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Optical coherence tomography (OCT) and OCT angiography (OCTA) findings in migraine with and without aura

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ABSTRACT | Purpose: To evaluate the relationships between retinal changes identified by optical coherence tomography in patients with migraine with aura or migraine without aura and the duration and severity of the disease, as measured by the *Headache Impact Test-6* questionnaire. **Methods:** In this cross-sectional study, 16 patients with migraine with aura and 15 patients with migraine without aura were compared with 16 age- and sex-matched controls without migraine. Retinal parameters were assessed using optical coherence tomography, and disease severity was evaluated using *Headache Impact Test-6* scores. **Results:** Foveal choroidal thickness was significantly reduced in migraine patients to controls ($p=0.040$). Negative correlations were observed between disease duration and total macular thickness ($p=0.037$), ganglion cell complex thickness ($p=0.017$), and choroidal thickness ($p=0.039$) in the migraine without aura Group. Additionally, *Headache Impact Test-6* scores showed an inverse correlation with peripapillary retinal nerve fiber layer thickness ($p=0.027$) in the migraine without aura Group. **Conclusion:** Individuals with migraine exhibited significant choroidal thinning compared with controls. Longer disease duration was associated with reduced total macular, ganglion cell complex, and choroidal thickness, while greater migraine-related disability correlated with thinner peripapillary retinal nerve fiber layers.

Keywords: Migraine with aura; Migraine without aura; Nerve fibers; Retina; Macula; Optic disc; Choroid; Tomography, optical coherence; Surveys and questionnaires.

INTRODUCTION

Migraine is one of the most common primary headaches worldwide, with an estimated prevalence of 15.2% in Brazil[1]. It is the second leading cause of disability globally and the leading cause of disability among individuals under 50 years of age[2].

Migraine is currently recognized as a neurovascular disorder. Pain attacks are thought to originate from dysfunction in hypothalamic nuclei and brainstem structures, leading to altered cortical excitability, activation of the trigeminovascular pathways and modulation of arterial vasomotor control. These attacks can result in central sensitization and further changes in cortical excitability, predisposing patients to chronic migraine[3].

The retina can be considered an extension of the central nervous system (CNS) because it shares the same embryological and vascular origins and exhibits similar tissue structure. Given these similarities, measurements of retinal and choroidal layer thickness using optical coherence tomography (OCT) may reflect neurovascular changes in patients with migraine. Several studies have investigated the association between migraine and retinal changes assessed by OCT[4]. Evidence suggests that structural alterations in the retinal ganglion cell layer

(RGCL), peripapillary retinal nerve fiber layer (pRNFL), and choroid occur in both migraine with aura (MwA) and migraine without aura (MwoA) during attack-free periods[4-9]. A meta-analysis published in 2021 found that pRNFL thickness is significantly reduced in migraine patients, particularly those with MwA, indicating that this parameter may help differentiate these patients[10].

Given the neurovascular mechanisms underlying migraine, OCT angiography (OCTA) may provide additional information beyond that obtained with OCT. Some studies have reported reduced vascular density (VD) and an enlarged foveal avascular zone in migraine patients compared with controls without headache[11-14]. Because the choroid is a highly vascularized tissue, it can be affected not only by migraine attacks but also by other vascular conditions, such as systemic arterial hypertension and diabetic retinopathy[15,16].

The severity and duration of migraine may influence the thickness of retinal and choroidal layers, as previously observed[6,11,17]. However, structural changes in the retina and choroid during the interictal phase of migraine remain inconsistent across studies. Therefore, the primary objective of this study was to evaluate the thickness of the retinal layers–specifically the RGCL, pRNFL, and total macula–as well as the choroid, using OCT and OCTA, in patients with MwA and MwoA compared with individuals without migraine. The secondary objective was to evaluate whether migraine duration and severity, measured by the Headache Impact Test-6 (HIT-6)[18], correlate with retinal and choroidal thickness.

METHODS

Study design

This cross-sectional study recruited migraine patients and age- and sex-matched controls without migraine from August 2022 to July 2023. Participants were evaluated at the tertiary headache units of the University Hospital of the *Universidade Federal de Juiz de Fora* and the *Hospital Regional de Barbacena*. OCT and OCTA examinations were performed at the *Hospital de Olhos de Juiz de Fora*, Minas Gerais. The control group consisted of family members and friends of patients and researchers. All participants provided written informed consent prior to enrollment.

Research participants and instruments

Participants included individuals aged ≤60 years who were diagnosed with MwA or MwoA by neurologists, according to the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria.[19]. The control group consisted of individuals aged ≤60 years without migraine, as confirmed by a neurologist (L.B.O). Inclusion criteria required participants to have spherical refraction within ± 5 diopters, cylinder correction within ± 4 diopters, and intraocular pressure between 10 and 21 mmHg. Exclusion criteria were as follows: (1) neurodegenerative disease of any origin, (2) structural CNS lesion, (3) previous ocular trauma, (4) glaucoma, (5) retinal disease of any cause, (6) myopia or hyperopia greater than four diopters, (7) astigmatism greater than six diopters, (8) cataracts, (9) systemic arterial hypertension, and (10) diabetes mellitus.

