

# Are They Same Diagnosis? Central Serous Chorioretinopathy or Erectile Dysfunction?

Bunlar Aynı Teşhis mi? Santral Seröz Koryoretinopati mi, Yoksa Erektile Disfonksiyon mu?

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## Abstract

**Purpose:** To investigate and compare the optical coherence tomography angiography (OCTA) findings of central serous chorioretinopathy (CSCR) in males with and without erectile dysfunction.

**Methods:** The study included 42 patients with chronic CSCR and 44 age- and sex-matched healthy controls. OCTA images were evaluated in both groups. The International Index of Erectile Function-15 (IIEF-15) was used to assess erection, orgasm, sexual desire, sexual satisfaction from intercourse, and overall sexual satisfaction in both the patient and control groups.

**Results:** Superficial capillary plexus vessel density, deep capillary plexus vessel density, and foveal density were statistically significantly lower in the CSCR group ( $p < 0.001$ ). The flow area of the superficial choroid layer in the CSCR group was also significantly lower than in the control group ( $1.86 \pm 0.29$  vs.  $2.12 \pm 0.09$ ,  $p < 0.001$ ). In the CSCR group, severe ED was diagnosed in three (5.2%) patients, moderate ED in 10 (17.2%), mild-to-moderate ED in seven (12.1%), and mild ED in 15 (25.9%), while no cases of severe or moderate ED were diagnosed in the control group. There was no significant difference in the vessel density of the superficial and deep retina or the choriocapillaris between the groups with and without ED ( $p = 0.302$ ,  $p = 0.064$ , and  $p = 0.970$ , respectively). However, in the ED CSCR group, radial peripapillary capillary density, all vessels and small vessels density in the whole area, all vessels and small vessels in the peripapillary area were significantly lower ( $p = 0.050$ ,  $p = 0.051$ ,  $p = 0.039$  and  $p = 0.029$ , respectively).

**Conclusion:** OCTA images showed that the frequency of ED was significantly higher in patients diagnosed with CSCR.

**Keywords:** central serous chorioretinopathy, erectile dysfunction, optical coherence tomography angiography

## Özet

**AMAÇ:** Erektile disfonksiyonu olan ve olmayan erkeklerde santral seröz korioretinopati (SSKR) tanısı almış hastaların optik koherens tomografi anjiyografi (OKTA) bulgularını araştırmak ve karşılaştırmak.

**YÖNTEMLER:** Çalışmaya kronik SSKR'li 42 hasta ve yaş ve cinsiyete uygun 44 sağlıklı kontrol dahil edildi. Her iki grupta da OKTA görüntüleri değerlendirildi. Hem hasta hem de kontrol gruplarında ereksiyon, orgazm, cinsel istek, cinsel ilişkiden alınan cinsel tatmin ve genel cinsel tatmini değerlendirmek için Uluslararası Erektile Fonksiyon İndeksi-15 (IIEF-15) kullanıldı.

**BULGULAR:** SSKR grubunda yüzeysel kılcal pleksus damar yoğunluğu, derin kılcal pleksus damar yoğunluğu ve fovea yoğunluğu istatistiksel olarak anlamlı derecede düşüktü ( $p < 0,001$ ). SSKR grubunda yüzeysel koroid tabakasının akım alanı da kontrol grubuna göre anlamlı derecede düşüktü ( $1,86 \pm 0,29$ 'a karşı  $2,12 \pm 0,09$ ,  $p < 0,001$ ). SSKR grubunda üç hastada (%5,2) şiddetli ED, 10 hastada (%17,2) orta şiddetli ED, yedi hastada (%12,1) hafif-orta şiddetli ED ve 15 hastada (%25,9) hafif ED tanısı konuldu; kontrol grubunda ise şiddetli veya orta şiddetli ED tanısı konulan vaka olmadı. Yüzeysel ve derin retinanın veya koryokapiller damar yoğunluğunda ED'li ve ED'siz gruplar arasında anlamlı bir fark yoktu (sırasıyla  $p = 0,302$ ,  $p = 0,064$  ve  $p = 0,970$ ). Ancak ED SSKR grubunda, radyal peripapiller kapiller yoğunluk, tüm alandaki tüm damarlar ve küçük damarlar yoğunluğu, peripapiller alandaki tüm damarlar ve küçük damarlar yoğunluğu anlamlı derecede düşüktü (sırasıyla  $p = 0,050$ ,  $p = 0,051$ ,  $p = 0,039$  ve  $p = 0,029$ ).

