



# Short Axial Length Is Related to Asymmetric Vortex Veins in Central Serous Chorioretinopathy

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**Purpose:** To investigate the clinical and morphologic factors related to asymmetric dilated vortex veins in central serous chorioretinopathy (CSC).

**Design:** Retrospective, comparative study.

**Participants:** One hundred fifty-eight eyes of 158 patients with CSC.

**Methods:** All patients with CSC underwent ophthalmic examination and multimodal imaging, including measurements of axial length (AL), fluorescein angiography, indocyanine green angiography, swept-source OCT, and anterior segment OCT. Using en face OCT images at the level of the outer choroid, the eyes were divided into 2 groups: eyes with symmetric vortex veins (symmetry group) and those with asymmetric vortex veins (asymmetry group).

**Main Outcome Measures:** Clinical and morphologic factors related to asymmetric vortex veins in CSC.

**Results:** Of the 158 eyes, 120 eyes (75.9%) were classified into the asymmetry group and 38 eyes (24.1%) were classified into the symmetry group. The asymmetry group showed significantly greater spherical equivalent ( $-0.32 \pm 1.78$  diopters [D] vs.  $-1.35 \pm 2.64$  D;  $P = 0.033$ ), shorter AL ( $23.52 \pm 0.86$  mm vs.  $24.10 \pm 1.06$  mm;  $P = 0.005$ ), and greater subfoveal choroidal thickness ( $414.6 \pm 105.3$   $\mu$ m vs.  $360.4 \pm 91.8$   $\mu$ m;  $P = 0.005$ ) than the symmetry group. No significant differences existed between the 2 groups regarding age, sex, or all scleral thicknesses at the superior, temporal, inferior, and nasal points. In the multivariate analyses, shorter AL (odds ratio, 0.56; 95% confidence interval, 0.36–0.88;  $P = 0.011$ ) was found to be significantly associated with the presence of asymmetric vortex veins.

**Conclusions:** The asymmetric dilated vortex vein is a common finding in patients with CSC. Our results suggest that certain biometric factors, such as short AL, may be associated with asymmetric dilated vortex veins developing in patients with CSC. *Ophthalmology Science* 2021;1:100071 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Central serous chorioretinopathy (CSC) is a common disease characterized by the accumulation of serous retinal detachment (SRD) with or without pigment epithelium detachment in the posterior pole of the eye.<sup>1,2</sup> Usually, CSC develops in middle-aged men.<sup>3</sup> In most cases of CSC, SRD is absorbed spontaneously, and the visual prognosis is relatively good. However, some patients with CSC may demonstrate recurrent or prolonged SRD and may sustain damage to the retinal pigment epithelium, resulting in irreversible vision loss.<sup>4</sup> From previous studies, it is well known that male gender,<sup>5</sup> type A personality,<sup>6</sup> psychological stress,<sup>7</sup> exposure to steroids,<sup>5</sup> pregnancy,<sup>8</sup> short axial length (AL),<sup>9,10</sup> scleral thickening,<sup>11</sup> and genetic factors<sup>12–17</sup> are associated with CSC. However, the exact pathologic mechanism of CSC is not fully understood.

Choroidal abnormalities are a well-known cause of CSC pathologic features. Using indocyanine green angiography (ICGA), researchers have observed signs of filling delays, dilated choroidal vessels, and choroidal vascular

hyperpermeability.<sup>18,19</sup> Owing to significant advances in OCT technology, such as enhanced depth imaging<sup>20</sup> and high-penetration swept-source (SS) OCT,<sup>21</sup> subfoveal choroidal thickness (SCT) in CSC eyes was found to be significantly greater than that in normal eyes.<sup>22</sup> After further research, a thick choroid was observed as a result of dilated choroidal vessels in the outer choroid.<sup>23</sup>

Recently, Pang et al<sup>24</sup> observed dilated outer choroidal vessels of the macular area associated with congested vortex vein ampullas before exiting the sclera using ultra-widefield ICGA. Hiroe and Kishi<sup>25</sup> showed that the patterns of outer choroidal vessels in the posterior pole were divided into asymmetric or symmetric vortex veins using en face OCT, and asymmetric dilated vortex veins were observed in all CSC eyes. Moreover, Kishi et al<sup>26</sup> reported that the asymmetric dilated vortex vein regions and filling delay areas on ICGA showed substantial overlap in acute CSC. Based on these findings, asymmetric dilated vortex veins in the outer choroid are expected to be related closely to CSC pathologic features.