All participants underwent comprehensive physical and neurological evaluations. Migraine patients completed the HIT-6 questionnaire[18]. A full ophthalmologic examination, including OCT and OCTA images, was performed for all participants and reviewed by ophthalmologist (L.P.C.) to identify any ocular conditions meeting exclusion criteria. OCT and OCTA scans for migraine patients were conducted during the interictal period, defined as at least 48 hours without a migraine attack.

OCT exam

Retinal and choroidal images were acquired in eyes dilated with 1% tropicamide under dark conditions during the same session. A Swept Source OCT device (DRI OCT Triton, Topcon Corporation, Tokyo, Japan) was used with a three-dimensional protocol. High-resolution images (512 × 256 A-scans) of the optic disc (6 × 6-mm) and macula (7 × 7-mm) were obtained[20]. Both eyes of each participant were imaged; however, only one eye per patient was included in the analysis. The eye with the best image quality was selected. If both eyes met inclusion criteria, one eye was randomly chosen using a simple coin-flip method (heads or tails). To minimize diurnal variation, all OCT and OCTA examinations were conducted in the morning between 9:00 and 11:00 AM.

The following structures were analyzed: pRNFL; total macula; RGCL plus inner plexiform layer (IPL) plus macular retinal nerve fiber layer (mRNFL), collectively termed the ganglion cell complex (GCC); and the choroid. Ophthalmologic parameters and measurement definitions followed the *Advised Protocol for OCT Study Terminology and Elements* (APOSTEL) for identification and measurement of the GCC, pRNFL and choroidal thickness[21].

pRNFL thickness was assessed using a three-dimensional optic disc protocol based on a 3.4-mm diameter circle centered on the optic disc. Thickness values were calculated automatically and divided into four quadrants: temporal, superior, nasal, and inferior (Figure 1A).

Total macular and choroidal thicknesses were automatically calculated according to the *Early Treatment Diabetic Retinopathy Study* (ETDRS) grid, divided into nine sectors: fovea, temporal inner, superior inner, nasal inner, inferior inner, temporal outer, superior outer, nasal outer, and inferior outer (Figures 1B and 1C).

Weighted averages of total macular and choroidal thickness were calculated considering the thickness of each of the nine sectors, as detailed in the supplementary material. For GCC measurements, the foveal sector was excluded from the weighted mean because the fovea lacks ganglion cells.

OCTA exam

Superficial VD measurements were acquired using OCTARA™ technology (Topcon Corporation, Tokyo, Japan). OCTARA is an algorithm that detects blood flow on the retinal surface by analyzing capillary motion from rapid in vivo Swept Source OCT scans, without the need for contrast injection. This technology allows differentiation between the superficial vascular plexus, located in the ganglion cell layer, and the deep capillary plexus in the inner nuclear layer[21].

OCTA images of the macula were acquired over a 6 x 6 mm area centered on the fovea, but analysis of the superficial capillary plexus was limited to a 3-mm diameter region. VD in the superficial layer was evaluated in five sectors: central, superior, inferior, nasal, and temporal. Values were expressed as percentages, and the mean VD
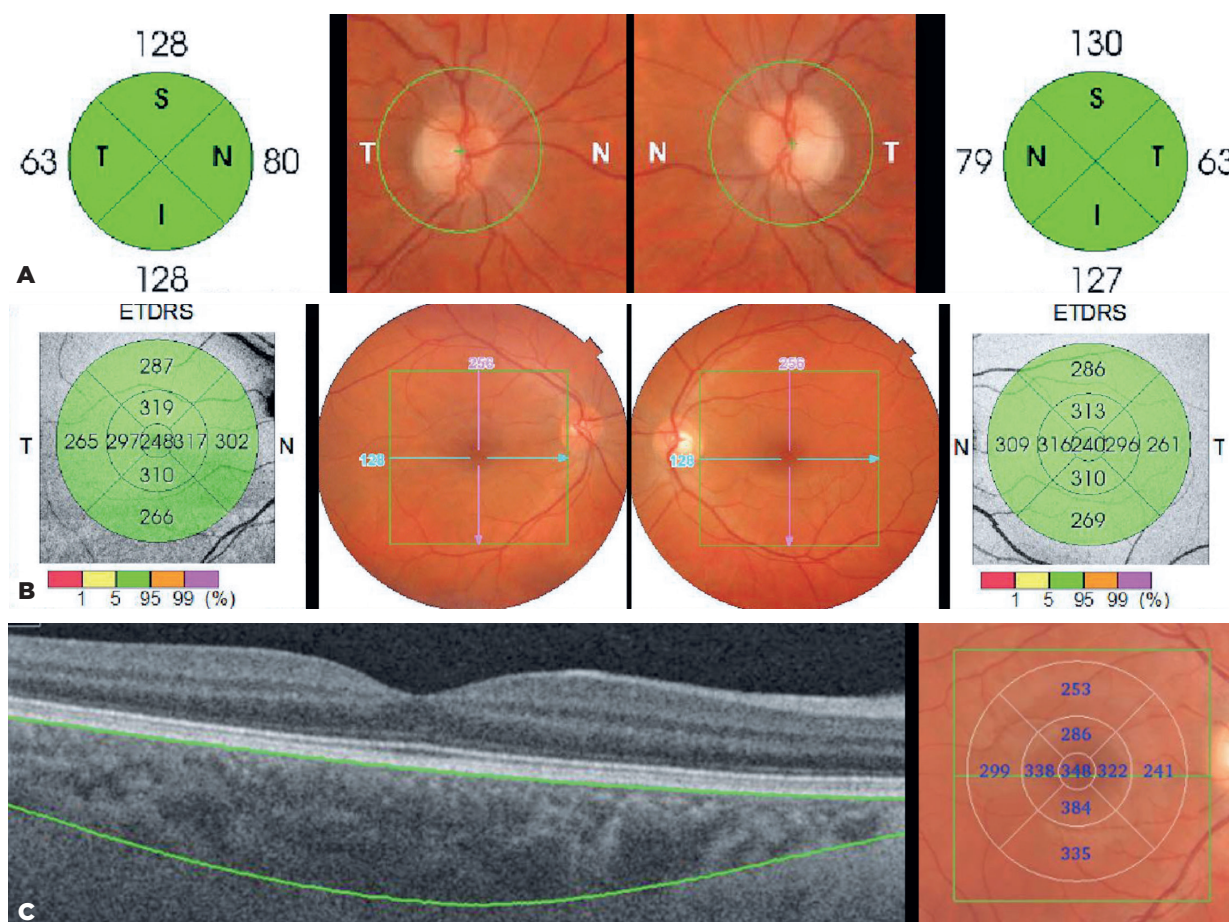