**SONUÇ:** OCTA görüntüleri, SSKR tanısı almış hastalarda ED sıklığının anlamlı derecede yüksek olduğunu göstermiştir.

**Anahtar Kelimeler:** central serous chorioretinopathy, erectile dysfunction, optical coherence tomography angiography.

Received: 16/10/2025

Accepted: 03/12/2025

Published Online: 30/08/2026

Cite this article: Bozkurt Gencer M, Yaprak L, Cetinkaya Yaprak A, et al. Are They Same Diagnosis? Central Serous Chorioretinopathy or Erectile Dysfunction? Turk J Health S. 2026;7:2:74-78. doi: 10.29228/tjhealthsport.87804

## INTRODUCTION

Central serous chorioretinopathy (CSCR) is a retinal disorder that primarily affects men aged 25 to 50 years and is characterized by a localized detachment of the neurosensory retina or a serous separation of the retinal pigment epithelium (RPE).[1] In most instances, the disease course is self-limiting, with gradual reabsorption of the subretinal fluid and subsequent improvement in visual acuity. However, approximately 20–30% of patients experience recurrent episodes, and about 5% develop a chronic form, typically associated with RPE dysfunction, leading to persistent subretinal fluid accumulation and prolonged visual impairment lasting three to six months or longer.[2]

Although the precise mechanisms underlying CSCR are not fully elucidated, several predisposing factors have been implicated, including male sex, exposure to stress-related hormones (particularly corticosteroids and catecholamines), type A personality traits, uncontrolled systemic hypertension, and irregular sleep patterns.[3,5] Psychological stress and emotional disturbances such as anxiety may induce retinal vascular dysregulation and angiospasm, thereby promoting macular leakage and fluid accumulation.[6,7]

Advances in ocular imaging modalities have provided substantial insights into the pathogenesis of CSCR. Findings such as choroidal vessel dilation and areas of impaired perfusion suggest that disturbances in choroidal hemodynamics contribute to focal RPE damage and subsequent subretinal fluid buildup.[8,9] Optical coherence tomography angiography (OCTA)—a noninvasive imaging technique offering depth-resolved visualization of retinal and choroidal vasculature—has enabled detailed evaluation of microvascular changes in CSCR. This tool has proven valuable for assessing vascular alterations, monitoring disease evolution, and detecting complications such as choroidal neovascularization or subepithelial fibrosis.[10]

Erectile dysfunction (ED) is defined as the persistent inability to attain or sustain a penile erection sufficient for satisfactory sexual performance. Its prevalence increases with age and is frequently associated with vascular comorbidities, adversely affecting the quality of life for both patients and their partners.[11] Endothelial dysfunction, by impairing the relaxation of arteriolar smooth muscle, leads to reduced vasodilation and consequently contributes to ED.[12] Moreover, men with ED are reported to have a 75% higher risk of developing peripheral vascular disease.[13] Interestingly, several overlapping risk factors—such as psychological stress, depression, anxiety, type A personality, elevated cortisol levels, hypertension, and sleep disorders—have been linked to both CSCR and ED.[14] Prior studies have demonstrated a notable association between the two conditions, suggesting

that pathophysiological mechanisms involved in CSCR may also predispose individuals to ED.[14,15]

Considering that CSCR and ED share a vascular etiology, the present study aimed to explore potential differences in OCTA parameters between CSCR patients with and without concomitant ED. Furthermore, given that ED serves as a clinical marker of systemic endothelial and cardiovascular dysfunction, we hypothesized that OCTA might reveal subclinical alterations in retinal and choroidal microvasculature among CSCR patients, providing insights into systemic vascular health.

## MATERIALS AND METHODS

**Ethical approval:** The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the Local Ethics Committee of Antalya Teaching and Research Hospital. Each participant was informed and consent was obtained.

**Study design:** The study included 42 male patients with chronic CSCR and flat, irregular pigment epithelium detachments who were followed up at the Ophthalmology Department of Antalya Training and Research Hospital, as well as 44 age- and sex-matched healthy controls.

The diagnosis of CSCR was considered as idiopathic serous macular detachment with choroidal thickening and focal RPE leakage with choroidal vascular hyperpermeability. (identified through fluorescein angiography). All participants were evaluated for age, sex, body mass index (BMI), comorbidities, known psychiatric disorders, history of pelvic injury or surgery, smoking habits, and medication use.