However, the mechanism underlying asymmetric dilated vortex vein development in CSC remains unclear. We previously studied the biometric aspects in CSC eyes and demonstrated that short AL,<sup>10</sup> hyperopic refractive error,<sup>10</sup> and thickened sclera<sup>11</sup> were associated with the pathogenesis of CSC. In contrast, patients with CSC accompanied by high myopia are seldom encountered in a clinical setting.<sup>27</sup>

This study investigated the relationship between the asymmetric dilated vortex vein and the clinical and morphologic factors. We conducted a comparative study in CSC eyes with symmetric or asymmetric vortex veins, paying particular attention to some biometric factors such as AL and scleral thickness.

## Methods

### Participants

This retrospective study was conducted in a single institution. The study was approved by the institutional review board of the University of the Ryukyus Hospital (approval no., 1503) and was conducted following the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants before their participation in this study.

We retrospectively reviewed the charts and imaging data of 158 eyes of 158 patients (28 women and 130 men; mean age, 52.0 years; standard deviation, 11.8 years) with CSC who visited the Macula Service of the University of the Ryukyus Hospital between October 2018 and November 2020. The right eye was used in patients with bilateral CSC.

Central serous chorioretinopathy was diagnosed by fundus ophthalmoscopy and multimodal imaging, including fluorescein angiography, ICGA, fundus autofluorescence photography, SS OCT, and OCT angiography. The clinical findings of CSC included the presence of SRD involving the macula on SS OCT and 1 or more leakage points at the level of the retinal pigment epithelium on fluorescein angiography and multifocal choroidal vascular hyperpermeability in mid- or late-phase ICGA. Fundus autofluorescence photography revealed at least 1 area of retinal pigment epithelium alteration. OCT angiography was also used to confirm the absence of choroidal neovascularization. Eyes with a history of any other retinal diseases, including choroidal neovascularization, a history of intraocular surgery, a history of photodynamic therapy, or a history of related systemic diseases associated with CSC, were excluded. Moreover, we also excluded patients with a history of taking systemic corticosteroids, considering the different causes of steroid-induced CSC.<sup>28–30</sup>

### Multimodal Imaging and Imaging Analysis

At the initial visit, all patients underwent complete ocular examinations with autorefractometry (ARK-1a; NIDEK), best-corrected visual acuity (BCVA) testing with Landolt C charts (SC-1000; TOMEY), measurements of the AL (IOL Master 700; Carl Zeiss Meditec), slit-lamp biomicroscopy with a noncontact fundus lens, color fundus photography and fundus autofluorescence photography (TRC-50DX; Topcon), fluorescein angiography and ICGA (Spectralis HRA + OCT; Heidelberg Engineering), SS OCT (DRI-OCT Triton; Topcon), OCT angiography (between October 2018 and March 2019: DRI-OCT Triton [Topcon]; between April 2019 and November 2020: Zeiss Plex Elite 9000 [Carl Zeiss Meditec]), and anterior-segment (AS) OCT (CASIA 2; TOMEY).

The spherical equivalent (SE) was defined as adding half of the cylindrical power to the principal spherical power. We measured SCT using B-scan images of the 12-mm horizontal line scans at the foveal center by measuring the distance from the hyper-reflective line corresponding to Bruch's membrane beneath the retinal pigment epithelium to the inner surface of the sclera using the calliper measurement tool of the SS OCT. To evaluate the symmetry of vortex veins in the outer choroid, we referred to the methods that used en face OCT described in a previous study.<sup>25</sup> First, the volume scan data were obtained using a raster scan protocol of 512 (horizontal) × 128 (vertical) B-scans, which covered a 12 × 9-mm area centered on the middle point of the foveal center and the optic disc. Then, en face OCT images were obtained as coronal slices from 3-dimensional OCT images that were flattened relative to Bruch's membrane using a software tool (EnView software; Topcon). The definition of a symmetric vortex vein was based on en face OCT images in the outer choroid showing a symmetric pattern between the superior and inferior vortex veins and the watershed horizontally passing through the macular region. The symmetry group (Fig 1) typically comprised patients with CSC with no difference in running pattern and vascular diameter between the superior and inferior vortex veins. The patients with CSC without symmetric vortex veins were categorized as having asymmetric vortex veins. The asymmetry group (Fig 2) typically showed dilated vortex veins extending over the horizontal line through the fovea. The symmetry or asymmetry groups were determined by 2 retinal specialists (N.T. and N.I.). Although the 2 examiners were blinded to the clinical findings, a third retinal specialist (S.S.) made the final decision in controversial cases. Interrater agreement was assessed by calculating Cohen's  $\kappa$  coefficient.

