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ORIGINAL PAPER

Evaluation of ophthalmic vascular and neural structures in female patients with fibromyalgia syndrome and their relationship with disease severity

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Abstract

Purpose This study aimed to evaluate choroidal and macular thickness, as well as vascular structures in female fibromyalgia syndrome (FMS) patients using optical coherence tomography angiography (OCTA) and optical coherence tomography (OCT), and to compare the results with healthy controls. Additionally, the relationship between these findings and disease severity was explored.

Methods The study included 62 female FMS patients and 60 healthy controls, conducted between January 2022 and October 2022 at the Antalya Training and Research Hospital. FMS patients were assessed based on American College of Rheumatology criteria. Tear production and stability were evaluated using Schirmer and Tear Break-Up Time (TBUT) tests, while OCTA and OCT were used to examine vascular and choroidal structures.

Results The mean age of the FMS group was 43.11 ± 7.94 years. No significant difference was found in the Schirmer test, but the TBUT was significantly lower in the FMS group ($p < 0.001$). OCTA showed significantly lower deep capillary plexus (DCP) values in the FMS group, with a weak negative correlation between DCP and disease severity ($r = -0.227$, $p = 0.012$). Foveal avascular zone (FAZ), non-flow, and choroidal thickness were significantly higher in FMS patients ($p < 0.050$).

Conclusion The study demonstrated a relationship between dry eye, vascular changes, and increased choroidal thickness with disease severity in female patients with FMS. The reduction in DCP, along with increases in FAZ, non-flow, and choroidal thickness, may be linked to vascular and inflammatory processes involved in FMS pathogenesis. The decrease in tear quality may be due to autonomic nervous system dysfunction. In conclusion, we suggest that autonomic dysfunction and inflammation in FMS may negatively affect retinal vascular structures and tear function.

Keywords Fibromyalgia · Optical coherence tomography · Choroidal thickness · Vascular changes · Dry eye

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Introduction

Fibromyalgia syndrome (FMS) is a chronic condition characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive dysfunction. Its prevalence ranges from 0.2 to 6.6%, occurring 6–9 times more frequently in women than in men [1, 2]. The pathophysiology of FMS involves central and peripheral sensitization, sympathetic dysfunction, neuroendocrine and autonomic system abnormalities, and psychosocial factors [3]. Central nervous system involvement in FMS may also lead to visual pathologies [4]. Symptoms such as dry eye, photopsia, diplopia, and blurred vision are commonly reported [5]. Dry eye in FMS may result from decreased corneal sensitivity, leading to reduced tear secretion, and suppression of tear film layer osmolarity following ocular surface inflammation [6, 7]. In one study, 20–35% of FMS patients reported dry eye symptoms [8].

Perfusion anomalies in the brain, vascular changes in the thalamus and caudate nucleus, optic nerve involvement, and neuroretinal changes have been reported in FMS. Axonal loss in the retinal nerve fiber layer (RNFL) has been observed in various neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, and Alzheimer's disease [4]. Garcia-Martin et al. observed significant thinning of the RNFL in FMS patients, suggesting the presence of neurodegenerative processes in this condition [9].

Choroidal thickness is influenced by various systemic and local factors, particularly inflammatory and vascular mechanisms [10]. Inflammatory rheumatologic diseases, such as Behçet's disease, ankylosing spondylitis, and psoriasis, have been associated with increased choroidal thickness, likely due to elevated pro-inflammatory cytokines (e.g., IL-6, TNF-α), which disrupt the blood-retinal barrier and increase vascular permeability [11–13]. In contrast, Ulusoy et al. reported reduced choroidal thickness in FMS patients, associating this finding with disease activity and suggesting that autonomic nervous system dysfunction may contribute to these choroidal changes [14].This variability in findings across studies indicates that autonomic dysfunction in FMS may manifest differently among patients, with alterations in sympathetic activity potentially influencing choroidal perfusion. These diverse mechanisms underscore the complex interplay of inflammation, vascular changes, and autonomic regulation in choroidal structural alterations observed in systemic conditions.

The imbalance between the sympathetic and parasympathetic nervous systems in FMS, along with changes in neurotransmitter and catecholamine concentrations, may affect ocular vascular perfusion [15]. Optical coherence tomography angiography (OCTA) plays a crucial role in evaluating neuroretinal, retinal, and choroidal vascular structures. In this study, based on potential vascular and inflammatory changes in FMS pathogenesis, we aimed to compare macular and choroidal thickness and vascular structures in female FMS patients, assessed by OCTA and optical coherence tomography (OCT), with healthy controls, and to explore the relationship between these findings and disease severity.

Methods

Patient selection

This study was designed as a single-center, prospective, cross-sectional study conducted in the Department of Physical Medicine and Rehabilitation at the University of Health Sciences (UHS) Antalya Training and Research Hospital. Before starting the study, ethical approval was obtained from the Clinical Research Ethics Committee of Antalya Training and Research Hospital (approval number 2/15, dated 20.01.2022). The study was conducted in accordance with the principles of the 2013 Declaration of Helsinki. Informed consent forms were signed by the patients.

Between January 2022 and October 2022, 62 newly diagnosed female patients with FMS aged 18–65 years who visited the Physical Medicine and Rehabilitation outpatient clinic of UHS Antalya Training and Research Hospital were included in the patient group, along with 60 healthy female individuals of the same age group without any additional systemic diseases, who were selected as the control group. The diagnosis of FMS was made according to the 2016 revised criteria of the American College of Rheumatology (ACR). Widespread pain was defined as pain in at least 4 out of 5 body regions:

the right and left sides of the body (jaw, shoulder, upper arm, forearm, hip, upper leg, lower leg) and the axial region (neck, back, lower back, chest, and abdomen), with pain lasting continuously for the past seven days. The widespread pain index (WPI) score was calculated between 0 and 19. The symptom severity scale (SSS) assessed fatigue, unrefreshed sleep, and cognitive symptoms over the past week, with a score from 0 to 3 (0 = no problem, 1 = mild, 2 = moderate, 3 = severe). The presence of headaches, lower abdominal pain/cramps, and depression in the past six months was also evaluated (0 = no, 1 = yes). The total score was calculated. A WPI score of ≥ 7 and an SSS score of ≥ 5, or a WPI score of 4–6 and an SSS score of ≥ 9, met the FMS diagnostic criteria. The fibromyalgia severity scale (FSS) was calculated by summing the WPI and SSS scores.

