Received: 19 November 2022 | Accepted: 5 June 2023 | Published online: 15 June 2023

DOI: 10.1111/opo.13187

OPO THE COLLEGE OF OPTOMETRISTS

ORIGINAL ARTICLE

# Choroidal vascularity index as an activity criterion and a treatment response measure in chronic central serous chorioretinopathy

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## Abstract

**Purpose:** This study aimed to evaluate the choroidal vascularity index (CVI) as an activity criterion in chronic central serous chorioretinopathy (CSC) and as a measure of treatment response after full-dose-full-fluence photodynamic therapy (fd-ff-PDT).

**Methods:** This fellow-eye-controlled, retrospective cohort study included 23 patients with unilateral chronic CSC treated with fd-ff-PDT (6 mg/m$^2$; 50 µcm$^2$; 83 s). Subfoveal choroidal thickness (SFCT, µm) and CVI (%) of the affected and fellow eyes at baseline as well as at 1, 3 and 6 months after fd-ff-PDT were compared.

**Results:** The patients' mean age was 43.4 ± 7.3 years, and 18 (78.3%) were male. CVI was comparable between the affected and fellow eyes at baseline (66.09 ± 1.56 vs. 65.84 ± 1.57, $p = 0.59$). However, it became significantly lower in the affected eyes 1 (64.45 ± 1.68 vs. 65.87 ± 1.19, $p = 0.002$), 3 (64.21 ± 2.08 vs. 65.71 ± 1.59, $p = 0.009$) and 6 (64.47 ± 2.19 vs. 65.62 ± 1.52, $p = 0.045$) months after fd-ff-PDT. The mean SFCT and the mean CVI were significantly decreased in the affected eyes at all follow-up visits compared with baseline after fd-ff-PDT ($p < 0.001$).

**Conclusion:** At baseline, CVI was comparable between affected and fellow eyes. Therefore, its use as an activity criterion in chronic CSC patients is questionable. However, it was significantly decreased in fd-ff-PDT-treated eyes, supporting its role as a measure of treatment response in chronic CSC.

**KEYWORDS**
central serous chorioretinopathy, choroidal vascularity index, subfoveal choroidal thickness

## INTRODUCTION

CSC is characterised by subretinal fluid and/or retinal pigment epithelium (RPE) detachment, generally localised in the macula and is associated with one or more focal lesions of RPE.[1] Choroidal vascular abnormalities such as hyperpermeability with dilatation of the choroidal vessels and leakage into the choroidal stromal area leading to subsequent RPE damage and subretinal fluid are thought to be the underlying factors.[1] The subretinal fluid spontaneously resolves within 3–4 months in acute CSC. However, in chronic CSC, it persists for more than 4–6 months resulting in RPE atrophy and photoreceptor damage.[1] Therefore, treatment modalities aim to reduce choroidal hyperpermeability, prevent fluid passage across the RPE and, thereby resolve subretinal fluid in managing chronic CSC.[1,2] One of the

This study was conducted at Marmara University School of Medicine, Department of Ophthalmology, Medical Retina Unit, Istanbul, Turkey.

This study was presented as an audio-narrated free paper at the 20th European Society of Retina Specialists (EURETINA 2020 Virtual) Congress, 2–4 October 2020.

management options, photodynamic therapy (PDT), has been shown to be effective regardless of whether full or reduced dose or full or reduced fluence is used.[3–7]

Recent imaging techniques such as spectral-domain optical coherence tomography (OCT) in enhanced depth imaging (EDI) mode and swept-source OCT have improved morphological analysis of the choroid, providing a better understanding of the pathophysiology of CSC.[8–10] It has been shown that CSC patients have a higher choroidal thickness in both the affected and fellow eyes than healthy controls, implicating the disease's bilaterality.[8,11–14] More recently, a novel OCT parameter was presented to assess choroidal vascular status termed the choroidal vascularity index (CVI). This was defined as the ratio between the choroidal vascular luminal area and the selected total choroidal area.[15] Studies conducted in acute or combined acute and chronic CSC cases showed that CSC patients have higher CVI values in their affected and clinically unaffected eyes than healthy controls.[16,17] It was suggested that CVI be used as a diagnostic parameter, disease activity criterion and measure of treatment response in CSC.[16,17]

To our knowledge, no studies in the literature have evaluated CVI exclusively in unilateral chronic CSC patients before and after fd-ff-PDT. Thus, this study aimed to assess the CVI, emphasising its use as a disease activity criterion and its longitudinal change as a treatment response parameter with fd-ff-PDT in affected eyes compared with the unaffected fellow eyes of chronic CSC patients.