Patients with definitive CSCR diagnoses who did not have any known comorbidities (e.g., hypertension and diabetes mellitus), were not overweight or obese ( $BMI < 28 \text{ kg/m}^2$ ), did not smoke, did not have a history of alcohol and/or substance abuse, and did not have any known psychiatric disorders were included in the study. The exclusion criteria were a history of ocular or pelvic surgery, previous treatments (e.g., photodynamic laser therapy or photocoagulation), the presence of other eye diseases that could affect the retinal microvascular flow (e.g., cataract, diabetic retinopathy, age-related macular degeneration, retinal vein occlusion, glaucoma, or macular epiretinal membrane), refractive error  $> +3.0$  diopters (D) or  $< -3.0$  D spherical equivalent, OCTA image quality below 7/10, and a history of glucocorticoid use.

Complete ophthalmological examinations, including best-corrected visual acuity, refractive error (KR-8900; Topcon, Tokyo, Japan), axial length (Lenstar LS 900, Haag-Streit AG, Switzerland), intraocular pressure (IOP, Full Auto Tonometer TX-F; Topcon), slit lamp examination of the anterior segment, dilated fundus examination, and OCTA imaging

(Optovue RTVue XR 100 Avanti, Freemont, California, USA) were performed in all participants. Color fundus images and autofluorescence images were captured using Visucam NM/FA (Carl Zeiss, Germany). OCTA and other ocular examinations were conducted by the same examiner on the same day, in the morning (8:00 a.m. to 12:00 p.m.) to minimize diurnal variations in retinal and choroidal vessel density (VD). The sexual function of all patients and controls was assessed using the 15-item International Index of Erectile Function-15 (IIEF-15) that evaluates the quality of erectile function within the previous four weeks. The Turkish version of the scale has been previously tested for validity and reliability.[16]

**OCTA** All subjects underwent optical coherence tomography angiography (OCTA) imaging using the RTVue XR100-2 Avanti device (Optovue, Inc., Fremont, CA, USA), which employs the split-spectrum amplitude-decorrelation angiography (SSADA) technique. Image analyses were performed using AngioAnalytics software (version 2018.0.0.14).

A single experienced examiner evaluated all OCTA images. The software automatically segmented full-thickness retinal scans into distinct vascular layers, including the superficial capillary plexus (SCP), deep capillary plexus (DCP), outer retina, and choriocapillaris (CC). It quantified vessel density (VD) in the SCP and DCP, delineated boundaries of these layers, and automatically calculated metrics such as the foveal avascular zone (FAZ) and foveal density (FD). The central circular flow area in both the outer retina and CC was measured and standardized to 3.144 mm<sup>2</sup>. Additionally, choroidal thickness was manually measured on horizontal sections by the same examiner.

The superficial choroidal capillary layer was defined anatomically as the region extending from 10 microns above to 30 microns below Bruch's membrane (BRM), or more broadly as the interface between the retinal pigment epithelium (RPE) and the sclera on horizontal B-scans. To evaluate peripapillary capillary density, high-definition AngioDisc imaging was utilized.

**IIEF-15 assessment:** Male sexual function was evaluated using the International Index of Erectile Function-15 (IIEF-15), which examines five domains—erection quality, orgasmic function, sexual desire, satisfaction with intercourse, and overall sexual satisfaction. Total scores range from 6 to 30, with erectile dysfunction categorized by severity as follows:

- 0–10 points: severe ED
- 11–16 points: moderate ED
- 17–21 points: mild-to-moderate ED
- 22–25 points: mild ED

## RESULTS

In this study, the patient group included 42 patients with chronic CSCR, with a mean age of 48.81 ± 9.65 years (range: 31–78 years), and the control group consisted of 44 healthy males, with a mean age of 44.41 ± 11.94 years (range: 21–72 years). No statistically significant differences were observed between the groups in terms of age or axial length. The demographic data of the patients are shown in Table 1.