Exclusion criteria included patients who had previously received or were receiving treatment for FMS; those with systemic, neurodegenerative, or rheumatologic diseases (rheumatoid arthritis, vasculitis, diabetes mellitus, hypertension, etc.); patients with spherical refractive errors outside the range of -3 to + 3 diopters or astigmatic refractive errors greater than 3 diopters; patients with retinal vascular pathologies such as diabetic retinopathy or retinal vein occlusion; patients with macular diseases such as senile macular degeneration or macular dystrophy; those with a history of uveitis, glaucoma, or optic nerve disease, or who had undergone ocular surgery or trauma; and participants with poor image quality due to movement artifacts or other factors, resulting in a signal quality score of less than 6/10.

All participants underwent refraction assessment with an autorefractometer (Nidek AR600A, Nidek Co., Japan), intraocular pressure measurement with a pneumatic tonometer (Nidek NT-2000 NCT, Nidek Co. Ltd., Hiroishi Gamagori, Aichi, Japan), and visual acuity evaluation. Anterior segment and fundus structures were assessed by biomicroscopic examination.

OCTA evaluation

OCTA is a non-invasive, rapid imaging method that provides a cross-sectional in vivo image of the dynamic microvascular system of the choroid and retina. In the OCT and OCTA imaging of the patients, the "Spectral-domain OCTA" (AngioVue; Optovue, Inc, Fremont, CA) device was used. OCTA measurements of the patient were performed at 6 × 6 mm HD angio retina and 4.5 × 4.5 mm angio disk scans. Images with poor quality due to motion artefact and other artefacts were not included in the study. Images with a signal quality greater than 8/10 were assessed. Foveal vascular density (FVD) was recorded as % of the vascular density in 1 mm diameter circle centered on fovea, parafoveal vascular density (PAFVD) was recorded as % of the vascular density in the circle from 1 to 3 mm, perifoveal vascular density (PEFVD) was recorded as % of the vascular density in the ring from 3 to 6 mm, and the total vascular density (TVD) was recorded as % of vascular density in 6 mm diameter circle centered on fovea. These areas provided the cross-sectional density measurement of the superfcial capillary area in automated mode Figs. 1, 2. The ratio of the vascular image in these areas (white areas) to the whole area provides the percentage of density. Foveal avascular zone (FAZ) was automatically calculated by the device; outer retinal flow (ORF) and choriocapillaris flow (CCF) automatically determined by the device were recorded as fow in mm^2 in the area with a central radius of 1 mm and area of 3.142 mm^2. Retinal nerve fiber thickness (RNFL) was measured and recorded automatically by the device on 3.4 mm diameter scanning circle centered on the optic disc Fig. 3. Retinal thickness: The retinal thickness between ILM and RPE in foveal, parafoveal and perifoveal zones was automatically measured and recorded by the device Fig. 4. Choroidal thickness: 2 diferent observers measured the subfoveal zone at "Enhanced HD line" cross-section. The average of values measured by the 2 observers was calculated Fig. 5. The RPE and sclerachoroidal junction was the border of subfoveal choroidal thickness.

Evaluation of schirmer and tear break-up time tests

The Schirmer test is a method used to measure tear quantity and aqueous production. A 5 mm wide and 35 mm long Whatman filter paper was used without local anesthesia. It was placed at the junction of the middle one-third and outer one-third of the lower eyelid. After five minutes, the amount of wetting on the filter paper was measured. When evaluated for dry eye, values between 0 and 5 mm were considered low, between 5 and 10 mm were suspicious, and values