Figure 1. A. Swept Source 3D Optic Disc Report protocol – OCT of both eyes to measure the peripapillary retinal nerve fiber layer (pRNFL). A 6 × 6-mm scanning area was centered on the optic disc, and analysis was performed along a 3.4-mm diameter circle divided into four quadrants (temporal, superior, inferior, nasal). Values are expressed in micrometers (μm). B. Swept Source 3D Macula Report analysis protocol – OCT of both eyes with a 7 × 7-mm scanning area and 6-mm map diameter divided into nine sectors according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. Values are expressed in micrometers (μm). C. Schematic of choroidal thickness measurement. Left, B-scan of the choroid; right, choroidal thickness map based on the ETDRS nine-sector grid (μm).

was calculated as a weighted average based on the area of each sector (Figure 2).

Both the superficial capillary plexus and total choroidal thickness were analyzed. Boundaries and segmentation for OCTA using the Swept-Source Triton were defined as follows:

a) Superficial capillary plexus: from 2.6-µm below the internal limiting membrane to 15.6 µm below the IPL

b) Deep capillary plexus: from 15.6-µm to 70.2-µm below the IPL

c) Outer retina: from 70.2-µm below the IPL to 29-µm below the retinal pigment epithelium (RPE); this layer is primarily avascular in normal eyes

d) Choriocapillaris: from 29-µm to 49 µm below the RPE

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are presented as frequencies and percentages. Associations between categorical variables were assessed using the chi-squared test or Fisher's exact test, as appropriate. Correlations between quantitative variables were assessed using Pearson's correlation coefficient. Differences in OCT and OCTA parameters between patients and controls were analyzed using Student's t-test for independent samples. Comparisons among MwA, MwoA, and control groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. Normality and homogeneity of variances were evaluated using the Kolmogorov-Smirnov and Levene tests, respectively. All analyses were conducted using SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Hypothesis tests were two-tailed, and p-values <0.05 were considered statistically significant. No formal statistical power calculation was performed prior to the study; the sample size was determined by convenience.