**Table 1. Demographic and clinical characteristics of patients with CSCR**

| Variables                                   | Values                             |
|---------------------------------------------|------------------------------------|
| Age (years)<br>mean ± SD                    | 48.81 ± 9.65                       |
| Visual acuity (LogMAR)<br>mean ± SD         | 0.168 ± 0.482                      |
| IOP (mmHg)<br>mean ± SD                     | 14.33 ± 3.13                       |
| Axial length (mm)<br>mean ± SD              | 23.09 ± 0.70                       |
| Sub-retinal fluid<br>(n) (%)                | (+) 21 (50 %)<br>(-) 21 (50 %)     |
| Intravitreal injection treatment<br>(n) (%) | (+) 22 (52.4 %)<br>(-) 20 (47.6 %) |

CSCR, central serous chorioretinopathy; SD, standard deviation; IOP, intraocular pressure

SCP VD, DCP VD, and FD were statistically significantly lower in the CSCR group ( $p < 0.001$ ). The flow area of the superficial choroid layer in the CSCR group was also significantly lower than in the control group ( $1.86 \pm 0.29$  vs.  $2.12 \pm 0.09$ ,  $p < 0.001$ ). The results are shown in Table 2.

**Table 2. Comparison of MMV measurements between the CSCR and control groups**

|            |                                                                     | CSCR group (n = 42)<br>(mean ± SD) | Control group (n = 44)<br>(mean ± SD) | p value |
|------------|---------------------------------------------------------------------|------------------------------------|---------------------------------------|---------|
| SCP VD (%) | Whole                                                               | 45.73 ± 3.46                       | 50.08 ± 2.37                          | < 0.001 |
|            | Foveal                                                              | 17.69 ± 6.93                       | 19.40 ± 6.35                          | 0.199   |
|            | Parafoveal                                                          | 48.41 ± 3.48                       | 52.81 ± 2.53                          | < 0.001 |
| DCP VD (%) | Whole                                                               | 48.26 ± 4.79                       | 53.06 ± 4.25                          | < 0.001 |
|            | Foveal                                                              | 30.27 ± 7.97                       | 36.14 ± 6.88                          | 0.001   |
|            | Parafoveal                                                          | 50.04 ± 5.10                       | 55.37 ± 3.90                          | < 0.001 |
|            | FAZ area in full retinal vasculature (mm <sup>2</sup> )             | 0.31 ± 0.13                        | 0.29 ± 0.10                           | 0.488   |
|            | FAZ perimeter (mm)                                                  | 2.16 ± 0.61                        | 2.10 ± 0.38                           | 0.213   |
|            | Foveal density (%)                                                  | 46.94 ± 5.44                       | 53.47 ± 3.31                          | < 0.001 |
|            | 1-mm CCFA (mm <sup>2</sup> )                                        | 1.86 ± 0.29                        | 2.12 ± 0.09                           | < 0.001 |
|            | Non-flow area in superficial retinal vasculature (mm <sup>2</sup> ) | 0.51 ± 0.21                        | 0.49 ± 0.13                           | 0.883   |

MMV, macular microvascular; CSCR, central serous chorioretinopathy; SD, standard deviation; SCP, superficial capillary plexus; DCP, deep capillary plexus; VD, vessel density; FAZ, foveal avascular zone; CCFA, choriocapillaris flow area

In the CSCR group, severe ED was diagnosed in three (5.2%) patients, moderate ED in 10 (17.2%), mild-to-moderate ED in seven (12.1%), and mild ED in 15 (25.9%), while no cases of severe or moderate ED were diagnosed in the control group. The results are shown in Table 3.

Table 3 Comparison of the CSCR and control groups according to the presence of ED

| ED                  | CSCR group (n = 42) | Control group (n = 44) | p value* |
|---------------------|---------------------|------------------------|----------|
| Severe ED           | 1                   | 0                      | 0,04     |
| Moderate ED         | 5                   | 0                      |          |
| Mild-to-moderate ED | 5                   | 5                      |          |
| Mild ED             | 11                  | 4                      |          |
| No ED               | 20                  | 35                     |          |

\*Fisher's exact test, CSCR, central serous chorioretinopathy; ED, erectile dysfunction

Further analysis of the data obtained from the CSCR group showed no significant differences in SCP VD, DCP VD, or CC between patients with and without ED ( $p = 0.302$ ,  $p = 0.064$ , and  $p = 0.970$ , respectively). The results are shown in Table 4.

