

# Correlation of subretinal fluid volume with choroidal thickness and macular volume in acute central serous chorioretinopathy

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## Abstract

**Purpose** To evaluate the correlation of subretinal fluid volume with choroidal thickness and macular volume in acute central serous chorioretinopathy (CSC).

**Methods** Twenty patients with acute unilateral treatment-naive idiopathic CSC and 20 age-matched normal eyes were included in this prospective cross-sectional study. Subretinal fluid volume (SRFV) of study eyes was estimated using a built-in segmentation-modifying tool of Spectralis spectral-domain optic coherence tomography (SD-OCT). Subfoveal choroidal thickness (SCT) (measured with enhanced depth imaging-OCT) and macular volume (MV) were also determined. The correlation of SRFV with SCT and MV was analyzed statistically.

**Results** There was no significant correlation of SRFV with SCT and MV in the study eyes ( $r = 0.062$ ,  $P = 0.796$  and  $r = -0.061$ ,  $P = 0.798$ , respectively). The mean SCT of the study eyes, the fellow eyes and the control eyes were  $461.4 \pm 101.4$ ,  $375.3 \pm 103.7$ ,  $287.6 \pm 62.5 \mu\text{m}$ , respectively ( $P < 0.001$ ). The mean modified MV (determined excluding SRF volume) of the study eyes, the macular volume of the fellow and the control eyes was  $8.57 \pm 0.59 \text{ mm}^3$ ,  $8.75 \pm 0.4 \text{ mm}^3$  and  $8.73 \pm 0.38 \text{ mm}^3$ , respectively ( $P > 0.05$ ).

**Conclusions** The current study shows that subretinal fluid volume does not correlate with subfoveal choroidal thickness. This novel finding suggests that formation of subretinal fluid is not solely associated with choroidal vasculature in acute CSC.

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## Introduction

Central serous chorioretinopathy (CSC) is a disorder characterized by serous retinal detachment and/or retinal pigment epithelial detachment (RPE), changes most often confined to the macula, and associated with leakage of fluid through the RPE into the subretinal space.<sup>1</sup> Two theories in the pathogenesis of CSC have been proposed: one is choroidal dysfunction and the other is RPE dysfunction theory.<sup>2</sup> Although the evidence for a choroidal vasculopathy in CSC is strong, the underlying mechanism of choroidal disease remains to be determined.

The availability of optical coherence tomography (OCT) has vastly enhanced the anatomical assessment and understanding of CSC by providing cross-sectional imaging of the macula and the presence of subretinal fluid. Recent advances in choroidal imaging with OCT, coupled with the enhanced depth imaging (EDI) technique,<sup>3</sup> have revealed choroidal thickening in eyes with CSC, and such thickening decreased after the treatment with photodynamic therapy.<sup>1</sup> Furthermore, various morphological features of CSC have been reported with OCT evaluation. The thickness of the outer nuclear layer, as measured with SD-OCT, appears to correlate with acuity in CSC.<sup>4</sup> OCT suggests that photoreceptor outer segments elongate in eyes with active serous

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detachment<sup>5</sup> and foveal thickness at presentation and after resolution of subretinal fluid (SRF) appear to correlate with acuity outcomes.<sup>6</sup> In one study, three-dimensional (3D) configuration of SRF was characterized in CSC using spectral-domain (SD) OCT and the 3D configurations were found to be different between acute and chronic CSC.<sup>7</sup>

Choroidal vascular hyperpermeability on ICGA is associated with an increase in subfoveal choroidal thickness on OCT.<sup>1</sup> Moreover, one study showed increase in choroidal thickness after administration of a selective inhibitor of cyclic guanosine monophosphate-specific phosphodiesterase-5, which acts as a vasodilator.<sup>8</sup> Another study reported that choroidal thickness in patients with CSC decreased after photodynamic therapy, which targeted choroidal vasculature.<sup>9</sup> In addition, the mean choroidal thicknesses of the affected eyes were found to be significantly greater than those of the unaffected fellow eyes in patients with unilaterally active CSC.<sup>10</sup> All these studies suggest that change in choroidal thickness may reflect the choroidal vasculature. On the other hand, in several hypotheses, hyperpermeable choroidal vasculature has been regarded as a strong candidate for the origin of SRF.<sup>1</sup> As a general rule, transport of fluid can be driven by hydrostatic pressure gradients. Thus, hyperpermeable choroidal vasculature is thought to produce increased tissue hydrostatic pressure, and leads to fluid accumulation between the retina and the RPE.<sup>1</sup> On the basis of all the aforementioned data, thicker choroid would be expected to cause the formation of more SRF.