RESULTS

A total of 62 individuals with migraine were invited to participate in the study. Eight were excluded due to clinical comorbidities, 16 did not attend ophthalmological evaluations, 6 had chronic migraine, and 1 was excluded due to poor-quality OCT/OCTA images. The final migraine cohort included 31 patients with episodic
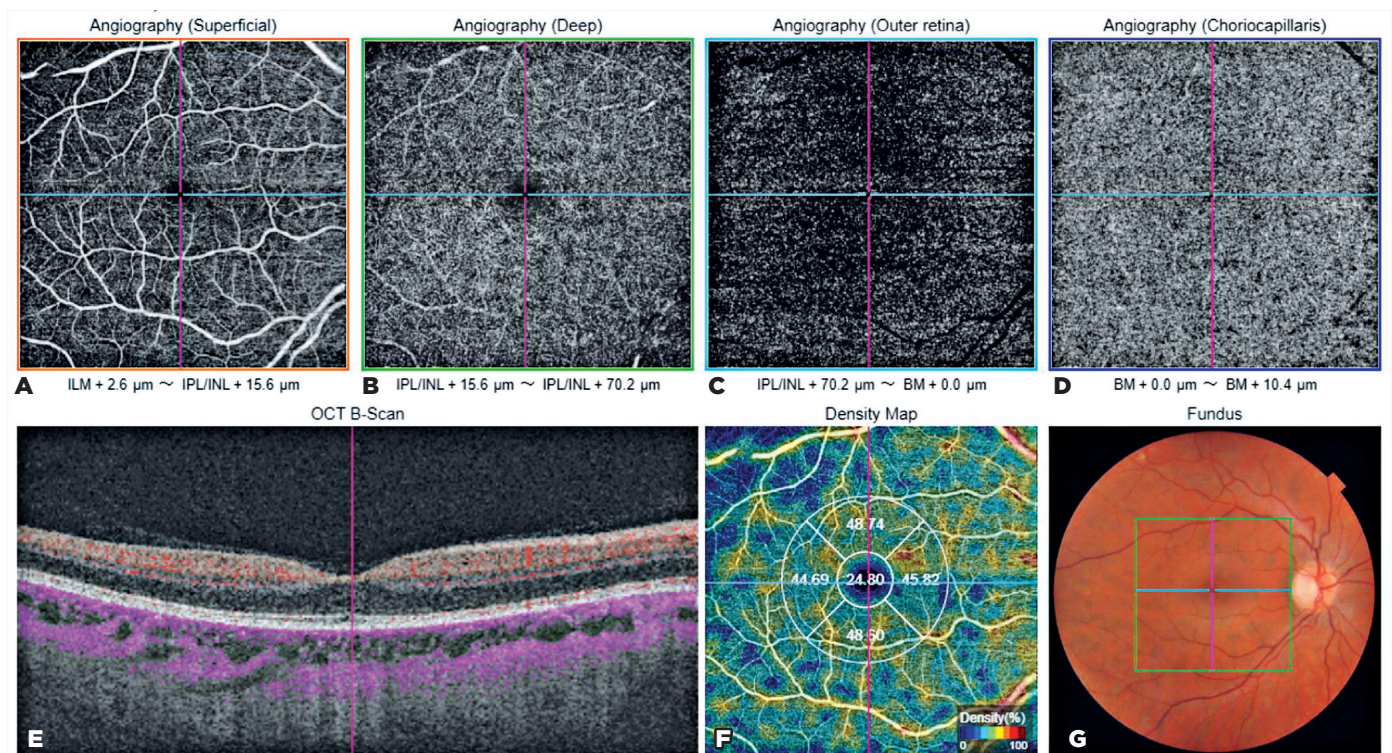

Figure 2. OCTA image acquisition protocol for the macula. A: Superficial capillary plexus angiography. B: Deep capillary plexus angiography. C: Outer retina angiography. D: Choriocapillaris angiography. E: OCT B-scan of the macula. F: Map of superficial layer vascular density divided into five regions (%). G: Fundus image of a 6 x 6-mm area around the fovea; analysis of the superficial capillary plexus was restricted to a 3-mm diameter.

migraine: 15 with MwA and 16 with MwoA. Eighteen individuals initially volunteered for the control group; two were excluded due to cataracts and referred for appropriate treatment. Sixteen controls were included in the analysis. There were no missing data. Participant characteristics are presented in table 1. No significant differences were observed between migraine patients and controls in terms of age or sex. Similarly, stratification into MwA (n=15) and MwoA (n=16) subgroups revealed no significant differences. Most participants were female (80.6% of patients and 75% of controls). The mean age ± SD was 33.7 ± 9.7 years for migraine patients and 33.2 ± 11.1 years for controls (p=0.861). Among migraine patients, the mean HIT-6 score ± SD was 62.7 ± 5.2, and the mean disease duration ± SD was 14.6 ± 11.6 years.

No statistically significant differences were observed between migraine patients and controls in pRNFL, GCC, or total macula thickness. Similarly, macular OCTA variables did not differ significantly between the groups (Tables 2 and 3). Choroidal thickness was significantly reduced in the right eyes of migraine patients compared with controls in the foveal (p=0.040), superior inner (p=0.018), temporal outer (p=0.027), and superior outer (p=0.016) regions, as well as in the average thickness (p=0.033) (Table 4).

Stratification by migraine subtype (MwA and MwoA) and comparison with controls using ANOVA revealed no significant differences in OCT variables (pRNFL, total macula, GCC, and choroid) or macular OCTA parameters.

Correlation analysis showed a positive, statistically significant relationship between disease duration and HIT-6 score (r=0.37; p=0.039; n=31). This correlation was stronger in MwA patients (r=0.64; p=0.010; n=15) but not significant in MwoA patients (r=0.14; p=0.611; n=16). Regarding OCT-derived retinal and choroidal thicknesses, negative correlations were observed between disease duration and total macula, GCC, and choroidal thicknesses, with stronger associations in MwoA patients (Table 5).

Analysis of the relationship between HIT-6 scores and OCT-derived thickness measurements revealed a statistically significant negative correlation in the average and superior regions of the pRNFL. For the average pRNFL thickness, correlations were observed in both the right (r=−0.55) and left eyes (r=−0.54), with no significant differences between MwA and MwoA Groups. In the superior pRNFL region, correlations were significant in the right (r=−0.45) and left eyes (r=−0.39), with stronger associations in the MwoA Group (right eye, r=−0.62; left eye, r=−0.58) (Table 6).