Table 4. Comparison of MMV measurements between patients with and without ED in the CSCR group

|                                                        |            | ED-positive patients with CSCR (n = 22) (mean $\pm$ SD) | ED-negative patients with CSCR (n = 20) (mean $\pm$ SD) | P value |
|--------------------------------------------------------|------------|---------------------------------------------------------|---------------------------------------------------------|---------|
| SCP VD (%)                                             | Whole      | 45.39 $\pm$ 3.49                                        | 46.10 $\pm$ 3.49                                        | 0.302   |
|                                                        | Foveal     | 16.64 $\pm$ 6.57                                        | 18.84 $\pm$ 7.30                                        | 0.413   |
|                                                        | Parafoveal | 48.06 $\pm$ 3.77                                        | 48.79 $\pm$ 3.20                                        | 0.419   |
| DCP VD (%)                                             | Whole      | 47.24 $\pm$ 3.96                                        | 49.39 $\pm$ 5.45                                        | 0.064   |
|                                                        | Foveal     | 29.07 $\pm$ 7.58                                        | 31.59 $\pm$ 8.38                                        | 0.427   |
|                                                        | Parafoveal | 48.93 $\pm$ 4.65                                        | 51.20 $\pm$ 5.41                                        | 0.049   |
| FAZ area in full retinal vasculature (mm2)             |            | 0.33 $\pm$ 0.15                                         | 0.29 $\pm$ 0.10                                         | 0.542   |
| FAZ perimeter (mm)                                     |            | 2.28 $\pm$ 0.56                                         | 2.04 $\pm$ 0.66                                         | 0.440   |
| Foveal density (%)                                     |            | 45.89 $\pm$ 5.53                                        | 48.09 $\pm$ 5.25                                        | 0.155   |
| Outer retina flow area (mm2)                           |            | 0.45 $\pm$ 0.27                                         | 0.50 $\pm$ 0.52                                         | 0.442   |
| 1-mm CCFA (mm2)                                        |            | 1.85 $\pm$ 0.29                                         | 1.87 $\pm$ 0.30                                         | 0.970   |
| Non-flow area in superficial retinal vasculature (mm2) |            | 0.55 $\pm$ 0.24                                         | 0.46 $\pm$ 0.15                                         | 0.242   |

CSCR, central serous chorioretinopathy; SD, standard deviation; SCP, superficial capillary plexus; DCP, deep capillary plexus; VD, vessel density; FAZ, foveal avascular zone; CCFA, choriocapillaris flow area

In terms of radial peripapillary capillary VD, the density values of the whole area all vessels, whole area small vessels, peripapillary area all vessels, and peripapillary area small vessels were significantly lower in the CSCR group with ED ( $p = 0.050$ ,  $p = 0.051$ ,  $p = 0.039$ , and  $p = 0.029$ , respectively). Peripapillary thickness was also significantly lower in the ED-positive group ( $p = 0.001$ ). The results are shown in Table 5.

Table 5 Comparison of RNFL and RPC measurements between patients with and without ED in the CSCR group

|     |                 |                                   | ED-positive patients with CSCR (n = 22) (mean $\pm$ SD) | ED-negative patients with CSCR (n = 20) (mean $\pm$ SD) | P value |
|-----|-----------------|-----------------------------------|---------------------------------------------------------|---------------------------------------------------------|---------|
| ONH | RNFL ( $\mu$ m) | Peripapillary thickness           | 111.32 $\pm$ 13.68                                      | 118.63 $\pm$ 13.04                                      | 0.001   |
|     |                 | Superior thickness                | 123.36 $\pm$ 14.58                                      | 140.84 $\pm$ 14.58                                      | 0.108   |
|     |                 | Temporal thickness                | 79.18 $\pm$ 22.84                                       | 76.32 $\pm$ 6.63                                        | 0.373   |
|     |                 | Inferior thickness                | 144.18 $\pm$ 25.63                                      | 148.11 $\pm$ 22.42                                      | 0.360   |
|     |                 | Nasal thickness                   | 101.86 $\pm$ 19.77                                      | 110.95 $\pm$ 21.34                                      | 0.113   |
| RPC | VD (%)          | Whole area, all vessels           | 55.95 $\pm$ 2.35                                        | 57.57 $\pm$ 2.37                                        | 0.050   |
|     |                 | Peripapillary area, all vessels   | 57.89 $\pm$ 2.45                                        | 59.81 $\pm$ 2.76                                        | 0.039   |
|     |                 | Inside-disc area, all vessels     | 59.86 $\pm$ 3.73                                        | 59.43 $\pm$ 4.79                                        | 0.896   |
|     |                 | Whole area, small vessels         | 49.30 $\pm$ 2.25                                        | 50.82 $\pm$ 2.34                                        | 0.051   |
|     |                 | Peripapillary area, small vessels | 51.23 $\pm$ 2.27                                        | 53.25 $\pm$ 2.97                                        | 0.029   |
|     |                 | Inside-disc area, small vessels   | 49.11 $\pm$ 4.40                                        | 48.73 $\pm$ 5.69                                        | 0.784   |