**Key points**

- The choroidal vascularity index is a relatively new quantitative marker proposed for diagnosis, activity assessment and treatment response monitoring in central serous chorioretinopathy.
- The choroidal vascularity index was comparable between the affected and fellow eyes in patients with unilateral chronic central serous chorioretinopathy, making its utility as an activity criterion questionable.
- The choroidal vascularity index was significantly decreased in the affected eyes of chronic central serous chorioretinopathy patients treated with full-dose-full-fluence photodynamic therapy, supporting its role as a measurement of treatment response.

## METHODS

This fellow-eye controlled, retrospective cohort study includes chronic CSC patients diagnosed initially as having acute CSC and then persistent subretinal fluid in their affected eye for more than 6 months between June 2017 and January 2019, followed in Marmara University Pendik Training and Research Hospital, Department of Ophthalmology. All patients received fd-ff-PDT, which resolved the subretinal fluid without recurrence for 6 months. The clinically unaffected fellow eyes were included as controls. The study protocol was approved by the Institutional Review Board of Marmara University School of Medicine (No. 09.2020.1320). The study was conducted following the Declaration of Helsinki ethical standards, and all patients provided written informed consent to use their medical information in the study analysis.

The diagnosis of acute CSC was made by the presence of the subretinal fluid on OCT images, focal leakage area at the RPE level in fundus fluorescein angiography and choroidal hyperpermeability in indocyanine green angiography. All cases were treated with oral carbonic anhydrase inhibitors (acetazolamide 250 mg, twice daily) for 2 weeks and topical brinzolamide (1%, twice daily) with topical nonsteroidal anti-inflammatory drugs (nepafenac 0.1%, 3× daily) for 6 months to see if any response was a decrease in the subretinal fluid. If the subretinal fluid persisted after 6 months of therapy with atrophic changes in the outer retina and RPE in OCT or fundus autofluorescence imaging, patients were diagnosed as chronic CSC and scheduled for indocyanine green angiography-guided PDT using full-dose (6 mg/m$^2$) verteporfin (Visudyne; Novartis AG, novartis.com) with full-fluence irradiation (50 J/cm$^2$; 83 s).

Patients with any recurrence of the subretinal fluid in the affected eye, findings of CSC in the fellow eye, a history of any ophthalmological disease other than CSC, any finding suggestive of macular neovascularisation or polypoidal choroidal vasculopathy in dilated fundus examination or retinal imaging (i.e., OCT, fundus fluorescein angiography and indocyanine green angiography), media opacity affecting image quality, ocular trauma or surgery, history of systemic or topical corticosteroid use and high levels of myopia (≤−6.00 D) or hyperopia (≥+3.00 D) were excluded from the study.

Patients received a complete ophthalmological evaluation, including assessment of best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, Goldmann applanation tonometry, dilated fundus examination and spectral-domain OCT (Spectralis®, Heidelberg Engineering, heidelbergengineering.com) in EDI mode before fd-ff-PDT. All assessments were repeated at the first, third and sixth month after fd-ff-PDT. BCVA obtained as the decimal equivalent was converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis.

The EDI-OCT B-scans passing through the fovea were obtained by the horizontal single-line scanning mode of the spectral-domain OCT device, averaging 100 frames for a single B-scan with its eye-tracking system. To ensure the exact B-scan location in consecutive visits, the follow-up function provided by the Spectralis® OCT device was used. Only the B-scans with a signal strength >25 db were used for subfoveal choroidal thickness (SFCT) measurement and CVI analysis. SFCT was calculated as the vertical distance between the manually segmented RPE/Bruch's complex's