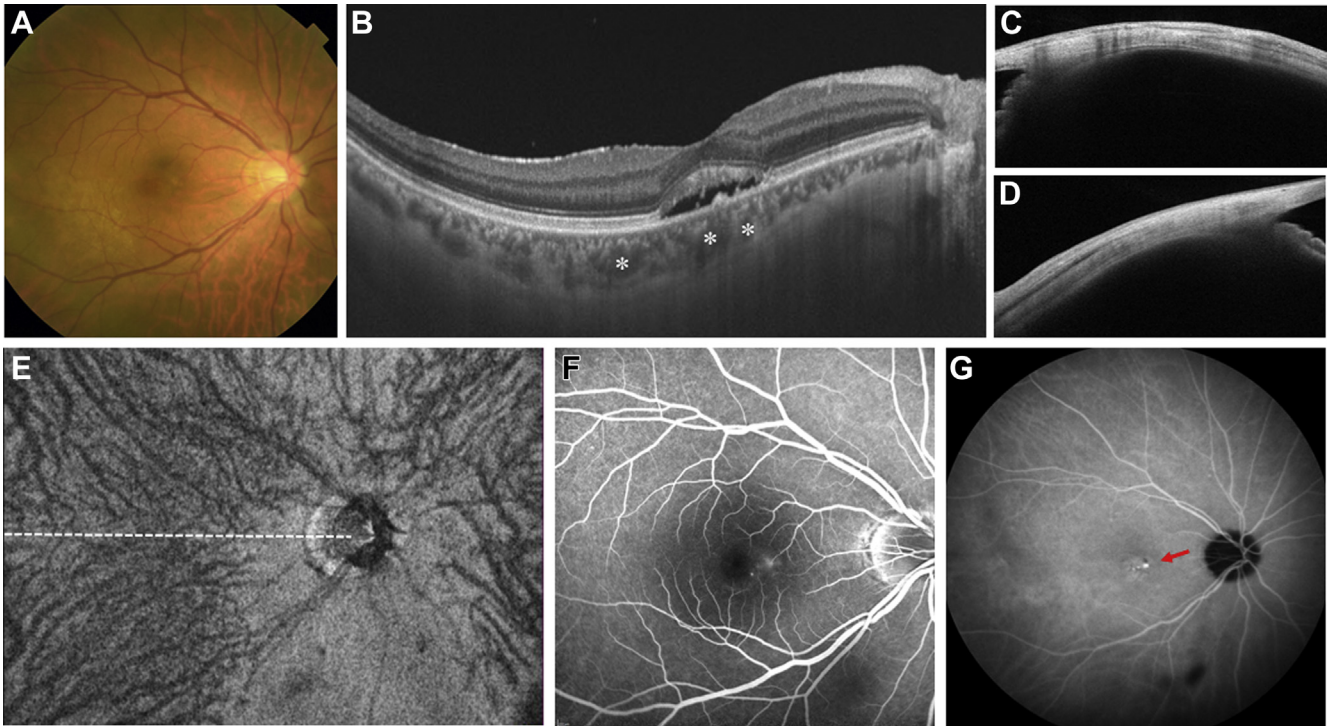
Using AS OCT, the scleral thickness was measured manually in 4 directions (superior, temporal, inferior, and nasal). In brief, we identified the upper scleral line based on the low brightness of each rectus muscle and delineated the lower scleral line from the difference in brightness. Scleral thickness was calculated vertically as the distance between the upper scleral line and the lower scleral line 6-mm posterior to the scleral spur using the calliper tool of the AS OCT. The detailed methodology for measuring scleral thickness has been described previously.<sup>11</sup>

### Outcomes

The symmetry and asymmetry groups were compared in terms of age, sex, SE, AL, SCT, and scleral thickness. Further, we investigated the possible factors related to the asymmetric vortex veins using multivariate logistic regression analyses.