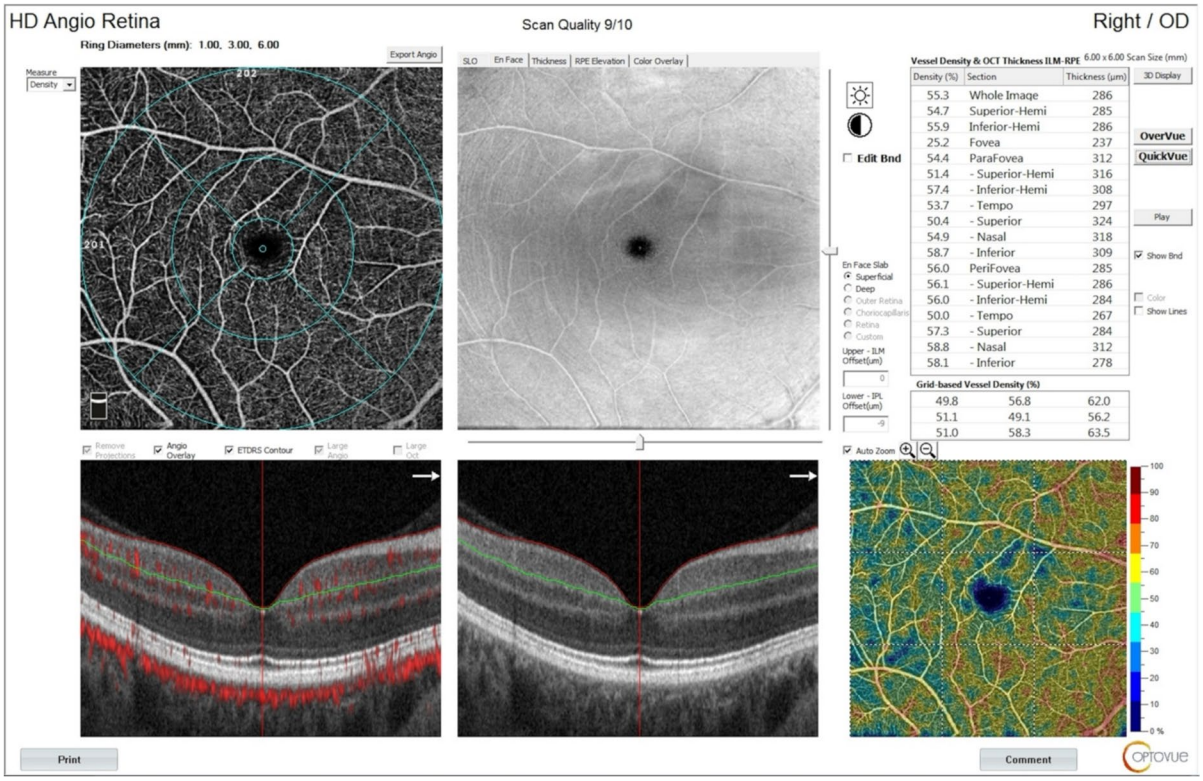


Fig. 1 Superficial vascular density assessment using optical coherence tomography angiography (OCTA)

above 10 mm were considered normal. A wetting measurement below 5 mm was regarded as significant for aqueous tear deficiency.

The Tear Break-Up Time (TBUT) test is a method used to evaluate tear stability. The patients' tears were stained using fluorescein-impregnated strips without topical anesthesia. The patient was instructed to blink once to allow the dye to spread across the ocular surface. The evaluation was performed using a wide light with a cobalt blue filter on a biomicroscope. The time between blinking and the first break in the dye on the ocular surface was measured. The test was repeated three times, and the average was taken; a time of less than 10 s was considered significant for dry eye.

All these procedures were performed by the same ophthalmologist. Measurements were made for both eyes; however, only the data obtained from the right eye were used for statistical analysis.

Statistical analysis

Descriptive statistics were presented using frequency, percentage, mean, standard deviation, median, 25th percentile, 75th percentile, minimum, and maximum values. In the analysis of categorical data, if the percentage of cells with expected values less than 5 was greater than 20%, Fisher's Exact Test was used; otherwise, Pearson Chi-Square Test was employed. The normality assumption was checked using the Kolmogorov–Smirnov Test. For the analysis of the difference between numerical data of the two groups, if the data followed a normal distribution, the Independent Samples t-test was used; if not, the Mann–Whitney U Test was applied. Relationships between numerical data were evaluated using the non-parametric Spearman Correlation Test and the parametric Pearson Correlation Test. Analyses were performed using SPSS version 23.0, and a p-value of less than 0.05 was considered statistically significant.

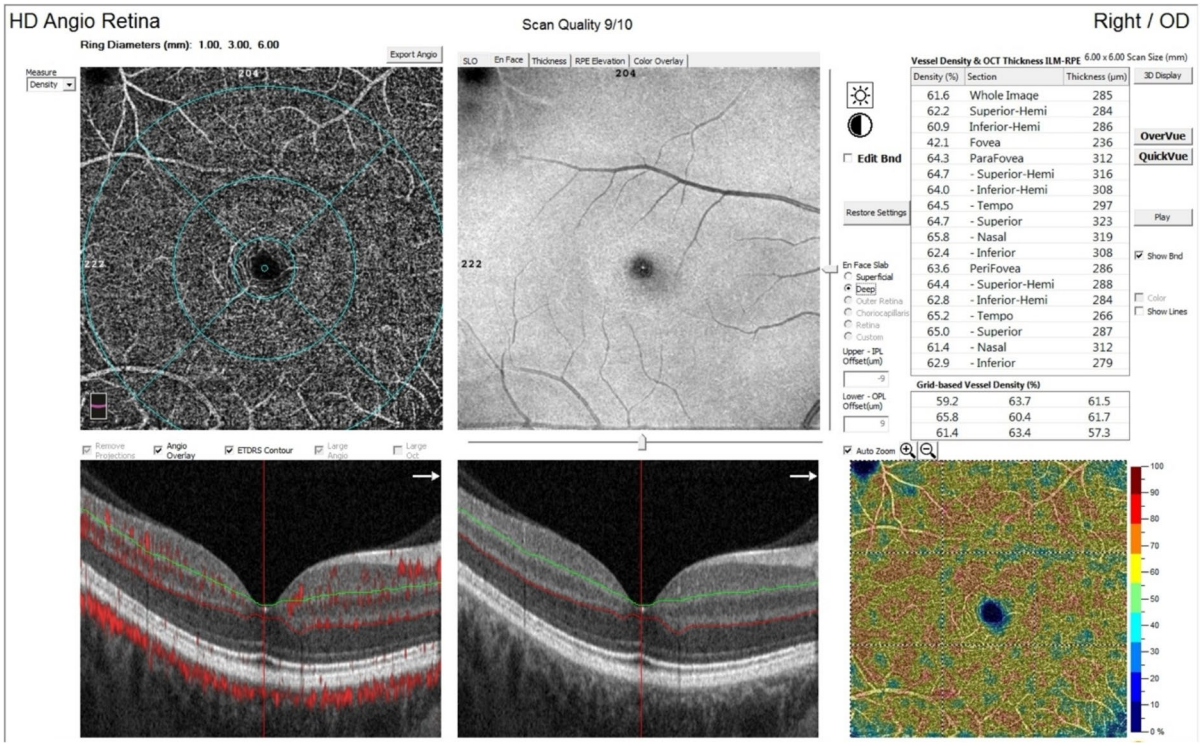


Fig. 2 Deep vascular density assessment using optical coherence tomography angiography (OCTA)

Result

A total of 62 women with FMS had a mean age of 43.11 ± 7.94 years (range: 19–59), while the healthy control group consisted of 60 women with a mean age of 40 ± 12.26 years (range: 18–64). The mean duration of the disease in the FMS group was 5.08 ± 3.97 years (range: 1–17). There was no statistically significant difference between the groups in terms of age and body mass index (BMI). The WPI score, SSS and FSS were significantly higher in the FMS group ($p < 0.001$). While there was no statistically significant difference between the groups in the Schirmer test, the TBUT test was significantly lower in the FMS group ($p < 0.001$) Table 1.