However, to the best of our knowledge, there has been no report thus far on the association of SRF volume that can be estimated using a built-in segmentation-modifying tool of SD-OCT<sup>11</sup> and choroidal thickness of the patients suffering from acute CSC. Thus, the principle objective of this study was to evaluate the correlation between these two parameters. The effect of SRF volume on macular volume was investigated, as well.

## Materials and methods

Twenty patients with acute, unilateral treatment-naive idiopathic CSC were included in this prospective cross-sectional study that was conducted at Retina Division, Ophthalmology Department of Kayseri Training and Research Hospital over a 12-month period. In addition, 20 healthy volunteers were included in the study as a control group.

The study followed the tenets of the Declaration of Helsinki and approved by local ethical committee. Each participant provided informed consent.

Inclusion criteria were diagnosis of idiopathic CSC with symptom duration of less than 1 month and

presence of subretinal fluid involving the macula associated with idiopathic leaks or mottling during fluorescein angiography (FA). Exclusion criteria were any prior treatment (such as laser photocoagulation, photodynamic therapy, or intravitreal injections of anti-VEGF), any presence of subretinal fluid or retinal pigment epithelium detachment in the fellow eyes at presentation and presence of subretinal fluid due to causes other than CSC (such as polypoidal choroidal vasculopathy).

Each patient underwent ophthalmologic examination, color fundus photography, fluorescein angiography (FA), and Spectralis spectral-domain OCT (Heidelberg Engineering Inc., Heidelberg, Germany). All OCT measurements were performed within a limited time (0900 to 1200 hours), which minimized the possibility of choroidal thickness change caused by diurnal variations.

For measurements of subfoveal choroidal thickness, 9 mm horizontal sections, which contained 100 duplicated scans, of the macula going through the foveola were obtained by the EDI-OCT maneuver previously described by Spaide *et al.*<sup>3</sup> Subfoveal choroidal thickness was manually measured using the contained Heidelberg eye explorer software (version 1.5.12.0, Heidelberg Engineering Inc.). Choroidal thickness was defined as the vertical distance from the hyperreflective line of Bruch's membrane to the innermost hyperreflective line of the chorio-scleral interface which was clearly visible in all eyes. Subfoveal choroidal thickness from the horizontal section was analyzed (Figure 1).

SRF volume was estimated using a built-in segmentation-modifying tool of SD-OCT.<sup>11</sup> Segmentation lines for internal limiting membrane and RPE were determined automatically for each of the volume scans, and the total macular volume of nine macular sectors as defined by the Early Diabetic Retinopathy Study was provided (Figure 2). The density of the macular volume scan was determined as 25 scans spaced 240  $\mu\text{m}$  apart. Using the modifying tool, the cursor line on the RPE was moved to the tips of the outer segments of the photoreceptors (Figure 3). The cursor lines were moved in all cuts so that the macular volume calculation could be accurately recalculated. If there was any pigment epithelial detachment, RPE line was moved to take that into account. With this movement, the modified macular volume was determined excluding SRF and was used as macular volume in the study eyes. The SRF volume was then calculated by subtracting this modified macular volume from the total macular volume.

The distributions of all variables determined with Shapiro-Wilk test were normal. The parameters were presented as mean  $\pm$  standard deviation. The analysis of variance (one-way ANOVA) was used to evaluate the

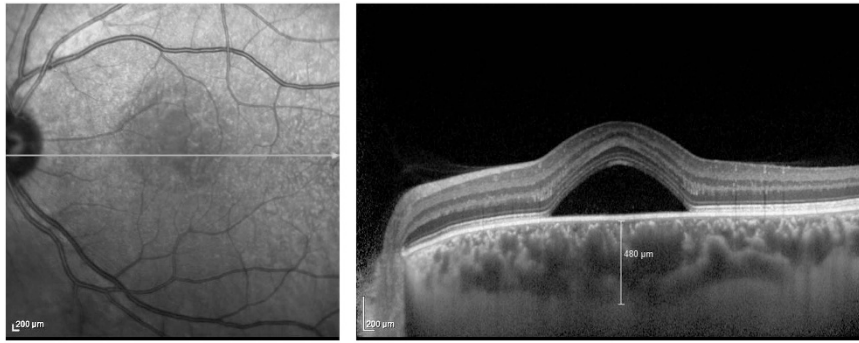


Figure 1 Manual measurement of subfoveal choroidal thickness with EDI-OCT.