DISCUSSION

The association between retinal and choroidal thickness changes in migraine patients has been investigated for nearly two decades. In the present study, no statistically significant differences were observed in pRNFL, total macula, GCC, or macular VD measured by OCTA between patients with episodic migraine and controls. In contrast, choroidal thickness was significantly reduced in the fovea, superior inner, temporal outer, and superior outer sectors, as well as in the average thickness, in migraine patients compared with controls.

These findings partially differ from previous studies. A 2012 meta-analysis by Lin et al.[10] reported that pRNFL thickness is reduced in patients with MwA compared with individuals without headache. Other studies have shown that both MwA and MwoA patients exhibited decreased pRNFL thickness compared with healthy controls[6,7]. and that RGCL thickness is reduced during the interictal phase in both MwA and MwoA[8,9]. However, similar to our results, Taşlı et al.[22] found no differences in pRNFL, GCC, or total macular thickness between MwoA patients and healthy controls. In addition, a population-

Table 1. Clinical characteristics of patients with migraine with aura, migraine without aura, and controls

Variables	Category/Measure	MwA (n=15)	MwoA (n=16)	Controls (n=16)	p-value
Age (years, mean ± SD)	-	33.27 ± 9.81	34.19 ± 9.91	33.19 ± 11.1	0.955[a]
Sex (n, %)	Female	12 (80.0)	14 (87.5)	12 (75.0)	0.664[b]
	Male	3 (20.0)	2 (12.5)	4 (25.0)	
Migraine days per month (mean ± SD)	-	1.89 ± 1.53	2.36 ± 2.08	-	0.509[c]
HIT-6 (mean ± SD)	-	61.6 ± 5.67	63.75 ± 4.63	-	0.250[d]
Disease duration (years, mean ± SD)	-	15.47 ± 11.68	13.71 ± 12.02	-	0.680[d]

HIT-6= Headache Impact Test; MwA= migraine with aura; MwoA= migraine without aura; SD= standard deviation. p<0.05 considered statistically significant.
[a]One-way ANOVA. [b]Chi-squared test. [c]Mann–Whitney U test. [d]Student's t-test for independent samples.

Table 2. Mean pRNFL, GCC, and total macula thickness (µm) in patients with MwA, MwoA, and controls