outer border and the choroid–sclera junction (Figure 1a,c). These same images used for SFCT measurement were binarised using open-access Fiji software (https:fiji.sc) for CVI analysis. Choroidal segmentation was applied using the manual method described by Agrawal et al.[16] Briefly, the image was converted to an 8-bit image using the default Fiji software settings. Then the area of the subfoveal 1500 μm (750 μm on each side of the fovea) was selected, and the image binarised with the Niblack auto-local threshold tool. The area between the RPE/Bruch's complex at the upper border and the choroid–scleral junction at the lower border was marked manually with the polygonal selection tool. The selected area was determined as the total choroidal area and uploaded to the region of interest manager. Then the binarised image was converted to a red, green, blue image with the colour threshold tool, and dark pixels were selected as luminal area. The software automatically calculated total choroidal area and luminal area, and the stromal area (light pixels) was calculated by subtracting the luminal area from the total choroidal area. CVI was calculated by dividing luminal area by total choroidal area (Figure 1b,d).

## Statistical analysis

Statistical Package for the Social Sciences version 22.0 (IBM Corp., ibm.com) for Windows was used for data analysis. The data distribution was determined by histograms and the Shapiro–Wilk test. Data with a normal distribution were presented as mean ± standard deviation (SD). Related samples were compared with the paired *t*–test, and independent samples were compared with the independent-sample *t*–test. A one-way repeated measures analysis of variance (ANOVA) with Bonferroni correction was conducted to determine the statistical significance of continuous related variables at different time points. The assumption of sphericity in repeated measures ANOVA was assessed with Mauchly's test of sphericity. If the assumption of sphericity was not met, then epsilon (ε) was calculated according to Greenhouse and Geisser to correct the one-way repeated measures ANOVA. $p < 0.05$ was considered statistically significant.

# RESULTS

Demographic and baseline clinical characteristics of the patients included are given in Table 1. The mean age of the 23 patients included in the study analysis was 43.4 ± 7.37 years, and 18 (78.3%) were male. The mean baseline BCVA of the affected and fellow eyes were 0.33 ± 0.22 logMAR (~6/12) and 0.01 ± 0.03 logMAR (~6/6), respectively ($p < 0.001$). There was no significant difference between the affected and fellow eyes regarding baseline manifest spherical equivalent refraction, SFCT and CVI (Table 1).

Baseline BCVA of the affected eyes was significantly improved after fd-ff-PDT ($F[1.39, 30.68] = 25.70$, $p < 0.001$, $\varepsilon = 0.47$), with an improvement of 0.17 logMAR (95% confidence interval [95% CI], 0.06–0.28) at the first, 0.20 logMAR (95% CI, 0.10–0.29) third and 0.23 logMAR (95% CI, 0.11–0.35) sixth months (Table 2).

The mean SFCT was significantly decreased in the affected eyes of the patients treated with fd-ff-PDT ($F[1.42, 31.32] = 40.38$, $p < 0.001$, $\varepsilon = 0.48$). The decrease in SFCT after fd-ff-PDT was 80.47 μm (95% CI, 47.86–113.09, $p < 0.001$) in the first month, 92.82 μm (95% CI, 53.82–131.82, $p < 0.001$) in the third month and 93.39 μm (95% CI, 53.53–133.24, $p < 0.001$) in the sixth month compared with baseline (Table 2). However, there was no significant change in the fellow control eyes ($F[1.48, 32.76] = 1.96$, $p = 0.17$, $\varepsilon = 0.50$) (Table 2).