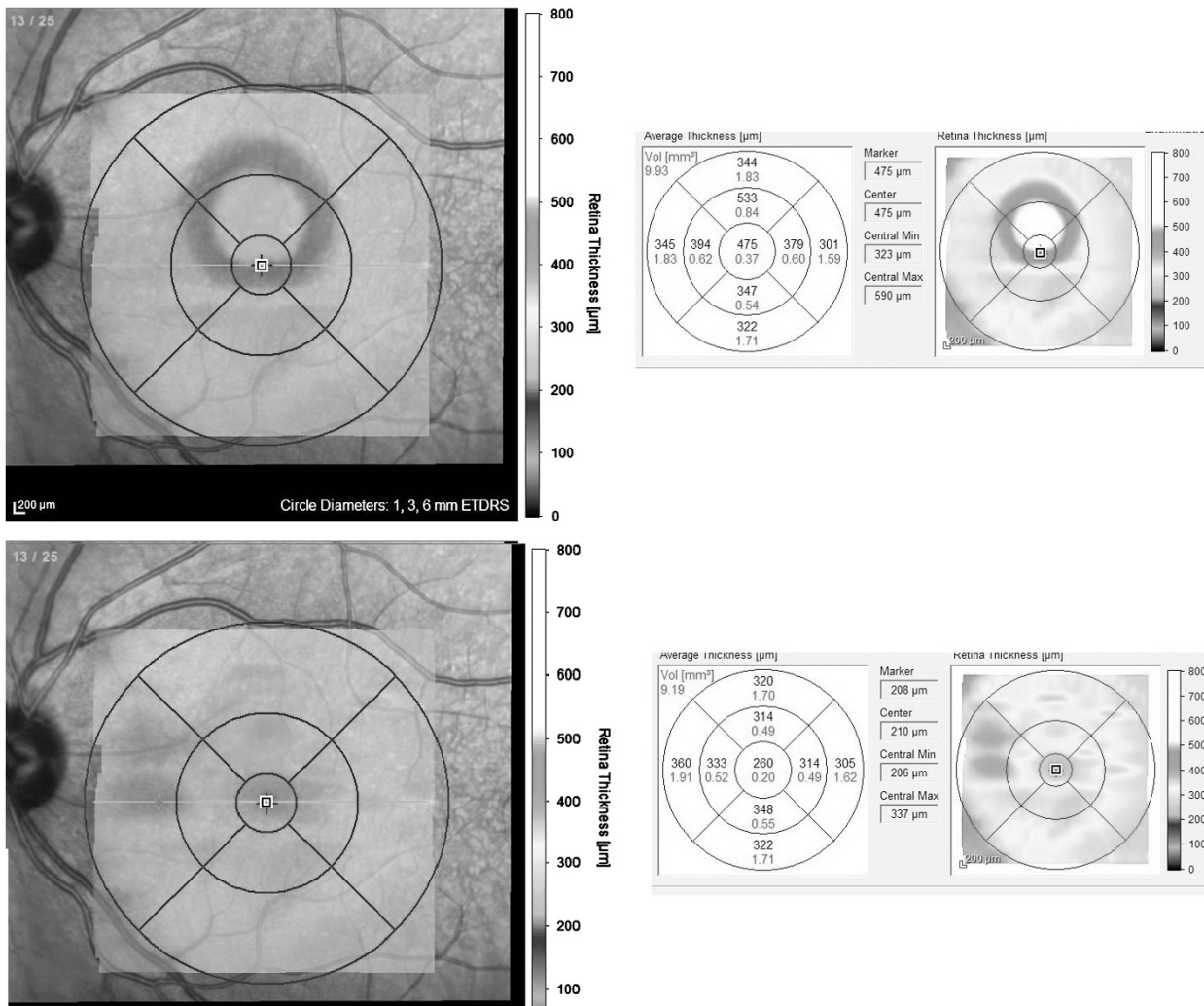
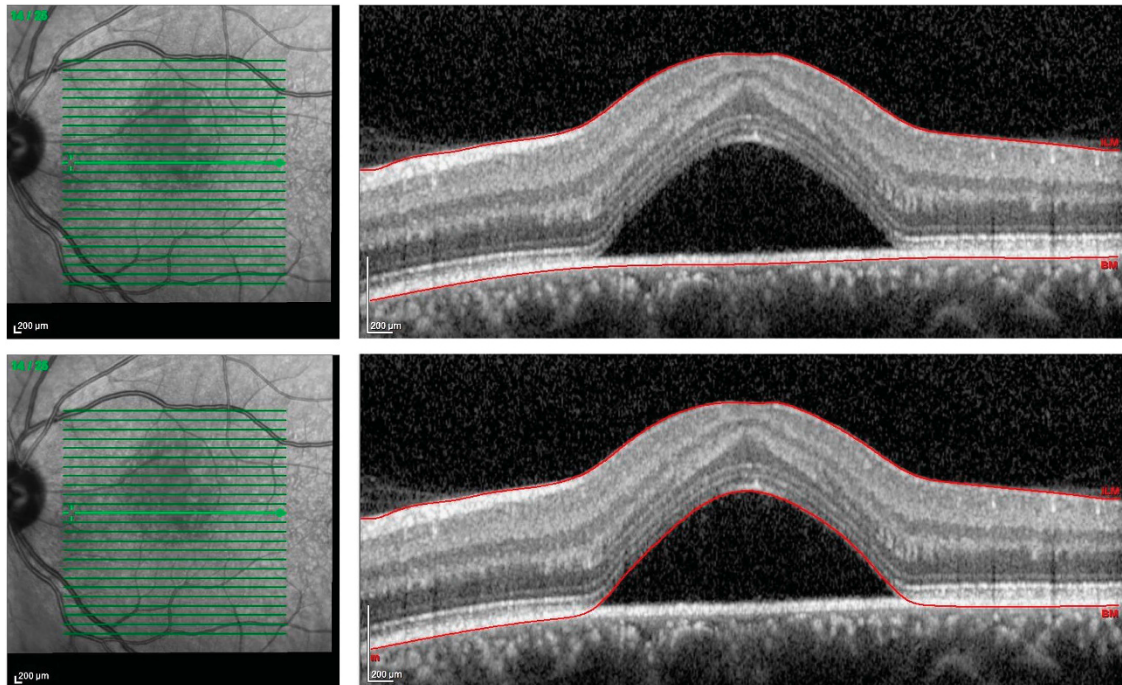