### Statistical Analysis

All data were analyzed using Statistical Analysis System software version 9.4 (SAS, Inc). Statistical significance was set at  $P < 0.05$ . Unless otherwise stated, the results were expressed as mean and standard deviation, and categorical data were assessed using the Fisher exact test. The Mann–Whitney  $U$  test was used to compare the quantitative variables between the 2 independent groups. The significantly associated factors in the univariate analysis were assessed further for their associations with the presence of asymmetric vortex veins using multivariate logistic regression analyses adjusting for possible confounders. The associations among the variables and the presence of asymmetric vortex veins in CSC eyes were assessed using odds ratios and their 95% confidence intervals by multivariate logistic regression analyses.



**Figure 1.** Images of the right eye of a 55-year-old man with central serous chorioretinopathy. Axial length is 26.44 mm, and spherical equivalent is  $-5.375$  diopters. **A**, Color fundus photograph revealing serous retinal detachment (SRD) involving the fovea. **B**, Horizontal B-scan OCT image through the fovea showing SRD with dilated choroidal vessels (asterisks). The subfoveal choroidal thickness is  $227 \mu\text{m}$ . **C**, Cross-sectional image of the sclera at the superior point showed with anterior-segment (AS) OCT. The scleral thickness is  $363 \mu\text{m}$ . **D**, Cross-sectional image of the sclera at the inferior point showed with AS OCT. The scleral thickness is  $415 \mu\text{m}$ . The mean value of scleral thicknesses at 4 directions is  $390 \mu\text{m}$ . **E**, En face OCT image of  $12 \times 9 \text{ mm}$  showing vortex veins in the outer choroid. The superior and inferior vortex veins demonstrate symmetric patterns, and the horizontal watershed zone passes through the fovea (white dashed line). This eye was classified in the symmetry group. **F**, Fluorescein angiogram within a  $30 \times 30$  range revealing diffuse leakage in the macular region. **G**, Indocyanine green angiogram within a  $55 \times 55$  range in the late phase revealing typical choroidal vascular hyperpermeability (red arrow).

## Results

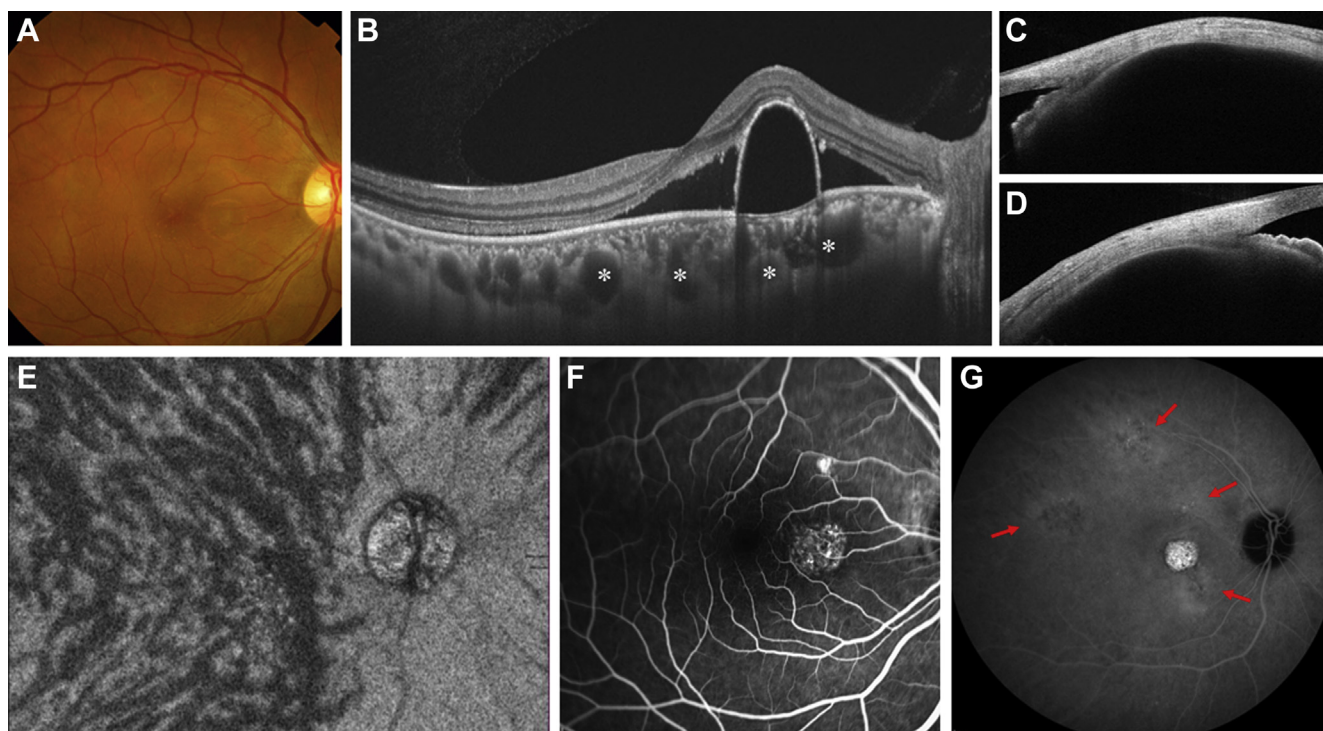
Of the 158 eyes, 120 eyes (75.9%) were classified into the asymmetry group and 38 eyes (24.1%) were classified into the symmetry group ( $\kappa$  statistic, 0.92; 95% confidence interval, 0.85–0.99;  $P < 0.001$ ). The demographic and clinical characteristics of the 2 groups are summarized in [Table 1](#). The asymmetry group showed significantly greater SE ( $-0.32 \pm 1.78$  diopters [D] vs.  $-1.35 \pm 2.64$  D;  $P = 0.033$ ), shorter AL ( $23.52 \pm 0.86$  mm vs.  $24.10 \pm 1.06$  mm;  $P = 0.005$ ), and greater SCT ( $414.6 \pm 105.3 \mu\text{m}$  vs.  $360.4 \pm 91.8 \mu\text{m}$ ;  $P = 0.005$ ) than the symmetry group. No significant differences existed between the 2 groups regarding age, sex, and all scleral thicknesses at the superior, temporal, inferior, and nasal points. Multivariate logistic regression analyses of the factors associated with asymmetric vortex veins are summarized in [Table 2](#). We included age and sex, which are clinically important confounders, in the final multivariate models, although they were not factors that were significantly associated in the univariate analysis. Because AL and SE were highly correlated ( $r_s = -0.50$ ;  $P < 0.001$ , Spearman rank correlation test), we needed to exclude 1 of these 2 variables from the multivariate logistic regression analyses. Therefore, 2 multivariate