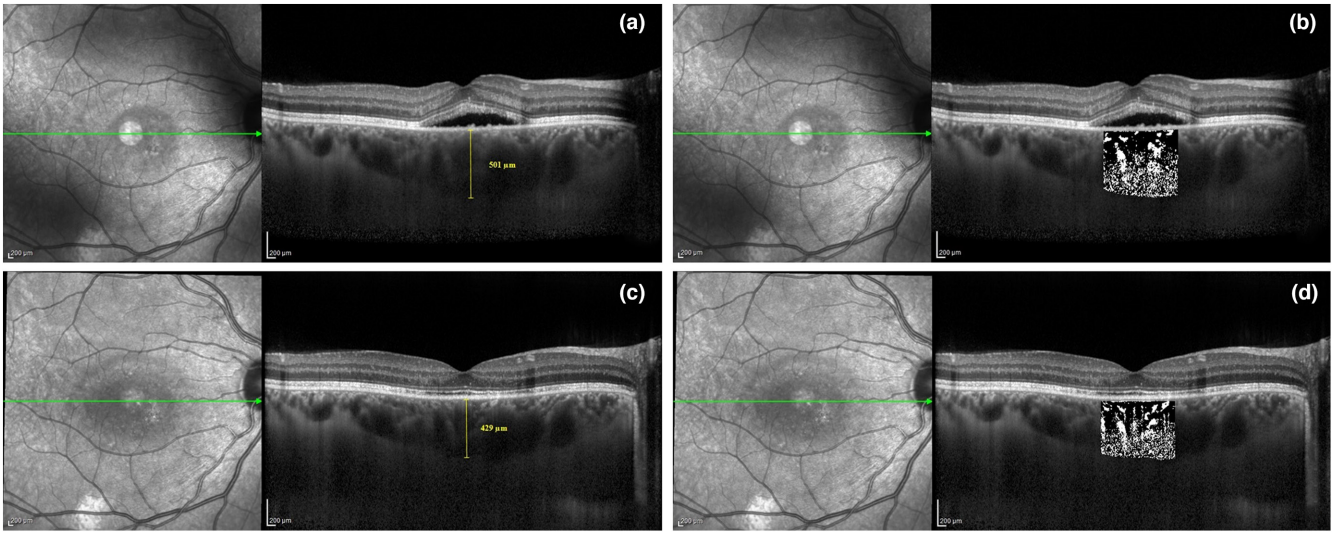


**FIGURE 1** Subfoveal choroidal thickness (SFCT) and choroidal vascularity index (CVI) measurements from the enhanced-depth imaging optical coherence tomography (OCT) B-scans of the right affected eye of a 34-year-old male patient included in the study analysis. (a) SFCT before full-dose-full-fluence photodynamic therapy (fd-ff-PDT). (b) CVI before fd-ff-PDT. (c) SFCT 6 months after fd-ff-PDT. (d) CVI 6 months after fd-ff-PDT.

**TABLE 1** Demographics and baseline clinical characteristics of the patients.

| | |
|---|---|
| Age, years | |
| Mean ± SD | 43.47 ± 7.37 |
| Range | 32–58 |
| Sex, *n* (%) | |
| Female | 5 (21.7) |
| Male | 18 (78.3) |
| Manifest SE refraction, mean ± SD dioptres | |
| Affected eyes | 0.43 ± 1.21 |
| Fellow eyes | 0.27 ± 1.44 |
| *p*-Value[a] | 0.47 |
| BCVA, mean ± SD logMAR (Snellen equivalent) | |
| Affected eyes | 0.33 ± 0.22 (~20/40) |
| Fellow eyes | 0.01 ± 0.03 (~20/20) |
| *p*-Value[a] | **<0.001** |
| SFCT, mean ± SD μm | |
| Affected eyes | 496.13 ± 87.51 |
| Fellow eyes | 458.95 ± 87.19 |
| *p*-Value[a] | 0.16 |
| CVI, mean ± SD % | |
| Affected eyes | 66.09 ± 1.56 |
| Fellow eyes | 65.84 ± 1.57 |
| *p*-Value[a] | 0.59 |

*Note*: The bold value indicates statistical significance. The changes in BCVA, SFCT and CVI of the affected eyes from baseline to the follow-up examinations in months after fd-ff-PDT are shown in Table 2.

Abbreviations: BCVA, best-corrected visual acuity; CVI, choroidal vascularity index; logMAR, logarithm of the minimum angle of resolution; SD, standard deviation; SE, spherical equivalent; SFCT, subfoveal choroidal thickness.

[a]Independent-sample *t* test.

When the mean SFCT of the affected and fellow eyes was compared, there was no significant difference at baseline (496.13 ± 87.51 vs. 458.95 ± 87.19, $p = 0.16$). Although there was a considerable amount of reduction in the SFCT of the fd-ff-PDT-treated affected eyes in the first month (80.47 μm), there was no significant difference between the affected and fellow eyes at the first month (415.65 ± 87.55 vs. 462.39 ± 85.68, $p = 0.07$) (Figure 2a). However, the SFCT of the affected eyes became significantly thinner than that of the fellow eyes in the third month (403.30 ± 84.34 vs. 467.82 ± 88.13, $p = 0.02$) and the sixth month (402.73 ± 82.13 vs. 462.39 ± 85.68, $p = 0.02$) after fd-ff-PDT (Figure 2a).

