invasive fundus autofluorescence (FAF) is useful in detecting the retinal pigment epithelium (RPE) alterations from previous episodes, and invasive fluorescein angiography indicates the origin of leakage at baseline.[1] The role of indocyanine green angiography (ICGA) is to provide more details about choroidal hemodynamic changes occurring in CSCR.[1,2]

Recently, enhanced-depth imaging and swept-source optical coherence tomography (SS-OCT) technologies have allowed deeper visualization of

the choroid which improves its morphological analysis.[3] In addition to the presence of subretinal fluid, pigment epithelial detachments (PEDs) and RPE leakage sites, there are choroidal changes observed with the help of enhanced-depth imaging and SS-OCT that have given newer insights into the pathogenesis of CSCR. There is evidence to suggest a reduction in choroidal thickness following resolution of CSCR.[4] However, Jirarattanasopa and colleagues[5] and Kuroda and colleagues[6] have described cases of typical CSCR which were not associated with increased choroidal thickness.

Majority of the studies related to choroidal thickness in CSCR have considered the mean central choroidal thickness.[7,8] There are, however, no studies to evaluate the regional differences in choroidal thicknesses and the correlation of choroidal thickness with retinal layer thickness in acute and recurrent CSCR. In addition, the correlation of these thicknesses after the resorption of subretinal fluid has not been studied.

This study aims to evaluate the regional differences in the choroidal thickness measurements, at presentation and at resolution of subretinal fluid (SRF) in acute and recurrent CSCR. The correlation of changes in choroidal thickness from baseline to resolution and its correlation with retinal layer thicknesses were also evaluated in these two groups of CSCR.

Methods

Eighteen eyes of 14 patients who were diagnosed to have either acute or recurrent CSCR without any previous treatment were included in our study. The data were collected between January 2015 and June 2015 at the vitreoretinal speciality clinic of a tertiary eye care institute. The CSCR patient's data were screened, and among them, we filtered patients who had undergone SS-OCT during baseline visit and follow-up after complete resolution with or without laser treatment. The complete resolution was necessary, as the choroidal remodelling will not reflect the true state of alterations unless the subretinal fluid had healed completely. This retrospective study was approved by the institutional review board of the organization (Ethics committee, Vision research foundation, IEC: 698-2018-P). Written informed consent for diagnostic and therapeutic procedures was obtained from all the patients.

Acute CSCR was defined as self-resolving subretinal defects (SRDs) within 4 months from the onset of symptoms. Recurrent CSCR is defined as an episode of acute CSCR following a previous episode with complete SRD resolution.[1] Around 20 patients with CSCR had baseline and follow-up SS-OCT evaluation during the study period, out of which only 14 patients had complete resolution during follow-up. Of the 14 patients, 5 patients (7 eyes) had acute and 9 patients (11 eyes) had recurrent CSCR. Out of seven eyes in the acute group, three eyes were advised focal laser photocoagulation to the leaks which was detected upon fluorescence angiography. The remaining four eyes were advised to avoid stress, steroid and were advised to come for a follow-up after 2 months. Out of the remaining 11 eyes in the recurrent group, three eyes were advised focal laser photocoagulation to the leaks, and the remaining eight eyes were advised to avoid stress and steroid in any form. The laser used was argon diode laser used to seal the leakage spots. The procedure for laser is pharmacological pupillary dilation followed by focal laser to the leakage point usually guided by angiography for precision.

All patients underwent comprehensive ophthalmic examination, which included assessment of refractive error, best corrected visual acuity (BCVA) using internally illuminated Snellen LED Vision Chart (ALVC-20; Appasamy Associates, Chennai, Tamil Nadu, India), slit-lamp examination, intraocular pressure using applanation tonometer and dilated fundus examination. All the patients underwent SS-OCT examination (imaging prototype; Topcon, Tokyo, Japan) at baseline and follow-up visit after complete or partial resolution of fluid in both acute and recurrent group. The average period between baseline and follow-up visit was around 6 months (190 days).