Table 2 shows the comparison between vascular densities in the superficial capillary plexus (SCP) and deep capillary plexus (DCP), as well as the foveal avascular zone (FAZ), choriocapillaris flow (CCF), outer retinal flow (ORF), and non-flow values of FMS patients and controls. In patients evaluated with OCTA, there were no statistically significant differences between the groups in the SCP TVD, SCP FVD, SCP PAFVD and SCP PEFVD parameters ($p > 0.050$). However, the DCP TVD, DCP FVD, DCP PAFVD and DCP PEFVD parameters were significantly lower in the FMS group ($p < 0.050$). While there were no statistically significant differences between the groups in CCF and ORF values ($p > 0.050$), the FAZ and non-flow parameters were found to be significantly higher in the FMS group ($p < 0.050$) Table 2.

Table 3 presents the comparison of OCT findings between the FMS and control groups. There was no statistically significant difference between the groups in RNFL, TRFT, TRPAFT, and TRPEFT values ($p > 0.050$); however, the choroidal thickness parameter was found to be significantly higher in the FMS group ($p < 0.050$) Table 3.

In the correlation examined between FMS severity and OCTA values, there is a statistically significant, weak negative relationship between DCP TVD and DCP PAFVD ($r = -0.227$, $p = 0.012$; $r = -0.192$, $p = 0.034$) Table 4

While there is a statistically significant, weak positive correlation between FMS severity and

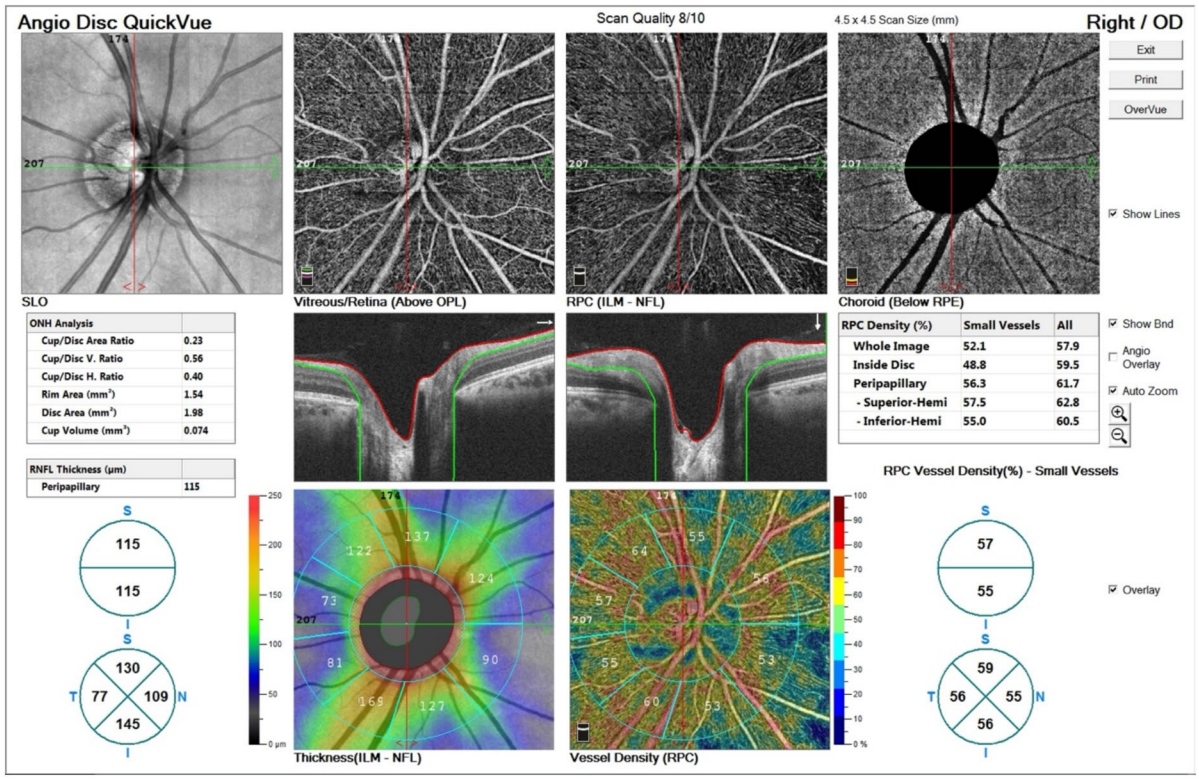


Fig. 3 Retinal nerve fiber layer (RNFL) thickness assessment using optical coherence tomography (OCT)

choroidal thickness ($r = 0.211$, $p = 0.02$), there is a weak negative correlation with the TBUT test ($r = -0.250$, $p = 0.005$) Table 5 No statistically significant relationship was found between FMS severity and other variables ($p > 0.050$) Tables 4 and 5.

Discussion

The abnormal sympathetic hyperactivity playing a role in the pathogenesis of FMS has been shown to lead to long-term disruption of blood pressure regulation, triggering endothelial dysfunction and vascular wall sclerosis, ultimately resulting in vasoconstriction and choroidal ischemia [16–18]. It has been suggested that this decrease in blood perfusion may be related to changes in the function of the autonomic nervous system. Numerous potential pathogenic mechanisms, such as the roles of inflammation and glial cell activation, are actively being investigated in the pathogenesis of FMS [19].