OCT parameters	Eye	MwA (n=15)	MwoA (n=16)	Controls (n=16)	p-value[a]
pRNFL					
Average (µm ± SD)	Right	111.0 ± 6.1	106.3 ± 7.4	106.1 ± 9.7	0.211
	Left	108.4 ± 6.3	107.0 ± 7.8	105.7 ± 10.3	0.666
Superior (µm ± SD)	Right	136.0 ± 11.1	127.8 ± 11.0	134.1 ± 16.4	0.199
	Left	137.1 ± 11.2	133.4 ± 12.2	133.6 ± 18.8	0.733
Temporal (µm ± SD)	Right	75.2 ± 7.2	72.6 ± 12.0	74.7 ± 9.5	0.749
	Left	70.8 ± 5.7	68.5 ± 9.4	69.6 ± 7.9	0.720
Inferior (µm ± SD)	Right	144.6 ± 12.6	138.3 ± 13.1	137.1 ± 13.8	0.244
	Left	140.9 ± 12.8	140.3 ± 14.2	139.4 ± 13.1	0.948
Nasal (µm ± SD)	Right	87.9 ± 11.8	86.3 ± 13.6	81.4 ± 12.2	0.330
	Left	84.5 ± 11.4	85.8 ± 13.5	80.6 ± 13.0	0.477
GCC					
Fovea (µm ± SD)	Right	46.9 ± 13.6	49.9 ± 9.6	47.5 ± 12.1	0.754
	Left	46.0 ± 13.7	48.5 ± 8.8	47.8 ± 10.8	0.826
Temporal inner (µm ± SD)	Right	110.8 ± 6.1	108.9 ± 7.7	109.1 ± 7.9	0.722
	Left	109.2 ± 6.2	107.8 ± 7.4	107.7 ± 7.5	0.802
Superior inner (µm ± SD)	Right	121.8 ± 7.5	120.3 ± 8.0	118.3 ± 8.5	0.473
	Left	122.6 ± 7.1	119.7 ± 7.9	118.2 ± 7.9	0.276
Nasal inner (µm ± SD)	Right	114.2 ± 8.8	116.2 ± 8.3	113.2 ± 12.0	0.675
	Left	116.4 ± 8.0	115.5 ± 7.4	115.4 ± 9.0	0.939
Inferior inner (µm ± SD)	Right	121.4 ± 7.0	120.4 ± 9.1	117.2 ± 9.9	0.386
	Left	120.9 ± 7.8	118.9 ± 7.5	116.9 ± 10.0	0.449
Temporal outer (µm ± SD)	Right	95.7 ± 9.3	95.0 ± 10.4	94.5 ± 8.7	0.937
	Left	92.8 ± 5.7	92.1 ± 11.1	93.8 ± 9.8	0.881
Superior outer (µm ± SD)	Right	107.9 ± 6.2	105.6 ± 8.5	105.6 ± 6.6	0.589
	Left	108.5 ± 6.7	102.7 ± 8.3	104.8 ± 6.5	0.094
Nasal outer (µm ± SD)	Right	120.4 ± 10.6	116.6 ± 14.9	119.4 ± 10.1	0.676
	Left	122.6 ± 7.2	117.9 ± 12.9	120.3 ± 10.6	0.467
Inferior outer (µm ± SD)	Right	106.0 ± 6.5	102.8 ± 7.4	104.9 ± 6.7	0.446
	Left	105.5 ± 5.8	102.8 ± 7.2	106.1 ± 7.7	0.396
Average (µm ± SD)	Right	109.7 ± 5.9	107.6 ± 7.4	108.0 ± 5.4	0.638
	Left	109.6 ± 5.3	106.5 ± 7.2	108.2 ± 5.4	0.377
Total macula					
Fovea (µm ± SD)	Right	228.2 ± 27.3	238.8 ± 16.8	235.1 ± 21.8	0.414
	Left	230.2 ± 25.4	238.1 ± 15.4	235.6 ± 21.1	0.567
Temporal inner (µm ± SD)	Right	295.1 ± 13.5	297.1 ± 18.7	297.6 ± 14.1	0.893
	Left	296.0 ± 13.3	295.5 ± 18.0	299.2 ± 14.2	0.758
Superior inner (µm ± SD)	Right	308.1 ± 13.4	311.8 ± 18.4	310.5 ± 12.5	0.782
	Left	311.0 ± 13.8	311.6 ± 18.6	313.0 ± 13.5	0.934
Nasal inner (µm ± SD)	Right	303.5 ± 16.3	310.9 ± 18.1	308.9 ± 14.4	0. 439
	Left	307.7 ± 15.8	311.3 ± 17.9	311.4 ± 15.1	0.770
Inferior inner (µm ± SD)	Right	304.3 ± 15.0	307.2 ± 19.3	307.2 ± 13.3	0.843
	Left	305.3 ± 15.5	303.1 ± 17.3	308.3 ± 12.2	0.620
Temporal outer (µm ± SD)	Right	258.1 ± 16.2	255.4 ± 15.8	258.3 ± 9.0	0.815
	Left	254.9 ± 14.0	253.6 ± 16.6	260.9 ± 15.5	0.370
Superior outer (µm ± SD)	Right	272.4 ± 11.9	273.5 ± 13.5	275.2 ± 9.3	0.801
	Left	274.9 ± 12.8	269.6 ± 15.0	277.6 ± 11.4	0.233
Nasal outer (µm ± SD)	Right	282.3 ± 16.6	288.1 ± 16.5	291.2 ± 12.5	0.269
	Left	286.4 ± 15.3	288.2 ± 17.6	291.2 ± 13.7	0.692
Inferior outer (µm ± SD)	Right	261.9 ± 12.7	259.1 ± 13.7	265.2 ± 9.3	0.364
	Left	261.7 ± 12.2	260.7 ± 13.3	266.8 ± 10.3	0.314
Average (µm ± SD)	Right	275.1 ± 12.5	276.5 ± 14.8	278.9 ± 12.6	0.694
	Left	276.3 ± 12.7	275.5 ± 14.6	280.6 ± 10.0	0.477

GCC= ganglion cell complex; MwA= migraine with aura; MwoA= migraine without aura; pRNFL= peripapillary retinal nerve fiber layer; SD= standard deviation.
p<0.05 considered statistically significant. [a]Student's t-test for independent samples.

-based study in Finland including 375 migraine patients and 1,489 controls reported no significant differences in pRNFL, macula, or RGCL-IPL thickness[23]. Likewise, Lamparter et al.[24], evaluating 1,973 individuals, found no significant associations between migraine and pRNFL thickness changes.

Most OCT studies in migraine patients have reported significant thinning of the choroid. Because the choroid is highly vascularized, its structural changes may reflect the neurovascular pathophysiology of migraine[3,25]. Electrophysiological evidence indicates direct activation of trigeminovascular neurons during migraine attacks[26].

Table 3. Mean macular OCTA values (in %) in patients with MwA, MwoA, and controls

Macula OCTA parameters	Eye	MwA (n=15)	MwoA (n=16)	Controls (n=16)	p-value[a]
Central (% ± SD)	Right	20.7 ± 6.0	21.6 ± 3.3	19.9 ± 3.9	0.589
	Left	18.9 ± 4.9	21.0 ± 3.2	19.9 ± 3.4	0.353
Superior (% ± SD)	Right	47.5 ± 3.0	47.5 ± 2.6	48.2 ± 2.3	0.662
	Left	46.3 ± 2.5	47.4 ± 2.2	47.1 ± 2.8	0.468
Inferior (% ± SD)	Right	46.5 ± 3.4	48.2 ± 2.7	48.2 ± 2.4	0.162
	Left	46.4 ± 2.5	46.4 ± 2.1	46.5 ± 3.0	0.985
Nasal (% ± SD)	Right	43.9 ± 2.7	44.9 ± 3.3	44.4 ± 2.5	0.626
	Left	43.7 ± 1.9	44.1 ± 2.8	44.4 ± 2.1	0.731
Temporal (% ± SD)	Right	47.0 ± 1.3	46.1 ± 1.6	46.0 ± 2.8	0.319
	Left	45.7 ± 2.6	45.0 ± 2.6	45.6 ± 2.3	0.695
Weighted average (% ± SD)	Right	43.3 ± 1.5	43.8 ± 1.7	43.7 ± 1.7	0.666
	Left	42.5 ± 1.2	42.9 ± 1.7	43.0 ± 1.8	0.711

MwA= migraine with aura; MwoA= migraine without aura; SD= standard deviation.
p<0.05 considered statistically significant. [a]Student's t-test for independent samples.