SS-OCT imaging

A single trained optometrist captured 12-mm radial scans using SS-OCT. Image registration was done for follow-up imaging. Both retinal and choroidal thicknesses were calculated using the built-in automated topographic mapping software provided by Topcon such as Early Treatment Diabetic Retinopathy Study (ETDRS) and rectangular grid. The rectangular grid gives a 6×6 rectangular area, where the length of one area is one-sixth the side length of the three-dimensional (3D) scan area which is 12×9 mm. The ETDRS grid consists of three concentric rings of 1-, 3- and 6-mm diameter and gives the mean thickness

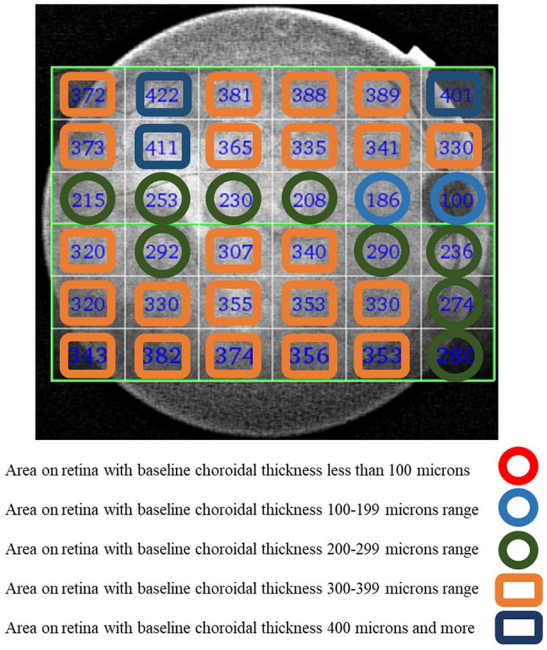

Figure 1. Classification of thickness into five zones on retina on basis of baseline choroidal thickness (in microns). The thickness in each sector indicates the choroidal thickness.

within the ring area. The foveal thickness (FT) and subfoveal choroidal thickness (SFCT) were measured manually for both acute and recurrent groups.

The thicknesses of the overall retina, choroid, ganglion cell layer (GCL) and retinal nerve fibre layer (RNFL) were obtained automatically using the rectangular grid in all 36 areas of the grid. The thickness of the retina was measured from the internal limiting membrane to the inner margin of the RPE tissue layer, and the thickness of the choroid was measured from the outer margin of RPE to the sclera–choroidal interface. The reference tissue layer or the segmentation lines provided by the automated mapping software can be altered in case of any error in marking by the software.

A similar protocol for measurements had been performed in Vogt Koyanagi Harada disease.[9] The pre-treatment or baseline choroidal thickness was categorized into five zones with respect to the thickness in each areas of the rectangular grid. The areas were divided as <100, 100 to <200, 200 to <300, 300 to <400 and $>400\,\mu m$ as shown in Figure 1. The average thicknesses of choroid, retina, GCL and RNFL of baseline were compared with follow-up in these five zones. There is no discrimination in the area measured at baseline and at follow-up, since image registration was done for all patients.

Statistical analyses

Statistical analyses were done using Microsoft Excel 2013 (Microsoft Corp., Redmond, WA, USA) and statistical software SPSS, version 21.0 (IBM Corp., Armonk, NY, USA). Kruskal–Wallis tests (the non-parametric equivalent of one-way ANOVA) were used to compare the variables among groups before the treatment. Wilcoxon-signed rank tests (the non-parametric equivalent of paired t-test) were used to compare the retinal layer and choroidal thicknesses between baseline and follow-up measurements. The change in relative retinal thicknesses was evaluated based on baseline choroidal layer thickness.