Figure 2 SRF volume was estimated using a built-in segmentation-modifying tool of SDOCT. Segmentation lines for internal limiting membrane and RPE were determined automatically for each of the volume scans, and the total macular volume of nine macular sectors as defined by the Early Diabetic Retinopathy Study was provided.

statistical significance over choroidal thickness and macular volume. All comparisons between the study eyes, the fellow eyes, and the control eyes were applied

using Tukey *post hoc* correction. Pearson's correlation coefficient was calculated to examine associations between choroidal thickness and SRF volume in the



**Figure 3** Using the modifying tool, the cursor line on the RPE was moved to the tips of the outer segments of the photoreceptors. With this movement, the modified macular volume was determined excluding SRF and was used as macular volume in the study eyes. The SRF volume was then calculated by subtracting this modified macular volume from the total macular volume.

study eyes. All statistical analyses were performed using SPSS Version 13.0 statistical analysis software (SPSS Inc., Chicago, IL, USA) and *P*-values <0.05 were considered statistically significant.

### Results

The study included 20 patients with a mean age of  $41.2 \pm 7.2$  (27–54) years and 12 patients were male. The mean age of the control group (13 male, 7 female) was  $39.3 \pm 6.9$  (25–48) years (*P* > 0.05). The mean symptom duration was  $18 \pm 6$  (7–30) days. The mean decimal visual acuity was  $0.51 \pm 0.13$  (0.3–0.7). The FA leakage patterns were: inkblot (55%), mottled pattern (40%) and smokestack (5%).