Table 4. Mean choroidal thickness (μm) in patients and controls

Indicator	Eye	Patients (n=31)	Controls (n=16)	p-value [a]
Choroidal thickness				
Fovea (μm)	Right	275.3 ± 67.3	316.8 ± 56.2	0.040*
	Left	284.8 ± 66.0	311.9 ± 67.3	0.193
Temporal inner (μm)	Right	276.0 ± 69.1	312.9 ± 50.5	0.065
	Left	285.4 ± 66.5	310.1 ± 58.5	0.217
Superior inner (μm)	Right	272.1 ± 69.9	321.2 ± 53.9	0.018*
	Left	275.1 ± 60.8	309.1 ± 52.1	0.063
Nasal inner (μm)	Right	259.2 ± 65.1	287.6 ± 56.8	0.147
	Left	258.7 ± 61.3	291.5 ± 58.4	0.084
Inferior inner (μm)	Right	270.9 ± 77.3	300.3 ± 58.6	0.189
	Left	280.3 ± 75.0	312.4 ± 69.3	0.161
Temporal outer (μm)	Right	258.7 ± 68.4	297.6 ± 46.5	0.027*
	Left	263.0 ± 63.0	291.7 ± 45.9	0.115
Superior outer (μm)	Right	269.7 ± 61.1	311.3 ± 48.8	0.016*
	Left	276.4 ± 63.7	309.4 ± 49.7	0.078
Nasal outer (μm)	Right	209.3 ± 54.1	239.2 ± 54.6	0.080
	Left	213.3 ± 59.3	240.1 ± 59.3	0.151
Inferior outer (μm)	Right	260.9 ± 70.7	296.8 ± 65.3	0.098
	Left	265.8 ± 59.8	289.5 ± 71.3	0.234
Average thickness	Right	254.7 ± 57.7	291.3 ± 45.7	0.033*
	Left	259.7 ± 54.8	288.6 ± 52.1	0.088

[a]Student's t-test for independent samples. *p<0.05.

Sensory innervation of the eye arises from the ophthalmic branch of the trigeminal nerve,[27] positioning the choroid as an input of the trigeminoautonomic system[9].

Consistent with prior studies and meta-analyses of observational data, migraine patients exhibited significantly reduced choroidal thickness compared with healthy

Table 5. Correlation coefficients between disease duration (years) and OCT-derived layer thicknesses in all patients and in MwA and MwoA subgroups (p-values in parentheses)

OCT parameters		Eye	Patients (n=31)	MWA (n=16)	MA (n=15)
			Disease duration		
Total macular thickness	Temporal inner	Right	−0.27 (0.142)	−0.45 (0.077)	0.02 (0.952)
		Left	−0.23 (0.215)	−0.47 (0.068)	0.12 (0.673)
	Superior inner	Right	−0.20 (0.273)	−0.44 (0.087)	0.17 (0.541)
		Left	−0.21 (0.253)	−0.49 (0.054)*	0.20 (0.468)
	Nasal outer	Right	−0.38 (0.035)*	−0.51 (0.045)*	−0.22 (0.420)
		Left	−0.39 (0.028)*	−0.61 (0.013)*	−0.12 (0.667)
	Superior outer	Right	−0.28 (0.128)	−0.53 (0.033)*	0.05 (0.872)
		Left	−0.42 (0.019)*	−0.64 (0.008)*	−0.19 (0.489)
	Average	Right	−0.27 (0.135)	−0.46 (0.073)	−0.02 (0.929)
		Left	−0.32 (0.081)	−0.52 (0.037)*	−0.06 (0.819)
GCC	Superior inner	Right	−0.12 (0.527)	−0.51 (0.042)*	0.33 (0.225)
		Left	−0.07 (0.699)	−0.51 (0.045)*	0.42 (0.118)
	Superior outer	Right	−0.21 (0.249)	−0.46 (0.071)	0.12 (0.673)
		Left	−0.37 (0.039)*	−0.56 (0.023)*	−0.25 (0.358)
	Nasal outer	Right	−0.60 (0.000)*	−0.75 (0.001)*	−0.44 (0.100)
		Left	−0.21 (0.252)	−0.33 (0.212)	−0.07 (0.797)
	Average	Right	−0.27 (0.134)	−0.54 (0.030)*	0.05 (0.847)
		Left	−0.34 (0.061)	−0.59 (0.017)*	−0.05 (0.847)
Choroidal thickness	Temporal outer	Right	−0.27 (0.134)	−0.39 (0.133)	−0.16 (0.559)
		Left	−0.40 (0.027)*	−0.57 (0.021)*	−0.21 (0.447)
	Superior outer	Right	−0.30 (0.101)	−0.25 (0.356)	−0.38 (0.156)
		Left	−0.39 (0.029)*	−0.49 (0.056)	−0.29 (0.297)
	Inferior outer	Right	−0.21 (0.215)	−0.33 (0.209)	−0.14 (0.618)
		Left	−0.19 (0.296)	−0.35 (0.183)	−0.04 (0.892)
	Average	Right	−0.27 (0.146)	−0.38 (0.145)	−0.17 (0.548)
		Left	−0.32 (0.083)	−0.52 (0.039)*	−0.09 (0.739)