The lacrimal gland is one of the target tissues in rheumatic diseases and can become dysfunctional due to lymphocytic infiltration. This condition can adversely affect tear production and the stability of the tear film, leading to disruptions in ocular surface homeostasis [20, 21]. Additionally, autonomic innervation of the cornea and periocular structures plays a role in regulating tear film secretion. Kötter et al. have demonstrated that the lacrimal gland can be affected in patients with FMS, similar to other rheumatic diseases [22]. Enríquez et al. suggested that inflammatory cytokines playing a role in the pathophysiology of FMS may be effective in suppressing tear osmolarity [23]. In a study by Tezel et al., investigating the prevalence of dry eye in individuals with FMS, TBUT values were found to be significantly lower in the FMS group, whereas no differences were detected in Schirmer test results between groups [24]. Similarly, Schuster et al. did not find a significant difference in Schirmer test results when assessing patients with FMS compared to the control group [25]. In our study, similarly, no

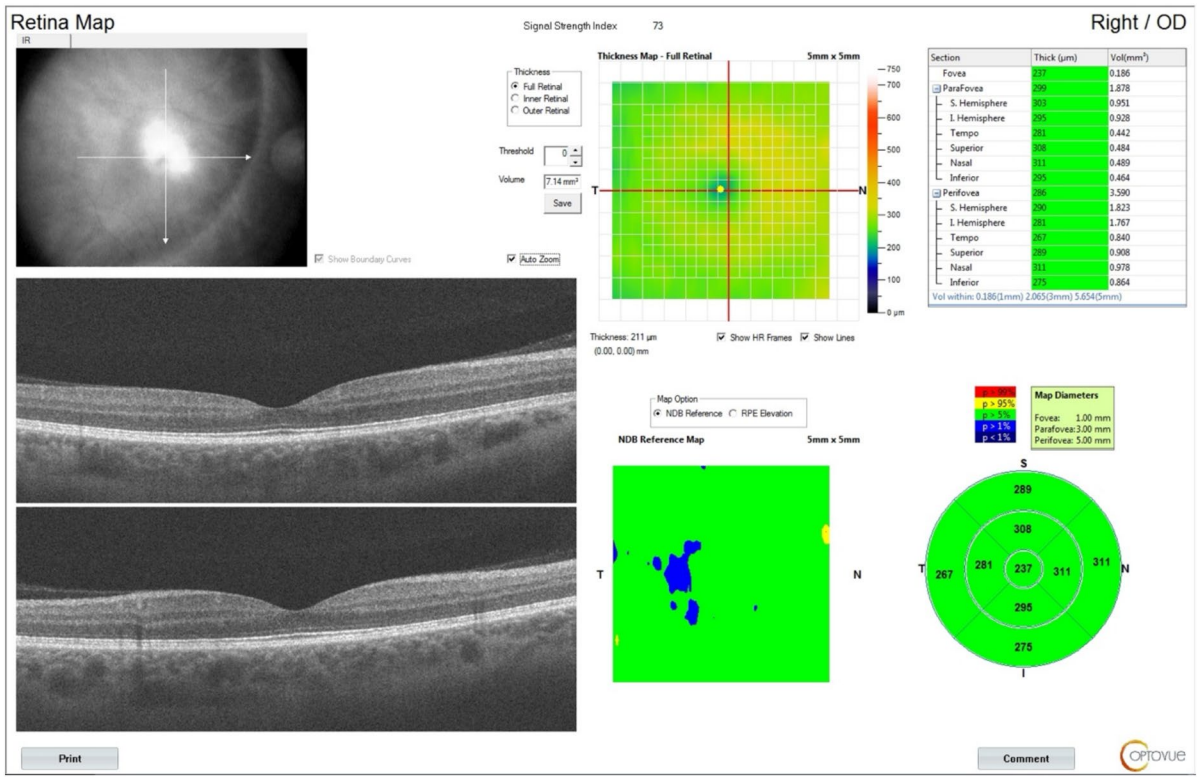


Fig. 4 Retinal thickness assessment using optical coherence tomography angiography (OCTA)

significant difference was found in Schirmer test results between individuals with FMS and the control group, while TBUT values were significantly lower in the FMS group, and it was observed that TBUT results significantly decreased as disease severity increased. Our findings suggest that the dysfunction of the autonomic nervous system observed in the pathogenesis of FMS affects the neural regulation of the lacrimal glands, leading to a decline in tear quality without directly impacting tear quantity. Additionally, chronic inflammation in FMS may disrupt the lipid and mucus layers of the tear film, resulting in more pronounced findings in TBUT, while not affecting the Schirmer test in the same manner.

In our study, the aim was to assess the macula and choroidal structures in female patients with FMS and to investigate their relationship with disease severity. Zhang et al. demonstrated changes in the retinal microvascular network in individuals with amnestic-type mild cognitive impairment, showing significant reductions in SCP and DCP vessel densities, in addition to decreased blood flow [26]. The authors also showed that parafoveal and peripapillary densities had a positive correlation with low scores on the Montreal Cognitive Assessment (MoCA). In a study by Bulut et al. it was shown that retinal vascular pathologies exhibited significantly lower retinal vascular density in all regions on patients with Alzheimer's-type dementia compared to healthy controls [27]. Both studies observed a reduction in retinal vessel density and a decline in blood flow. These findings suggest that in chronic neurodegenerative diseases, vascular problems may be associated with the disruption of the blood–brain barrier and hypoperfusion. Similarly, the observation of vascular changes in chronic conditions like FMS may suggest the presence of disruptions in blood flow and decreases in vessel density, especially at the microvascular level. In our study, while no significant difference was observed in SCP in the FMS group, significant reductions were seen in DCP. Additionally, a weak negative correlation was detected between FMS severity and DCP TVD and DCP PAFVD. In