The mean CVI was significantly lower by 1.63% (95% CI, 0.29%–2.9%, $p = 0.01$) at the first month, 1.88% (95% CI, 0.58%–3.17%, $p = 0.002$) at the third month and 1.61% (95% CI, 0.30%–2.9%, $p = 0.01$) at the sixth month after fd-ff-PDT in the affected eyes compared with baseline ($F[3, 66] = 7.87$, $p < 0.001$) (Table 2). However, there was no significant change in the fellow eyes ($F[2.17, 47.76] = 0.30$, $p = 0.75$, $\varepsilon = 0.72$) (Table 2). When the mean CVI of the affected and fellow control eyes was compared, there was no significant difference at baseline (66.09 ± 1.56 vs. 65.84 ± 1.57, respectively, $p = 0.59$) (Figure 2b). However, it was significantly lower in all visits after fd-ff-PDT (at the first month: 64.45 ± 1.68 vs. 65.87 ± 1.19, $p = 0.002$; third month: 64.21 ± 2.08 vs. 65.71 ± 1.59, $p = 0.009$ and sixth month: 64.47 ± 2.19 vs. 65.62 ± 1.52, $p = 0.045$) (Figure 2b).

No systemic or local adverse events were attributed to fd-ff-PDT in any patients for the 6-month follow-up period.

## DISCUSSION

To our knowledge, this is the first study evaluating CVI and the effects of fd-ff-PDT on CVI in exclusively chronic CSC patients. The longitudinal analysis showed comparable baseline CVI between the affected and fellow eyes. However, it was significantly decreased in the fd-ff-PDT-treated eyes and became lower than the fellow eyes in the first month, which was maintained over the 6 months of the study.

The efficacy of PDT with full or lower doses or fluences in chronic CSC management has been proven in many studies.[3–7] PDT causes choroidal capillary hypoperfusion in the short term, resulting in shrinkage of the vascular lesion with endothelial damage, platelet aggregation and vaso-occlusion, and in the long term, it causes a decrease in choroidal congestion with vascular remodeling, reducing the fluid passage into the subretinal area.[18–20] After being introduced for the treatment of chronic CSC, PDT is considered the most efficient therapy among the options available, such as pharmacotherapy with topical nonsteroidal anti-inflammatory drugs, topical or systemic carbonic anhydrase inhibitors, systemic mineralocorticoid receptor antagonists and intravitreal anti-vascular endothelial growth factors and traditional or subthreshold laser photocoagulation.[1,2,18–20]

Concerns of potential complications due to fd-ff-PDT, including choroidal ischemia, RPE atrophy and secondary macular neovascularisation, have led to safety-enhanced protocols for chronic CSC such as half-dose (3 mg/m$^2$) full-fluence, full-dose half-fluence (25 J/cm$^2$), half-dose (3 mg/m$^2$) half-fluence (25 J/cm$^2$) and even half-time (42 s) full-dose-full-fluence PDT.[4–7] These safety-enhanced protocols were also shown to be effective in treating CSC, with reduced but not eliminated complication rates and an emergence of increased rates of recurrences and retreatments.[4–7] In the present study, the subretinal fluid was resolved entirely in the first month after fd-ff-PDT; BCVA was significantly improved at all visits compared with baseline without recurrence and complications for 6 months, suggesting that fd-ff-PDT is an effective treatment option in chronic CSC. Furthermore, considering previous reports that secondary macular neovascularisation usually complicates PDT in the 3 months after therapy,[19,21–23] the absence of complications in our 6-month evaluation period can be interpreted as a favourable safety profile for fd-ff-PDT. However, our study's exclusion criteria and relatively short follow-up period prevent us from commenting on the recurrence rates after fd-ff-PDT in chronic CSC patients. Nevertheless, it should be