The mean OCT parameters of the study eyes, fellow eyes, and control eyes were shown in Table 1.

The mean subfoveal choroidal thicknesses of the study eyes, the fellow eyes, and the control eyes were  $461.4 \pm 101.4$ ,  $375.3 \pm 103.7$ ,  $287.6 \pm 62.5 \mu\text{m}$ , respectively. The mean choroidal thicknesses of the study eyes were significantly greater than those of the fellow eyes and the control eyes (*P* < 0.001). Also, the mean choroidal thicknesses of the fellow eyes were significantly greater than those of the control eyes (*P* < 0.001).

The mean modified macular volume (determined excluding SRF volume) of the study eyes was  $8.57 \pm 0.59 \text{ mm}^3$ . The macular volume of the fellow eyes

and the control eyes were  $8.75 \pm 0.43$  and  $8.73 \pm 0.38 \text{ mm}^3$ , respectively. However, the differences did not reach a statistical significance (*P* > 0.05).

Pearson correlation analysis revealed no significant correlation of choroidal thickness with SRF volume in the study eyes (*r* = 0.062 and *P* = 0.796; Figure 4a). There was no significant correlation between macular volume and SRF volume in the study eyes (*r* = -0.061 and *P* = 0.798; Figure 4b).

### Discussion

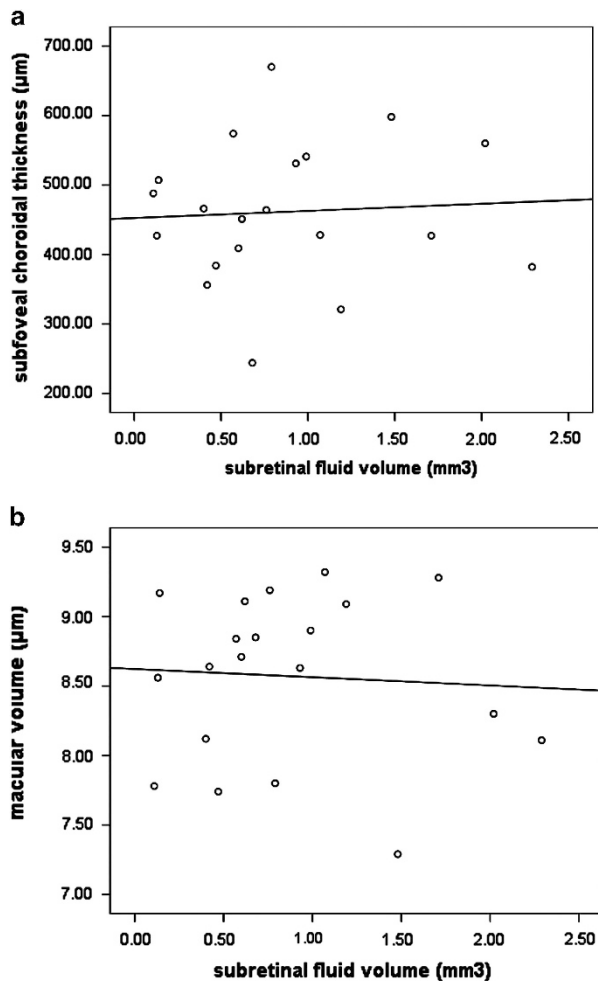
The results of this study revealed that choroidal thickness was significantly increased in the affected eyes compared with unaffected fellow eyes of unilaterally active CSC patients and control eyes, confirming previous reports.<sup>10,12,13</sup> To our knowledge, the unique aspect of the current study is the measurement of subretinal fluid volume and its correlation with subfoveal choroidal thickness and macular volume. The analysis showed that SRF volume does not correlate with subfoveal choroidal thickness and macular volume.

The mean subfoveal choroidal thicknesses of the study eyes, the fellow eyes, and the control eyes were  $461.4 \pm 101.4$ ,  $375.3 \pm 103.7$ ,  $287.6 \pm 62.5 \mu\text{m}$ , respectively. The differences were statistically significant. The pathogenesis of CSC is still partly controversial; however, its mechanism has been postulated to be

**Table 1** Mean OCT parameters

	Study eyes	Fellow eyes	Control eyes	P
SCT ( $\mu\text{m}$ )	461.4 $\pm$ 101.4	375.3 $\pm$ 103.7	287.6 $\pm$ 62.5	<0.001
MV ( $\text{mm}^3$ )	8.57 $\pm$ 0.59	8.75 $\pm$ 0.43	8.73 $\pm$ 0.38	>0.05
SRFV ( $\text{mm}^3$ )	0.87 $\pm$ 0.61			

Abbreviations: MV, macular volume; SCT, subfoveal choroidal thickness; SRFV, subretinal fluid volume.