Results

Table 1 shows the baseline and follow-up characteristics of both acute and recurrent groups. The mean age group of the acute group was 45.80 ± 6.46 years and that of the recurrent was 45.00 ± 11.08 years. ($p = 0.248$). In the acute group, 60% of the patients were male and in the recurrent group, all were male ($p = 0.048$). In the acute group, 42.86% of eyes were advised for focal laser photocoagulation to leak and in the recurrent group, this number was 27.27% ($p = 0.498$). The mean baseline visual acuity in the acute group was 0.36 logMAR (6/14 approximate Snellen equivalent) and in the recurrent group was 0.54 logMAR (6/21 approximate Snellen equivalent). The baseline clinical parameters were not statistically significant between acute and recurrent groups. There was no statistically significant difference between baseline and follow-up logMAR visual acuity, spherical equivalent, intraocular pressure, central retinal thickness or SFCT in either acute or recurrent group.

Table 2 shows the comparison of mean retinal, outer retinal, GCL and RNFL thicknesses at baseline in five zones depending on the choroidal thickness. The outer retinal thickness was higher in areas of thicker choroid and less in areas of thinner choroid ($p = 0.01$) in acute CSCR, which was not seen in recurrent CSCR.

The separate layer thicknesses in the rectangular grid were averaged and were compared between

Table 1. Clinical characteristics of study group.

Characteristics	Acute (*N* = 5 patients)			Recurrent (*N* = 9 patients)		
	Baseline	Follow-up	*p* value	Baseline	Follow-up	*p* value
Age (in years)	45.80 ± 6.46	–	–	45.00 ± 11.08	–	–
Gender (Male/female)	3/2	–	–	9/0	–	–
	N = 7 eyes			*N* = 11 eyes		
Intervention						
Focal laser to leak, *N* (%)	3 (42.86%)	–	–	3 (27.27%)	–	–
Nil, *N* (%)	4 (57.14%)	–	–	8 (72.73%)	–	–
Mean best correction visual acuity (in logMAR)	0.36 ± 0.36	0.26 ± 0.36	0.563	0.54 ± 0.48	0.56 ± 0.54	0.700
Mean spherical equivalent (in diopters)	0.66 ± 1.51	0.73 ± 1.52	0.569	0.63 ± 0.94	0.45 ± 0.57	0.538
Mean intraocular pressure (in mmHg)	14.57 ± 2.23	13.29 ± 0.76	0.196	14.27 ± 2.97	13.09 ± 1.38	0.239
Mean central retinal thickness (in μm)	322.71 ± 135.64	238.29 ± 188.87	0.368	244.64 ± 173.48	186.09 ± 101.04	0.093
Mean subfoveal choroidal thickness (in μm)	378.29 ± 84.05	332.14 ± 50.73	0.088	445.50 ± 82.55	447.27 ± 97.60	0.736

P values > 0.05, hence differences between baseline and follow-up were not significant.

baseline and follow-up visits. Table 3 shows the comparison of retinal layer, choroidal layer, GCL and RNFL thicknesses difference between baseline and follow-up visits. In the acute group, except for choroidal thickness, all other layers such as total retina, GCL and RNFL showed statistically significant decrease in thickness ($p < 0.005$). In the recurrent group, choroidal and GCL layer thickness showed statistically significant difference with $p < 0.0001$, whereas total retina and RNFL did not. The choroidal layer was found to be increased in follow-up visit, whereas the GCL layer showed a decrement in follow-up visit.

Table 4 shows the comparison of average baseline and follow-up total retinal, choroidal, outer retinal, GCL and RNFL thicknesses in each zone described according to baseline choroidal thickness. In the acute group, the choroidal thickness reduced at follow-up in areas with more baseline choroidal thickness (300–399 μm), $p = 0.04$. Likewise, the overall retinal thickness and outer retinal thickness also showed a reduction in areas with more baseline choroidal thickness (300–399 μm), $p = 0018$. The RNFL thickness reduces in the areas of choroidal thickness (200–299 μm). In the recurrent group, there was no significant reduction of choroidal thickness at follow-up. Like the acute group, the overall retinal thickness and outer retinal thickness were also reduced in the recurrent CSCR; however, the reduction was not only seen in areas of thicker choroid, but also in the areas of lesser choroidal thickness. Unlike the acute CSCR, the GCL thickness showed a significant reduction in the areas of thicker baseline choroidal thickness ($p = 0.008$) for the recurrent group.