**TABLE 2** Changes in BCVA, SFCT, and CVI of the affected and fellow eye after fd-dd-PDT.

| Parameter (mean ± SD) | Baseline (A) | After fd-ff-PDT | | | One-way repeated measures ANOVA | | |
|---|---|---|---|---|---|---|---|
| | | First month (B) | Third month (C) | Sixth month (D) | *F* | *p* | Post hoc test* |
| BCVA, logMAR (Snellen equivalent) | | | | | | | |
| Affected eyes | 0.33 ± 0.22 (~6/12) | 0.16 ± 0.16 (~6/10) | 0.13 ± 0.16 (~20/28) | 0.10 ± 0.16 (~6/8) | 25.70[a] | **<0.001**[a] | A versus B, ***p* = 0.001**<br>A versus C, ***p* < 0.001**<br>A versus D, ***p* < 0.001**<br>B versus C, *p* = 0.47<br>B versus D, ***p* = 0.02**<br>C versus D, *p* = 0.30 |
| Fellow eyes | 0.01 ± 0.03 (~6/6) | 0.01 ± 0.03 (~6/6) | 0.01 ± 0.03 (~6/6) | 0.01 ± 0.03 (~6/6) | — | — | — |
| *p*[b] | **<0.001** | **<0.001** | **0.001** | **0.008** | — | — | — |
| SFCT, μm | | | | | | | |
| Affected eyes | 496.13 ± 87.51 | 415.65 ± 87.55 | 403.30 ± 84.34 | 402.73 ± 82.13 | 40.38[c] | **<0.001**[c] | A versus B, ***p* < 0.001**<br>A versus C, ***p* < 0.001**<br>A versus D, ***p* < 0.001**<br>B versus C, *p* = 0.47<br>B versus D, *p* = 0.50<br>C versus D, *p* > 0.99 |
| Fellow eyes | 458.95 ± 87.19 | 462.39 ± 85.68 | 467.82 ± 88.13 | 462.39 ± 85.68 | 1.96[d] | 0.17[d] | — |
| *p*[b] | 0.16 | 0.07 | 0.02 | 0.02 | — | — | — |
| CVI, % | | | | | | | |
| Affected eyes | 66.09 ± 1.56 | 64.45 ± 1.68 | 64.21 ± 2.08 | 64.47 ± 2.19 | 7.87 | **<0.001** | A versus B, ***p* = 0.01**<br>A versus C, ***p* = 0.002**<br>A versus D, ***p* = 0.01**<br>B versus C, *p* > 0.99<br>B versus D, *p* > 0.99<br>C versus D, *p* > 0.99 |
| Fellow eyes | 65.84 ± 1.57 | 65.87 ± 1.19 | 65.71 ± 1.59 | 65.62 ± 1.52 | 0.30[e] | 0.75[e] | — |
| *p*[b] | 0.59 | 0.002 | 0.009 | 0.045 | — | — | — |

*Note*: Bold values indicate statistical significance.

Abbreviations: ANOVA, analysis of variance; BCVA, best-corrected visual acuity; CVI, choroidal vascularity index; fd-dd-PDT, full-dose-full-fluence photodynamic therapy; logMAR, the logarithm of the minimum angle of resolution; SFCT, subfoveal choroidal thickness; SD, standard deviation.

**p* Values adjusted for multiple comparisons with Bonferroni correction.

[a]Sphericity assumption not met, Greenhouse–Geisser $\varepsilon = 0.47$.

[b]Paired-sample *t*-test.

[c]Sphericity assumption not met, Greenhouse–Geisser $\varepsilon = 0.48$.

[d]Sphericity assumption not met, Greenhouse–Geisser $\varepsilon = 0.50$.

[e]Sphericity assumption not met, Greenhouse–Geisser $\varepsilon = 0.72$.

borne in mind that if PDT was chosen as the management method, then the available evidence suggests half-dose-full-fluence or full-dose-half-fluence PDT as the treatment of choice in chronic CSC.[1]

In studies conducted on CSC patients with subretinal fluid, whether acute or chronic, SFCT measurements were significantly higher in the affected than in fellow eyes.[8,11–13] These findings support the possible use of SFCT as a diagnostic parameter for CSC. However, unlike these investigations, the SFCT of the affected and fellow eyes of the chronic CSC patients in the present study did not show a statistical difference at baseline. In addition, since we did not have a healthy control group, we could not conclude that SFCT is a diagnostic parameter for patients presenting with unilateral subretinal fluid. However, the decline in SFCT after fd-ff-PDT observed here is in line with previous reports evaluating the effect of PDT on choroidal thickness.[24,25]