**Figure 4** (a, b) The scatter-plot showing no significant correlation of subretinal fluid volume with subfoveal choroidal thickness (a) and macular volume (b).

hyperpermeability of the choroidal vessels and consequent increased choroidal hydrostatic pressure.<sup>1</sup> This also was confirmed by a series of ICGA study,<sup>14</sup> in which CSC was augmented by hyperfluorescein leakage from the choriocapillaris or large vessels. These facts led to the expectation that the choroid might become thickened in CSC, and the current study confirmed this using EDI-OCT and consistent with previous studies.<sup>10,12,13</sup>

However, it remains unclear as to whether or not thicker choroid on OCT is associated with larger SRF volume. If this is indeed the case, the assessment of choroidal thickness may prove to be a useful clinical indicator for the monitoring of SRF volume. To analyze this, the correlation of SRF volume and subfoveal choroidal thickness was investigated in the current study. But, no association was found between these two parameters. This novel finding suggests that formation of subretinal fluid is not solely associated with choroidal vasculature. Some factors such as RPE dysfunction other than choroidal disease may have a role in the pathogenesis of CSC. However, these data need to be clarified by further studies.

Macular volume analysis revealed that there was no significant difference between the affected, the unaffected eyes, and the control eyes. The mean modified macular volume (determined excluding SRF volume) of the study eyes was  $8.57 \pm 0.59 \text{ mm}^3$ . The macular volume of the fellow eyes and the control eyes were  $8.75 \pm 0.43$  and  $8.73 \pm 0.38 \text{ mm}^3$ , respectively. The differences were not statistically significant. On the other hand, Matsumoto *et al*<sup>5</sup> showed that the median distance between the internal limiting membrane (ILM) and the external limiting membrane (ELM) at the central fovea was approximately  $135 \mu\text{m}$  (range, 115 to  $175 \mu\text{m}$ ) in the 10 normal eyes. In the 20 eyes with CSC, the median distance was approximately  $75 \mu\text{m}$  (range, 60 to  $130 \mu\text{m}$ ) at the central fovea, where the retina was always detached. In short, the distance between the ILM and the ELM was found to be significantly shorter in eyes with CSC than in normal eyes.<sup>5</sup> Although there seems to be inconsistency between the current study and the study done Matsumoto *et al*, symptom duration was shorter in the current study (18 days *vs* 3.5 months). For this reason, there would not be enough time for the apoptosis of the photoreceptors occurs in the detached retina.

One limitation of this study was small sample size. The reason for this, unilateral treatment-naive idiopathic CSC patients with symptom duration of <1 month were chosen. Another limitation was manual measurement of subfoveal choroidal thickness. However, authors found high interobserver correlation,<sup>3</sup> high repeatability,<sup>15</sup> and high intersystem, interexaminer, and intervisit reproducibility<sup>16</sup> in choroidal thickness measurements. Finally, our study cannot answer the question of cause-effect relationship. In other words, we cannot definitively conclude that subretinal fluid volume does not go parallel to subfoveal choroidal thickness in CSC. Therefore, randomized-controlled studies are needed to further explain this issue.

In conclusion, the current study shows that subretinal fluid volume does not correlate with

subfoveal choroidal thickness. This novel finding suggests that formation of subretinal fluid is not solely associated with choroidal vasculature in acute CSC.

### Summary

#### What was known before

- There has been no report thus far on the association of SRF volume that can be estimated using a built-in segmentation-modifying tool of SD-OCT and choroidal thickness of the patients suffering from acute CSC.

#### What this study adds

- The current study shows that subretinal fluid volume does not correlate with subfoveal choroidal thickness. This novel finding suggests that formation of subretinal fluid is not solely associated with choroidal vasculature in acute CSC.

### Conflict of interest

The author declares no conflict of interest.

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