logistic regression models, model 1 including AL and model 2 including SE, were used for further analyses. In model 1, multivariate analysis revealed that AL (odds ratio, 0.56; 95% confidence interval, 0.36–0.88;  $P = 0.011$ ) was the sole variable significantly associated with asymmetric vortex veins in CSC. Age, sex, and SCT were not significantly associated with asymmetric vortex veins in CSC. In model 2, we did not find statistically significant associations among age, sex, SE, SCT, and asymmetric vortex veins in CSC. [Table 3](#) shows the distribution of the symmetry or asymmetry groups with the AL subgroup. With a shorter AL, the prevalence of the asymmetry group was significantly higher than that of the symmetry group in the AL subgroup dataset ( $P < 0.001$ ).

## Discussion

An asymmetric dilated vortex vein in the outer choroid is a newly identified morphologic feature associated with pachychoroid-related diseases.<sup>25</sup> The current study investigated the relationship between asymmetric vortex veins and the clinical and morphologic features of CSC. We revealed the following: (1) the asymmetric vortex vein





**Figure 2.** Images of the right eye of a 37-year-old man with central serous chorioretinopathy. Axial length is 21.33 mm, and spherical equivalent is +1.000 diopter. **A**, Color fundus photograph revealing serous retinal detachment (SRD) with pigment epithelium detachment in the macular region. **B**, Horizontal B-scan OCT image through the fovea showing SRD with dome-shaped pigment epithelium detachment and significantly dilated choroidal vessels (asterisks). The subfoveal choroidal thickness is 452  $\mu\text{m}$ . **C**, Cross-sectional images of the sclera at the superior point showed with anterior segment (AS) OCT. The scleral thickness is 432  $\mu\text{m}$ . **D**, Cross-sectional images of the sclera at the inferior point showed with AS OCT. The scleral thickness is 470  $\mu\text{m}$ . The mean value of scleral thicknesses at 4 directions is 450  $\mu\text{m}$ . **E**, En face OCT image of 12  $\times$  9 mm showing dilated vortex veins in the outer choroid. The horizontal watershed zone has disappeared because of the superior dilated vortex veins evident in more than the upper half of the posterior pole. This eye was classified in the asymmetry group. **F**, Fluorescein angiogram within a 30°  $\times$  30° range revealing typical leakages in the macular area. **G**, Indocyanine green angiogram within a 55°  $\times$  55° range in the late phase, revealing multifocal areas of choroidal vascular hyperpermeability (red arrows).

was seen in 75.9% of CSC eyes; (2) the asymmetry group showed greater SE, shorter AL, and greater SCT than the symmetry group in the univariate analysis; and (3) shorter AL was the sole factor associated with asymmetric vortex veins in CSC in the multivariate regression analyses.