CVI is a more stable method for evaluating the vascular structure of the choroid than the measurement of choroidal thickness, since it shows smaller measurement variability and is less affected by physiological factors such as age, axial length and intraocular pressure.[15,26] Agrawal et al.[16] were the first to evaluate CVI as a marker of reproducible quantification of the vascular abnormalities that indocyanine green angiography had already demonstrated in CSC patients. They showed that acute CSC eyes with subretinal fluid had significantly higher CVI (70.54 ± 0.15 μm) than acute CSC eyes with resolved subretinal fluid (65.44 ± 0.10 μm), apparently normal fellow eyes (64.42 ± 0.08 μm) and healthy controls (65.18 ± 0.20 μm) ($p < 0.001$ for all).[16] The authors

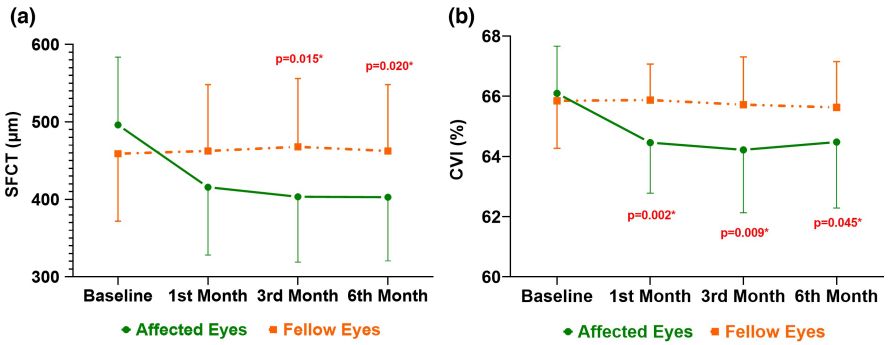


**FIGURE 2** Comparison of the subfoveal choroidal thickness (SFCT) (a) and choroidal vascularity index (CVI) (b) between the affected and fellow eyes of the patients. *Statistical significance with the independent-sample *t* test.

proposed that CVI could be used to diagnose CSC, monitor disease activity and evaluate the treatment response in CSC patients.[16] However, further reports make the proposition of CVI as an activity criterion questionable.[17,27,28] A recent study evaluating CVI in a three-dimensional manner using swept-source OCT covering a 12 × 12 mm area centred on the fovea failed to show such a difference between acute CSC eyes with subretinal fluid and unaffected fellow eyes.[17] However, these authors demonstrated that both eyes had significantly higher CVI than healthy control eyes, supporting the proposition of CVI as a diagnostic criterion.[17] Another multicentre study evaluating choroidal anatomical alterations after full-dose-half-fluence or half-dose-full-fluence PDT for chronic CSC also did not demonstrate a significant difference between the CVI of PDT-treated and fellow eyes in their 64 subjects.[27] However, 24 of the 64 fellow eyes included in the analysis showed signs of CSC, including RPE alterations or extrafoveal subretinal fluid not requiring treatment.[27] Topographical distribution of CVI with three-dimensional mapping and Early Treatment of Diabetic Retinopathy Study grid-based quantification also failed to show differences in any zones when comparing affected and fellow eyes of unilateral acute and chronic CSC patients.[28] The comparison of CVI in the affected and fellow eyes of chronic CSC patients in the present study also did not show a significant difference at baseline, making the value of the CVI as an activity criterion in chronic CSC again questionable.

Recent research has focused on the utility of CVI in the treatment response for CSC patients.[7,27,29,30] The effect of PDT on CVI was evaluated in a retrospective study comparing full-dose-full-fluence, full-dose-half-fluence and half-dose-half-fluence PDT in a mixed group of acute and chronic CSC patients.[7] Park et al. demonstrated a significant decrease in CVI and improvement in BCVA for full-dose-full-fluence and full-dose-half-fluence PDT-treated patients after 3 months, compared with baseline.[7] However, in the half-dose-half-fluence PDT group, CVI was significantly increased without any improvement in BCVA, suggesting no effect compared with the other two treatment protocols.[7] In a further study evaluating safety-enhanced PDT protocols, Izumi et al.[29] showed a significant reduction in CVI 3 months after half-dose-full-fluence PDT.