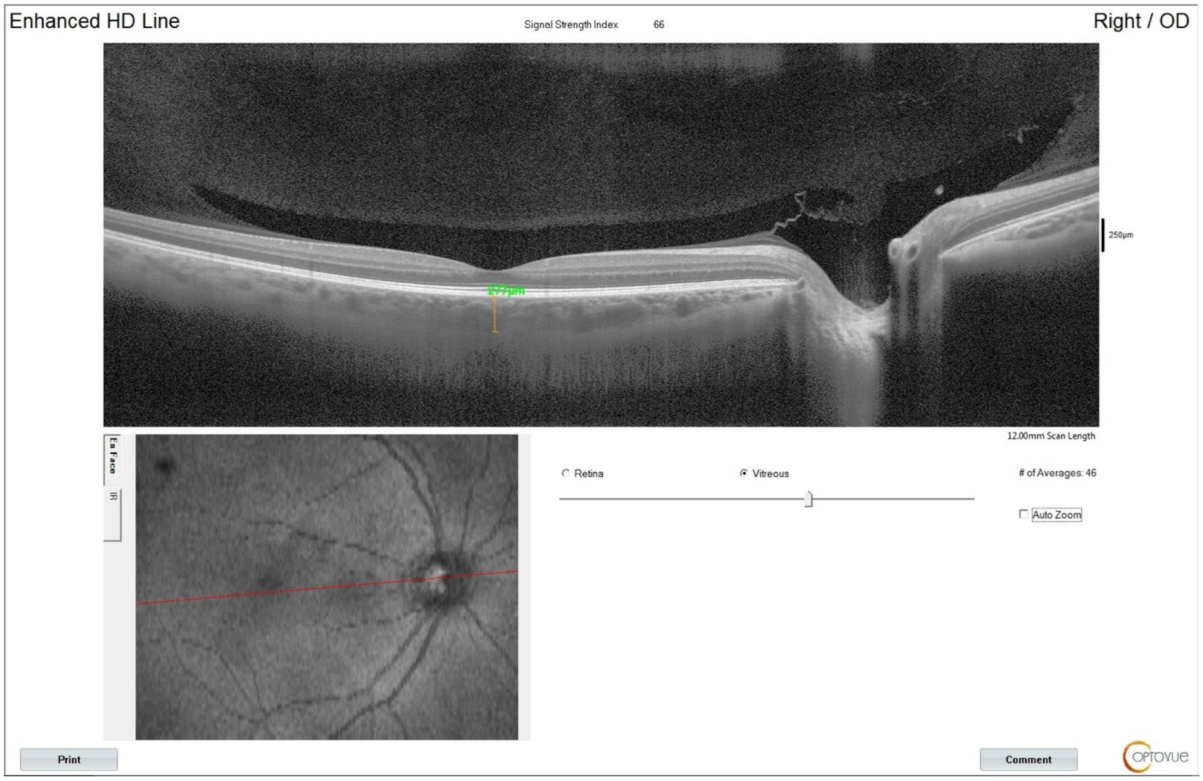


Fig. 5 Choroidal thickness assessment using optical coherence tomography (OCT)

another study conducted by Bulut et al. on Familial Mediterranean fever (FMF) patients, similar results were reported. The authors found that there was no significant change in SCP compared to the control group, while a significant reduction was observed in DCP. Also a weak negative correlation was found between disease duration and DCP structures on FMF patients [28]. We believe that the increase in inflammation in these rheumatological diseases may lead to disrupted blood pressure regulation, endothelial dysfunction, and vasoconstriction in the vascular walls, which may be linked to a decrease in capillary plexus density.

The differing responses of SCP and DCP in FMS may be attributed to their distinct anatomical and functional properties [29]. The SCP, which primarily supplies the inner retina, possesses a robust autoregulatory mechanism mediated by pericytes and endothelial cells, allowing it to maintain relatively stable blood flow despite systemic or local inflammatory processes [30]. In contrast, the DCP is more vulnerable to hemodynamic disturbances due to its reliance on choroidal circulation and its direct connection to larger vasculature [31]. This anatomical relationship exposes the DCP to greater fluctuations in perfusion pressure, rendering it more susceptible to ischemia, hypoxia, and inflammatory damage [32]. The negative correlation between disease severity and DCP density further supports this hypothesis, suggesting that vascular impairment in FMS primarily affects the deeper retinal layers.

Changes in pro-inflammatory cytokines and chemokines playing a role in the pathogenesis of FMS have been reported [33]. In our study, an increase in choroidal thickness values was noted. We thought that the significant correlations with FMS severity could be attributed to the increase in inflammation in FMS patients and the subsequent increase in vascular permeability. Similarly, in a study conducted by Ağın et al., an increase in choroidal thickness was found in children with

Table 1 Demographic and clinical characteristics of fibromyalgia syndrome (FMS) patients and healthy controls

Parameters	Group (n)	Mean ± SD (Min.-Max)	Median (Q1-Q3)	P
Mean age, (years)	FMS (n = 62)	43.11 ± 7.94(19–59)	43(39–49)	0.182[2]
	Control (n = 60)	40 ± 12.26(18–64)	40(28.5–49.5)	
BMI (kg/m^2)	FMS (n = 62)	26.01 + 4.26(16.42–35.25)	25.62(23.53–28.91)	0.151[1]
	Control (n = 60)	24.95 ± 4.49(16.42–35.25)	24.53(21.64–27.99)	
Disease duration (years)	FMS (n = 62)	5.08 ± 3.97 (1–17)	4(1–7)	–
	Control (n = 60)	–	–	
Widespread pain index (WPI) score	FMS (n = 62)	13.5 ± 3.01(8–19)	14(11–15)	***< 0.001***[2]
	Control (n = 60)	0.58 ± 1.08(0–4)	0(0–1)	
Symptom Severity Scale (SSS)	FMS (n = 62)	9.39 ± 1.96(5–12)	10(8–11)	***< 0.001***[2]
	Control (n = 60)	0.53 ± 1.08(0–4)	0(0–0.5)	
The fibromyalgia severity scale (FSS)	FMS (n = 62)	22.92 ± 4.15(15–31)	23.5(20–25)	***< 0.001***[2]
	Control (n = 60)	1.12 ± 2.03(0–6)	0(0–2)	
Schirmer test (mm)	FMS (n = 62)	17.19 ± 9.65(3–35)	16.5(8–24)	0.437[2]
	Control (n = 60)	18.33 ± 8.72(3–36)	17(12–24)	
TBUT test (s)	FMS (n = 62)	7.76 ± 4.28(3–19)	6(5–12)	***< 0.001***[2]
	Control (n = 60)	10.47 ± 3.87(4–18)	11(8–13)	

Bolditalic values indicate statistically significant results ($p < 0.05$)

SD: Standard deviation, Q1: 25th percentile, Q3: 75th percentile, FMS: Fibromiyalgia syndrome, BMI: Body Mass Index, TBUT: Tear Break-Up Time

[1]Independent t test

[2]Mann Whitney U test were used

systemic lupus erythematosus compared to the healthy group [34]. Additionally, hypoxia-inducible mechanisms may contribute to this finding. Chronic pain and altered muscle metabolism in FMS can create systemic hypoxia-like conditions, stimulating angiogenesis and vascular remodeling via vascular endothelial growth factor (VEGF) pathways [35, 36]. However, also contrasting findings exist in the literature, suggesting that choroidal structural changes in FMS may be influenced by multiple factors, including individual variations in disease severity, autonomic function, and vascular regulation [14]. These interconnected mechanisms likely contribute collectively to increased choroidal thickness in FMS. Further studies incorporating biomarkers such as VEGF and autonomic function assessments are needed to better elucidate these complex interactions.