These findings suggest that a shorter AL may be associated with the development of asymmetric vortex veins and the pathogenesis of CSC.

Choroidal circulation is formed by short posterior ciliary arteries, long posterior ciliary arteries, and anterior ciliary

Table 1. Demographic and Clinical Characteristics of Patients with Asymmetric and Symmetric Vortex Veins in Central Serous Chorioretinopathy

Characteristic	Asymmetry Group (n = 120)	Symmetry Group (n = 38)	P Value
Age (yrs)	52.8 $\pm$ 12.1	49.7 $\pm$ 10.6	0.300*
Female sex	23 (19.2)	5 (13.2)	0.473 <sup>†</sup>
SE (D)	-0.32 $\pm$ 1.78	-1.35 $\pm$ 2.64	0.033*
AL (mm)	23.52 $\pm$ 0.86	24.10 $\pm$ 1.06	0.005*
SCT ( $\mu\text{m}$ )	414.6 $\pm$ 105.3	360.4 $\pm$ 91.8	0.005*
Scleral thickness ( $\mu\text{m}$ )			
Superior	417.5 $\pm$ 60.8	405.2 $\pm$ 60.7	0.220*
Temporal	437.0 $\pm$ 55.9	425.3 $\pm$ 51.0	0.226*
Inferior	450.3 $\pm$ 58.0	440.0 $\pm$ 64.2	0.194*
Nasal	434.6 $\pm$ 61.0	430.7 $\pm$ 56.7	0.580*

AL = axial length; D = diopter; SCT = subfoveal choroidal thickness; SE = spherical equivalent.

Data are presented as mean  $\pm$  standard deviation or no. (%), unless otherwise indicated.

\*Mann-Whitney U test.

<sup>†</sup>Fisher exact test.

Table 2. Multivariable Logistic Regression Analysis of the Factors Associated with Asymmetric Vortex Vein in Central Serous Chorioretinopathy

Variable	Model 1			Model 2		
	Odds Ratio	95% Confidence Interval	P Value	Odds Ratio	95% Confidence Interval	P Value
Age (yrs)	1.03	0.99–1.07	0.147	1.03	0.99–1.07	0.187
Male (vs. female)	1.46	0.48–4.46	0.503	1.75	0.58–5.24	0.321
AL (mm)	0.56	0.36–0.88	0.011	—	—	—
SE (D)	—	—	—	1.20	0.99–1.47	0.071
SCT (µm)	1.00	1.00–1.01	0.051	1.00	1.00–1.01	0.055

D = diopter; AL = axial length; SCT = subfoveal choroidal thickness; SE = spherical equivalent; — = analysis not carried out.

arteries as inflow vessels and vortex veins as outflow vessels. The vortex veins were located in each of the 4 quadrants. These vortex veins form an ampulla and penetrate the sclera at the equator. The boundary of each vortex vein region is called a *watershed zone*. It is observed as a border separating each vortex vein region, usually passing horizontally through the disc area and vertically through the papillomacular area.<sup>31</sup> However, various choroidal venous vascular patterns exist, such as the asymmetric vortex vein.<sup>32</sup> In the current study, of the 158 CSC eyes, 120 eyes (75.9%) were in the asymmetry group and 38 eyes (24.1%) were in the symmetry group. Hiroe and Kishi<sup>25</sup> reported the running patterns of the vortex veins in 38 eyes with CSC using en face OCT and ICGA images, and asymmetric vortex veins were observed in all CSC eyes. Although the observed prevalence of asymmetric vortex veins in CSC eyes was higher than that detected in a large cohort in our study, our results are seemingly much higher than those in normal participants.<sup>25</sup> Shiihara et al<sup>33</sup> also analyzed the running pattern of the choroidal vessels in en face OCT images determined by a machine learning-based quantitative method and showed that CSC eyes harbored dilated and asymmetric vessels running in the outer choroid. The pathogenesis of CSC is presumably involved in venous congestion and increased venous pressure associated with these morphologic features, such as asymmetric dilated vortex veins.