The CVI was calculated as the ratio of the luminal area, corresponding to the vascular component of the choroid, to the total choroidal area, which is the total area of the choroid with both its vascular and stromal components.[15] Therefore, it is affected by the relative changes in the components of the choroidal structure.[15,26] In an investigation of the effects of half-dose-full-fluence and full-dose-half-fluence PDT on the choroid in chronic CSC, a considerable decrease in the luminal area was demonstrated and the total choroidal area calculated by an automated algorithm after 1 month, but there was no change in CVI.[27] The authors concluded that the CVI changed only if one of the two parameters (luminal area or total choroidal area) varied more than the other one; therefore, the luminal area and the total choroidal area may also provide additional information about the anatomical response to treatment.[27] In a prospective study comparing the effects of half-dose-full-fluence PDT and high-density subthreshold micropulse laser in chronic CSC patients, van Rijssen et al.[30] found no significant change in the CVI of the treated eyes after 7–8 months for each modality. Therefore, they argued that the treatment effect after half-dose-full-fluence PDT and high-density subthreshold micropulse laser might be based on mechanisms of action other than the decrease in CVI.[30] In the present study, CVI significantly decreased in the fd-ff-PDT-treated eyes in the first month, and remained significantly lower than baseline in the third and sixth months. Furthermore, although the baseline CVI of affected and fellow eyes was comparable, the CVI of the fd-ff-PDT-treated eyes became significantly lower than that of the fellow eyes in the first month and maintained this treatment effect during the follow-up period. Although the evaluation of changes in separate choroidal components is beyond the scope of this study, our findings strongly support the vascular remodeling effect of fd-ff-PDT and CVI's value in monitoring treatment response in chronic CSC patients.

The strengths of the present study are its fellow-eye controlled design, thereby eliminating interpatient differences, and the longitudinal evaluation of the patients rather than comparing before and after effects of the intervention in a single visit. However, the study's limitations that should be considered while interpreting the results

are its single-centre retrospective nature, relatively small sample size and short follow-up period. Furthermore, instead of a single line for choroidal thickness measurement, a more consistent determination could be obtained by taking multiple lines from the relevant EDI-OCT B-scans and averaging them. In addition, CVI was assessed only in the subfoveal 1500 μm, which could have been evaluated from the whole subfoveal B-scan.

## CONCLUSION

In conclusion, the baseline comparable CVI values in the affected and fellow eyes of chronic CSC patients argue for its utility as an activity criterion. CVI decreased significantly in the fd-ff-PDT-treated eyes and became significantly lower than that of fellow control eyes of the chronic CSC patients for 6 months. These findings support the role of CVI as a measurement of treatment response in fd-ff-PDT-treated chronic CSC patients. However, studies involving larger study samples with more extended follow-up periods are required to demonstrate the validity and sustainability of these findings.

### AUTHOR CONTRIBUTIONS

**Mehmet Orkun Sevik:** Conceptualization (equal); data curation (equal); formal analysis (lead); investigation (equal); methodology (lead); supervision (equal); writing – original draft (lead); writing – review and editing (equal). **Aslan Aykut:** Conceptualization (equal); investigation (equal); methodology (equal); supervision (equal). **Furkan Çam:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); writing – original draft (equal); writing – review and editing (equal). **Volkan Dericioğlu:** Investigation (equal); methodology (equal); software (equal); writing – review and editing (equal). **Özlem Şahin:** Methodology (equal); supervision (equal); validation (equal); writing – review and editing (equal).

### FUNDING INFORMATION

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

### CONFLICT OF INTEREST STATEMENT

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or nonfinancial interest in the subject matter or materials discussed in this manuscript.

### DATA AVAILABILITY STATEMENT

The data supporting the study findings are available from the corresponding author upon request.

### INFORMED CONSENT

The study was conducted following the Declaration of Helsinki ethical standards, and all patients provided written informed consent to use their medical information in the study analysis.

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**How to cite this article:** Sevik MO, Aykut A, Çam F, Dericioğlu V, Şahin Ö. Choroidal vascularity index as an activity criterion and a treatment response measure in chronic central serous chorioretinopathy. *Ophthalmic Physiol Opt*. 2023;43:1203–1210. https://doi.org/10.1111/opo.13187