RNFL, retinal nerve fiber layer; CSCR, central serous chorioretinopathy; RPC, radial peripapillary capillary; ONH, optic nerve head; SD, standard deviation; VD, vessel density

DISCUSSION

The limitations of our study include its single-center design, the inclusion of only male participants, and its cross-sectional nature. However, the findings of the present study revealed that macular microvascular parameters were significantly reduced in the CSCR group compared with the control cohort. Consistent with our results, earlier investigations utilizing laser Doppler flowmetry have also demonstrated a marked decline in choroidal blood flow in eyes affected by CSCR relative to their unaffected fellow eyes.[18]

Within the CSCR patient population, comparative analysis indicated no statistically significant differences between patients with and without erectile dysfunction (ED) regarding superficial capillary plexus (SCP) vessel density, deep capillary plexus (DCP) vessel density, or choroidal thickness (CT). In contrast, individuals with concurrent ED exhibited notably diminished radial peripapillary capillary vessel density values—including total vessel area, small vessel area, peripapillary total area, and peripapillary small vessel area—with corresponding p-values of 0.050, 0.051, 0.039, and 0.029, respectively. Moreover, peripapillary retinal thickness was significantly lower among ED-positive patients ( $p = 0.001$ ). These microvascular alterations may reflect generalized endothelial compromise. Supporting this, Blumentals et al. documented a 75% increased likelihood of peripheral vascular disease in men with ED.[13] Both conditions share several predisposing factors—such as advancing age, hypertension, diabetes mellitus, hyperlipidemia, and tobacco use—all of which can impair nitric oxide (NO) bioavailability within vascular and penile tissues. The resultant NO dysregulation is proposed as a unifying mechanism linking ED with systemic vascular pathology.[13]

In a population-based study, Tsai et al. further observed that men diagnosed with CSCR had a significantly higher risk of developing ED compared with those without CSCR, even

after adjustment for demographic and comorbid variables. This observation supports the hypothesis that pathogenic mechanisms driving CSCR may concurrently contribute to erectile dysfunction.<sup>14</sup>

The underlying mechanisms responsible for choroidal thickening in CSCR are yet to be fully delineated. Given that choroidal vasculature is modulated by the autonomic nervous system, systemic influences likely contribute to the hyperperfusion characteristic of the disease. Identifying systemic abnormalities in CSCR patients may therefore help elucidate its pathophysiology. Previous reports have implicated several systemic contributors—including male gender, psychological stress, and corticosteroid exposure—in disease development.[19] The vasoconstrictive potential of glucocorticoids on retinal microvessels offers a plausible explanation for these associations. Experimental data indicate that topical or systemic glucocorticoid administration can induce vascular constriction, promote platelet aggregation, and elevate blood viscosity, predisposing to microthrombosis. Consistently, elevated circulating glucocorticoid levels have been detected in patients with CSCR.[20]

It has been proposed that excess endogenous cortisol disrupts RPE and choroidal vascular integrity, leading to capillary fragility, hyperpermeability, and subsequent subretinal fluid leakage.[21] The interplay of heightened catecholamine levels and sympathetic overactivity—often seen in individuals with sleep disorders—may further exacerbate choroidal vascular instability. Conversely, psychosocial stress, a recognized precipitant of CSCR, could itself increase the risk of sleep dysregulation.[17] Despite these insights, data on endothelial function in CSCR remain scarce, underscoring the need for further studies to clarify the contribution of systemic endothelial dysfunction to the disease process.

In summary, our results demonstrate a significant association between OCTA parameters and the presence of ED in patients with CSCR. These findings suggest that vascular and endothelial mechanisms implicated in CSCR may also underlie erectile impairment. Nevertheless, additional prospective, large-scale studies are required to confirm this association and to elucidate the shared pathophysiological pathways between ocular and systemic vascular dysfunction.

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