In this study, shorter AL seemed to be the sole factor associated with the presence of asymmetric vortex veins in CSC eyes using multivariate regression analyses. We

recently proposed that the thick sclera may play a role in the pathogenesis of CSC by showing significantly greater scleral thickness in CSC eyes than in normal control eyes.<sup>11</sup> Therefore, we postulated that the thick sclera was considered to disturb the choroidal venous outflow. Unexpectedly, the scleral thickness was not significantly associated with the presence of an asymmetric vortex vein in the current study. Furthermore, previous reports have shown that asymmetric vortex veins also are present in healthy participants.<sup>25,33</sup> These facts imply that the asymmetric vortex vein may be a congenital morphologic factor and may be related to the misalignment of the watershed associated with the shorter AL. In addition to the presence of asymmetric vortex veins, thick sclera may stagnate the choroidal circulation further or may enlarge the choroidal vessels, leading to the development of CSC.

Central serous chorioretinopathy is a multifactorial disease, typically caused by many physiologic and psychological factors,<sup>34,35</sup> and is also influenced by genetic factors.<sup>12–17</sup> Notably, Hosoda et al<sup>13</sup> reported significant associations between *CFH* and *VIPR2* genes and choroidal thickness. They proposed that *CFH* and *VIPR2* contribute to the pathogenesis of CSC via their effect on choroidal thickness. These genetic factors and anatomic features, such as short AL, may play an essential role in asymmetric vortex vein development.

This study has several limitations. First, only eyes with CSC were analyzed in this study. It is necessary to consider whether the results apply to both CSC eyes and healthy eyes. Second, because this study was hospital-based, the enrolled CSC eyes

Table 3. Distribution of Asymmetry or Symmetry Groups with the Axial Length Subgroup

Variable	Asymmetry Group (n = 120)	Symmetry Group (n = 38)	P Value
AL subgroup (mm), no. (%)			< 0.001*
21–< 22	5 (4.2)	0 (0)	
22–< 23	24 (20.0)	6 (15.8)	
23–< 24	55 (45.8)	15 (39.5)	
24–< 25	30 (25.0)	10 (26.3)	
25–< 26	6 (5.0)	4 (10.5)	
26–< 27	0 (0)	3 (7.9)	

AL = axial length.

\*Fisher exact test.

consisted of mainly severe cases referred to our hospital for treatment, and few mild CSC cases were found. Third, the en face images used in this study covered  $12 \times 9$  mm of the posterior pole. We observed asymmetric dilated vortex veins in the posterior pole. Still, we were unable to observe the full features of the vortex veins from the macular region to the ampulla before entering the sclera. Fourth, we measured the scleral thickness 6 mm posterior to the scleral spur. Therefore, the morphologic features of the sclera surrounding the vortex veins remain unclear. Finally, the diagnosis of symmetric or asymmetric vortex veins was made subjectively based on the previous literature.<sup>25</sup> More objective and quantitative methods are needed for future analyses.

In conclusion, this study analyzed the relationship between asymmetric vortex veins and the clinical and

morphologic features of CSC. We showed that a shorter AL is associated with solely asymmetric vortex veins in CSC. Therefore, certain biometric factors, such as shorter AL, may be associated with asymmetric dilated vortex veins developing in eyes with CSC. To better understand the morphologic features of the vortex veins, it is necessary to further investigate the features of asymmetric vortex veins from their posterior pole to the ampulla using widefield images.

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HUMAN SUBJECTS: Human subjects were included in this study. This retrospective study was conducted in a single institution. The study was approved by the institutional review board of the University of the Ryukyus Hospital and was conducted following the tenets of the Declaration of

Helsinki. Informed consent was obtained from all participants before their participation in this study.

No animal subjects were included in this study.

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Abbreviations and Acronyms:

AL = axial length; AS = anterior-segment; CSC = central serous chorioretinopathy; D = diopter; ICGA = indocyanine green angiography; SCT = subfoveal choroidal thickness; SE = spherical equivalent; SRD = serous retinal detachment; SS = swept-source.

Keywords:

Asymmetric dilated vortex vein, Axial length, Central serous chorioretinopathy, Choroidal thickness, Choroidal vascular hyperpermeability, Pachychoroid, Scleral thickness.

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