The apparent contradiction between the findings of increased choroidal thickness and reduced DCP density can be reconciled by considering the complexity of vascular dynamics and the interplay of multiple pathophysiological mechanisms in FMS.

Firstly, increased vascular permeability and choroidal thickness may primarily reflect the effects of inflammation. Elevated levels of pro-inflammatory cytokines such as IL-6 and TNF-α in FMS can lead to endothelial dysfunction, disruption of the blood-retinal barrier, and subsequent leakage, resulting in increased choroidal thickness [10]. This process is likely to occur in the larger choroidal vasculature, which has a higher capacity for vascular remodeling and is more prone to inflammation-induced changes.

On the other hand, the reduction in DCP density may be driven by different mechanisms, such as ischemia and vasoconstriction. The DCP, as discussed earlier, is particularly sensitive to hemodynamic disturbances due to its lack of autoregulatory smooth muscle cells and its direct communication with larger vascular structures [31]. Chronic ischemia, likely exacerbated by autonomic dysfunction and microvascular dysregulation, may

Table 2 Comparison of optical coherence tomography angiography (OCTA) findings between fibromyalgia syndrome patients and healthy controls

Retinal vasculer density (%)	Group (n)	Mean ± SD (Min.-Max)	Median (Q1-Q3)	P
SCP total vascular density	FMS (n = 62)	51.15 ± 2.93(44.5–59.7)	51.45(49.3–53.6)	0.653[1]
	Control (n = 60)	50.91 ± 3.04(44.1–57.1)	51.3(48.75–52.8)	
SCP foveal vascular density	FMS (n = 62)	17.68 ± 6.79(5.08–34.8)	16.15(13.04–22.5)	0.059[2]
	Control (n = 60)	19.99 ± 7.75(5.8–56.5)	18.8(15.55–24)	
SCP parafoveal vascular density	FMS (n = 62)	52.9 ± 5.16(23.9–61.1)	53.45(51.1–56.1)	0.868[2]
	Control (n = 60)	53.06 ± 3.59(44.5–59)	53.7(50.7–55.8)	
SCP perifoveal vascular density	FMS (n = 62)	51.14 ± 4.74(22.3–60.9)	51.4(50–53.7)	0.705[2]
	Control (n = 60)	51.36 ± 2.96(46.2–57.6)	51.35(49.15–53.7)	
DCP total vascular density	FMS (n = 62)	51.09 ± 5.14(39–61)	51.3(47.2–54.9)	***0.002***[2]
	Control (n = 60)	53.87 ± 5.23(39.1–62.5)	54.8(51.15–56.95)	
DCP foveal vascular density	FMS (n = 62)	34.2 ± 7.42(17.09–49.9)	33.9(28.4–39.6)	***0.019***[1]
	Control (n = 60)	37.28 ± 6.92(20.7–51.3)	37.2(32.9–42.7)	
DCP parafoveal vascular density	FMS (n = 62)	55.52 ± 3.91(44.5–61.6)	56(53.6–58.7)	***0.011***[2]
	Control (n = 60)	57.09 ± 3.94(41–62.6)	57.65(55.35–59.8)	
DCP perifoveal vascular density	FMS (n = 62)	52.81 ± 5.77(37.6–63.1)	52.7(48.9–57)	***0.009***[2]
	Control (n = 60)	55.05 ± 6.28(32.2–63.9)	56.6(52.75–58.75)	
Foveal avascular zone (FAZ) mm^2	FMS (n = 62)	0.34 ± 0.13(0.08–0.77)	0.34(0.25–0.41)	***0.003***[1]
	Control (n = 60)	0.28 ± 0.1(0.06–0.49)	0.30(0.2–0.35)	
Choriocapillaris flow (CCF)	FMS (n = 62)	2.066 ± 0.112(1.781–2.291)	2.074(2.016–2.138)	0.784[2]
	Control (n = 60)	2.071 ± 0.135(1.582–2.29)	2.075(1.992–2.177)	
Outer retina flow (ORF)	FMS (n = 62)	0.6 ± 0.341(0.12–1.571)	0.513(0.367–0.771)	0.786[2]
	Control (n = 60)	0.614 ± 0.332(0.178–1.774)	0.525(0.361–0.793)	
Nonflow	FMS (n = 62)	0.563 ± 0.126(0.268–0.921)	0.596(0.474–0.65)	***0.042***[1]
	Control (n = 60)	0.515 ± 0.132(0.19–0.916)	0.513(0.426–0.583)	

Bolditalic values indicate statistically significant results ($p < 0.05$)

SD: Standard deviation, Q1: 25th percentile, Q3: 75th percentile, FMS: Fibromiyalgia syndrome, SCP: Superficial Capillary Plexus, DCP: Deep Capillary Plexus

[1]Independent *t* test

[2]Mann Whitney U test were used

selectively affect the DCP, leading to capillary dropout and reduced vascular density.

These two processes—choroidal thickening due to inflammation and DCP loss due to ischemia—are not mutually exclusive and may occur simultaneously in FMS.

The findings reflect distinct, yet interconnected processes occurring at different levels of the retinal and choroidal vasculature. Increased choroidal thickness and reduced DCP density represent the combined effects of inflammation, vascular permeability, ischemia, and hemodynamic dysregulation in FMS.