Table 5 shows the average baseline and follow-up thicknesses of different retinal layers according to baseline choroidal thickness in the observation group and the laser treatment group. In the observation group, the overall retinal thickness was reduced in areas where the choroidal thickness was high (>200 μm). There was an effect on the other retinal layers on follow-up in this group. However, in the laser treated eyes, the overall retinal thickness reduced in the areas of thicker choroid (300–399 μm) only. There were reductions in

Table 2. Comparison of mean retinal, outer retinal, GCL and RNFL thicknesses at baseline in five zones of retina.

Parameter (μm)	Zones based on baseline choroidal thickness (μm)					*p* value
	<100	**100–199**	**200–299**	**300–399**	**⩾400**	
Acute						
Mean choroidal thickness	87.44	154.49	256.1	327.93	412.25	**<0.0001***
Mean retinal thickness	273.04	268.62	251.85	299.4	202.75	0.358
Mean GCL thickness	118.51	117.69	100.44	104.99	56.5	0.278
Mean RNFL thickness	69.56	69.97	56.37	42.48	21.63	0.113
Mean outer retinal thickness	84.97	80.96	95.04	151.92	124.62	**0.010***
Recurrent						
Mean choroidal thickness	81.26	165.46	255.8	333.4	425.5	**<0.0001***
Mean retinal thickness	269.11	273.45	259.44	253.65	250.17	0.773
Mean GCL thickness	116.45	116.56	96.98	100.8	82.67	0.143
Mean RNFL thickness	43.02	53.82	46.67	48.93	29.5	0.454
Mean outer retinal thickness	109.64	103.07	115.79	103.92	138	0.978

**P* values statistically significant. Note the five columns indicate the five regions of retina divided based on baseline choroidal thickness (indicated in bold under the group names); the rows indicate the average value of thicknesses in μm of each layer at the respective zones of the column. GCL, ganglion cell layer; RNFL, retinal nerve fibre layer.

Table 3. Comparison of retinal layer, choroidal layer, GCL and RFNL thicknesses between baseline and follow-up.

Indices	Mean of average area thickness (overall), μm		*p* value
	Baseline	**Follow-up**	
Acute			
Overall retinal layer	269.84	251.9	**0.001***
Overall choroidal layer	229.18	226.55	0.564
Overall ganglion cell layer	107.14	101.28	**0.003***
Overall retinal nerve fibre layer	56.96	49.33	**0.003***
Recurrent			
Overall retinal layer	261.35	237.99	0.411
Overall choroidal layer	254.58	262.55	**<0.0001***
Overall ganglion cell layer	103.43	94.01	**<0.0001***
Overall retinal nerve fibre layer	47.14	43.31	0.100

Bold values indicates statistical significance.
**P* values statistically significant. GCL, ganglion cell layer; RNFL, retinal nerve fibre layer.

Table 4. Average baseline and follow-up thickness of different retinal layers according to baseline choroidal thickness in both acute and chronic groups.

Parameters (μm)	Acute (*N* = 7)					Recurrent (*N* = 11)				
	Zones based on baseline choroidal thickness (μm)					Zones based on baseline choroidal thickness (μm)				
	<100	100–199	200–299	300–399	⩾400	<100	100–199	200–299	300–399	⩾400
Mean choroidal thickness										
Baseline	87.44	154.49	256.1	327.93	412.25	81.26	165.46	255.8	333.0	425.5
Follow-up	125.69	166.52	246.29	305.39	340.38	78.14	185.12	257.2	333.34	394
P value	0.144	0.237	0.484	**0.043***	–	0.109	0.575	0.515	0.678	0.285
Mean retinal thickness										
Baseline	273.04	268.62	251.85	299.40	202.75	269.11	273.45	259.44	253.65	250.17
Follow-up	264.02	265.67	241.35	250.22	203.13	232.63	251.93	231.76	234.62	235
P value	0.273	0.499	0.093	**0.018***	–	0.285	**0.036***	**0.038***	**0.008***	0.109
Mean outer retinal thickness										
Baseline	84.97	80.96	95.04	151.92	124.62	109.64	103.07	115.79	103.92	138
Follow-up	85.94	88.71	97.89	119.51	150.38	111.87	91.94	93.4	102.13	130.17
P value	0.715	0.398	0.779	**0.018***	–	1.000	**0.017***	0.139	**0.008***	0.109
Mean ganglion cell layer thickness										
Baseline	118.51	117.69	100.44	104.99	56.5	116.45	116.56	96.98	100.8	82.67
Follow-up	113.44	113.52	97.36	94.71	44.25	91.2	105.11	93.13	92.41	74.67
P value	0.465	0.173	0.123	0.091	–	0.593	0.484	0.314	**0.008***	1.000
Mean retinal nerve fibre layer thickness										
Baseline	69.56	69.97	56.37	42.48	21.63	43.02	55.82	46.67	48.93	29.5
Follow-up	64.63	63.45	46.1	36	8.5	29.56	54.88	45.23	40.09	30.17
P value	0.273	0.499	**0.05***	0.128	–	0.109	0.674	0.441	0.859	0.285

**P* values statistically significant. Note the five columns in each group indicate the five regions of retina divided based on baseline choroidal thickness (indicated in bold under each group); the rows indicate the average value of thicknesses in μm at baseline and follow-up of each layer at the respective zones of the column and *p* values comparing the thicknesses between baseline and follow-up.

GCL thickness and RNFL thicknesses in areas of choroidal thickness >200 μm.

Discussion

In this study, we assessed the retinal and choroidal layer thicknesses during baseline (visit with activity) and follow-up (visit with reduction in or resolution of activity) in patients with acute and recurrent CSCR. During the activity of the disease, the retinal changes in areas corresponding to choroidal changes were noted in acute CSCR but not in recurrent CSCR. Reduction in retinal layer thickness was noted in both acute and recurrent groups. In the acute group, the retinal thickness showed significant reduction only in few areas, whereas in the recurrent group, the retinal thickness showed significant reduction in almost all areas. Reduction in choroidal and retinal layers thickness was better in eyes that underwent laser treatment compared with the observation group. This study is important as more recently

Table 5. Average baseline and follow-up thickness of different retinal layers according to baseline choroidal thickness in observation group *versus* laser treatment group.

Parameters (μm)	In observation group (*N* = 12)						In laser treatment group (*N* = 6)					
	Zones based on baseline choroidal thickness (μm)						Zones based on baseline choroidal thickness (μm)					
	Overall	<100	100–199	200–299	300–399	⩾400	Overall	<100	100–199	200–299	300–399	⩾400
Mean choroidal thickness												
Baseline	241.40	78.31	163.06	251.92	329.82	425.50	227.18	87.67	154.71	258.54	325.89	–
Follow-up	245.98	171.24	177.07	233.37	308.75	365.28	223.27	96.25	151.58	239.94	302.79	–
P value	1.000	0.285	0.646	0.657	0.508	0.655	0.345	0.180	0.753	0.345	0.173	–
Mean retinal thickness												
Baseline	256.37	274.34	260.53	254.89	259.67	164.31	260.94	251.59	279.19	253.42	295.99	–
Follow-up	235.68	276.77	248.30	228.37	237.52	169.19	248.08	194.17	267.01	245.41	245.39	–
P value	0.131	0.109	0.114	**0.013***	**0.013***	1.000	0.173	0.655	0.116	0.463	**0.028***	–
Mean ganglion cell layer thickness												
Baseline	103.17	111.34	103.84	93.20	100.27	152.25	113.13	104.43	115.82	118.38	102.39	–
Follow-up	105.98	128.81	93.24	108.43	103.82	143.25	104.03	90.39	116.44	97.65	103.94	–
P value	0.534	0.686	**0.016***	0.799	0.345	0.180	**0.028***	0.109	0.463	**0.046***	0.068	–
Mean retinal nerve fibre layer thickness												
Baseline	50.38	63.20	56.68	48.18	42.29	28.25	97.58	46.94	64.71	53.58	57.72	–
Follow-up	47.02	66.47	55.01	43.11	39.97	33.33	48.29	23.50	62.62	48.64	35.18	–
P value	0.131	0.285	0.575	0.041	0.037	0.655	0.173	0.180	0.345	0.753	**0.028***	–