In our study, we found that the FAZ area and non-flow parameters were higher in the FMS group compared to the healthy control group. This can be associated with the dilation of FAZ due to ischemia caused by vascular damage. Consistent with our study findings, Temel et al., shown that the FAZ area was larger in diabetic patients compared to controls due to microvascular changes in the retina [37].

The autonomic dysfunction that arises in the FMS process can negatively affect the function of retinal vessels by causing endothelial damage. This process can lead to reduced blood flow and microvascular damage, thereby causing structural changes in retinal cells. Garcia-Martin et al. demonstrated that there was a reduction in RNFL thickness in patients with FMS, while the vascular density levels in the macular region were similar to those of

Table 3 Comparison of optical coherence tomography (OCT) findings between fibromyalgia syndrome patients and healthy controls

Variables	Group (n)	Mean ± SD (Min.-Max)	Median (Q1-Q3)	*p*
Retinal nerve fiber layer (RNFL) µm	FMS (n = 62)	117.92 ± 11.67(85–145)	117(112–125)	0.162[1]
	Control (n = 60)	114.97 ± 11.51(93–139)	113(106–124)	
Total retinal foveal thickness µm (TRFT)	FMS (n = 62)	244.34 ± 20.88(201–304)	243(231–257)	0.052
	Control (n = 60)	251.42 ± 18.93(218–298)	248(237–266)	
Total retinal parafoveal thickness µm (TRPAFT)	FMS (n = 62)	314.68 ± 22.23(278–447)	313(303–322)	0.665
	Control (n = 60)	314.18 ± 12.76(289–340)	312(305–324)	
Total retinal perifoveal thickness µm (TRPEFT)	FMS (n = 62)	286.74 ± 17.75(189–313)	289.5(280–297)	0.984
	Control (n = 60)	287.78 ± 10.73(262–309)	288(280.5–294.5)	
Choroidal thickness µm	FMS (n = 62)	321.55 ± 62.12(180–569)	316(278–352)	***0.004***[2]
	Control (n = 60)	287.08 ± 46.1(180–379)	298(253–312)	

Bolditalic values indicate statistically significant results ($p < 0.05$)

SD: Standard deviation, Q1: 25th percentile, Q3: 75th percentile, FMS: Fibromiyalgia syndrome

[1]Independent t test

[2]Mann Whitney U test were used

Table 4 The correlation between optical coherence tomography angiography (OCTA) values measured with fibromyalgia syndrome (FMS) severity

Variables	r	p
SCP total vascular density	0.040	0.660
SCP foveal vascular density	−0.108	0.237
SCP parafoveal vascular density	0.042	0.645
SCP perifoveal vascular density	0.044	0.633
DCP total vascular density	**−0.227***	***0.012***
DCP foveal vascular density	−0.112	0.220
DCP parafoveal vascular density	**−0.192***	***0.034***
DCP perifoveal vascular density	−0.173	0.057
Foveal avascular zone (FAZ) mm^2	0.175	0.054
Choriocapillaris flow (CCF)	−0.063	0.487
Outer retina flow (ORF)	0.007	0.941
Nonflow	0.150	0.100

Bold values indicate correlation coefficients (r) with statistically significant *p*-values ($p < 0.05$)

Bolditalic values indicate statistically significant results ($p < 0.05$)

r: Spearman's Rank Correlation Coefficient. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed)

SCP: Superficial Capillary Plexus, DCP: Deep Capillary Plexus

Table 5 The correlation between optical coherence tomography (OCT) measurement thicknesses, Schirmer, and Tear Break-Up Time (TBUT) values with fibromyalgia syndrome (FMS) severity

Variables	**r**	**p**
Retinal nerve fber layer (RNFL) µm	0.146	0.109
Total retinal foveal thickness µm (TRFT)	−0.129	0.155
Total retinal parafoveal thickness µm (TRPAFT)	−0.001	0.989
Total retinal perifoveal thickness µm (TRPEFT)	−0.013	0.885
Choroidal thickness µm	**0.211***	***0.020***
Schirmer test (mm)	−0.017	0.853
TBUT test (s)	**−0.250****	***0.005***

Bold values indicate correlation coefficients (r) with statistically significant *p*-values ($p < 0.05$)

Bolditalic values indicate statistically significant results ($p < 0.05$)

r: Spearman's Rank Correlation Coefficient. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed)

TBUT: Tear Break-Up Time

healthy control subjects [3]. Öztürk et al. found slight differences in TRFT and TRPAFT values in patients with FMS. However, they noted that no significant vascular or neurodegenerative changes were observed compared to healthy controls [15]. In our study, no significant differences were found in RNFL, TRFT, TRPAFT, and TRPEFT values between patients with FMS and healthy individuals.

The lack of significant changes in TRFT, TRPAFT, and TRPEFT values in our study can be explained by factors such as different sample characteristics, methodological approaches used, and disease severity compared to previous studies.

Our study has some limitations. First, the small number of patients limits the generalizability of the results obtained. Additionally, not grouping patients according to disease stages and symptom durations may have prevented us from observing different clinical effects. Moreover, the absence of long-term follow-up limited the opportunity to more comprehensively assess the dynamics of changes and symptoms observed over time. These limitations are important factors to consider in future studies.

Conclusion

This study presents significant findings regarding ophthalmic vascular and choroidal changes in patients with FMS. The notable decrease observed in the DCP, the increase in FAZ and non-flow areas, and the increase in choroidal thickness indicate the negative effects of autonomic dysfunction and inflammation on vascular structures in the pathogenesis of FMS. Additionally, the significant decrease in TBUT test suggests that chronic inflammation in FMS adversely affects tear quality. The use of modern imaging techniques, such as OCTA and OCT, enables a more detailed and precise assessment of the effects of FMS on eye health. Future studies involving larger patient groups and long-term follow-ups will be beneficial for better understanding the impact of FMS on eye health and providing important contributions to the treatment and management of this condition.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 2013 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Clinical Research Ethics Committee of Health Sciences University Antalya Training and Research Hospital (decision number: 18/13, date: September 29, 2022).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Written consent was acquired by all participants.

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