**P* values statistically significant. Note the five columns in each group indicate the five regions of retina divided based on baseline choroidal thickness (indicated in bold under each group); the rows indicate the average value of thicknesses in μm at baseline and follow-up of each layer at the respective zones of the column and *p* values comparing the thicknesses between baseline and follow-up.

CSCR is considered as a part of pachychoroid spectrum. Pachychoroid is defined as focal or diffuse abnormal increase in choroidal thickness, which is generally associated with dilated outer choroidal vessels. The absolute choroidal thickness may be less in case the choriocapillaries and Sattler layer vessels are attenuated. Pachychoroid is associated with choroidal hyperpermeability on ICGA.[4]

Jirarattanasopa and colleagues[5] had assessed the change in choroidal thickness in different zones using the rectangular grid and correlated the changes with angiographic features. They found that choroidal thickness was greater in the area with leakage points on FA than in area without leakage. It was postulated that the reason of this focal thickening of the choroid was due to an increase in focal hydrostatic pressure within the choroid in areas with choroidal vascular hyperpermeability, resulting in focal leakage of the fluid into the subretinal spaces. In corresponding areas of focal increase in choroidal thickness, this focal hydrostatic pressure leads to increase in the movement of fluid to outer retinal layers resulting in increased thickness. This theory explains the reason why an increased outer retinal thickness was found in areas of thicker choroid when compared to the outer retinal thickness in areas of thinner choroid in CSCR patients.

In our study, the average choroidal thickness, when compared with other retinal layer thickness, showed higher variation between acute and

recurrent groups. It was found to be more prominent in the recurrent than the acute and the thickness significantly increased during follow-up in recurrent group. Chan and colleagues[10] evaluated the choroidal vascular remodelling after photodynamic therapy with verteporfin in CSCR. It was emphasized that the disturbance in choroidal vasculature was the primary cause of the disease, and the treatments proposed in the literature were capable of rapid resolution of the subretinal fluid, however, unable to treat the underlying pathology responsible for recurrence.[11–14] Hence the choroidal thickness variation which results from hyperpermeability and vascular changes of choroid, could be an indicator for recurrence as suggested by the results from our study. Supporting this, the acute group did not show any change in choroidal thickness in our study.

We found a local reduction in retinal thickness in area with thick choroid in the acute group, whereas the same was found in areas with both moderate and increased choroidal thickness in the recurrent group. Previous studies had shown that the outer retinal or the photoreceptor layer was found to be more increased in the recurrent group when compared to the acute group and reduces after resolution of the subretinal fluid.[15–17] The area of involvement of retina in recurrent was more compared to acute CSCR. Previous studies had evaluated the retinal thickness in various areas; however, the correlation between the involvement of choroid and consecutive change in retinal layers in various areas of retina was not done previously.

To the best of our knowledge, this is the first study illustrating the changes in various areas of choroid and correlating it with changes in different layers of retina in CSCR. The strengths of our study were all patients involved in the study were treatment-naive during baseline; the OCT evaluation was standardized by a single trained optometrist, and automated software was used for measuring the retinal and choroidal thickness in various areas of retina which reduces intra-observer variability; comparison of changes between acute and recurrent groups. The limitations of our study were small sample size in each group, shorter follow-up period and lack of fundus fluorescein angiography or ICGA to correlate the thickness changes with vascular abnormalities.

To conclude, change in choroidal thickness in various areas of retina in SS-OCT and correlating the changes in retinal thickness might be a very good tool to evaluate both the extent of pathology and to predict the rate of recurrence of CSCR. Future studies with a large sample size and a prolonged follow-up duration are required to validate this; however, this study stands as a preliminary report.

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Conflict of interest statement

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