*p<0.05. GCC: ganglion cell complex (GCL + IPL + mRNFL). MwA= migraine with aura; MwoA= migraine without aura; OCT= optical coherence tomography.

Table 6. Correlation coefficients between HIT-6 scores and mean pRNFL thickness (µm) in all patients and in MwA and MwoA subgroups (p-values in parentheses)

pRNFL	Eye	Patients (n=31)	MA (n=15)	MWA (n=16)
		HIT-6		
Superior (µm ± SD)	Right	−0.451 (0.011)*	−0.237 (0.395)	−0.617 (0.011)*
	Left	−0.388 (0.031)*	−0.173 (0.539)	−0.580 (0.019)*
Inferior (µm ± SD)	Right	−0.054 (0.774)	0.500 (0.057)	−0.505 (0.046)*
	Left	0.015 (0.935)	0.456 (0.088)	−0.473 (0.064)
Nasal (µm ± SD)	Right	−0.241 (0.191)	−0.262 (0.345)	−0.213 (0.429)
	Left	−0.339 (0.62)	−0.469 (0.078)	−0.264 (0.323)
Temporal (µm ± SD)	Right	0.147 (0.439)	0.495 (0.061)	−0.016 (0.954)
	Left	0.167 (0.370)	0.519 (0.048)*	0.010 (0.972)
Average (µm ± SD)	Right	−0.255 (0.167)	0.165 (0.558)	−0.551 (0.027)*
	Left	−0.246 (0.182)	0.094 (0.740)	−0.540 (0.031)*

*p<0.05.
HIT-6= Headache Impact Test; pRNFL= peripapillary retinal nerve fiber layer; SD= standard deviation.

controls[25]. However, this difference was not observed when patients were stratified into MwA and MwoA. This may be explained by the fact that migraine pain primarily involves activation of the trigeminovascular system via peripheral nociceptive neurons, and most migraine attacks occur without aura[4]. Consequently, choroidal vascular changes are likely proportional to the frequency and intensity of pain attacks rather than the presence of aura. In line with this, we observed a significant negative correlation between disease duration and choroidal thickness, consistent with findings reported by Abdellatif et al. in 2018[6].

We observed a significant inverse correlation between disease duration and both total macular and GCC thickness. This suggests that longer migraine duration may lead to greater activation of the trigeminovascular system, resulting in vasoconstriction that affects not only the choroid but also the macula and GCC through prolonged oligemia[6]. The reduction in choroidal thickness, alongside normal OCTA findings, may indicate a pathophysiological mechanism involving transient ischemia during migraine attacks that spares vascular structures in the interictal period but induces long-term changes in non-vascular components of the choroid and retina. An alternative explanation is direct neurogenic damage to choroidal and retinal tissues, primarily affecting non-vascular structures.

Regarding migraine-related disability, assessed using the HIT-6 questionnaire, we found a statistically significant inverse correlation with average and superior pRNFL thickness. Similar findings have been reported by Martinez et al.[17], who observed an inverse correlation between pRNFL thickness and migraine severity. Abdellatif et al. also demonstrated that migraine severity significantly influences pRNFL and GCC thinning[6]. Assessing headache-related disability is a valuable tool for guiding treatment selection, and the HIT-6 is a reliable, widely applicable, and easy-to-use instrument for this purpose[28].

Migraine, particularly with aura, is a recognized risk factor for ischemic stroke and cardiovascular disease[29], which is partly explained by its neurovascular pathophysiology. Previous studies have reported reduced peripapillary and macular VD and an increased foveal avascular zone in patients with MwA[12,13]. However, microvascular changes in the retina may manifest primarily when neuroaxonal damage is present. As shown by other authors[30,31], reductions in RNFL and GCC thickness, which reflect neuroaxonal injury, strongly correlate with decreased VD. Accordingly, VD reduction is typically observed alongside significant RNFL and GCC thinning, consistent with findings from prior studies[12-14]. These changes may be influenced by disease duration and severity, as supported by our results and previous reports demonstrating inverse correlations between disease duration and GCC thickness, and between migraine severity and RNFL thickness[6,17]. In contrast, we observed significant choroidal thinning even in the absence of neuroaxonal damage, suggesting that structural changes in this highly vascularized layer may occur earlier in the disease process in migraine patients.

The variability in retinal layer thickness and macular VD reported across studies may be influenced by differences in study populations (e.g., MwA vs. MwoA, episodic vs. chronic migraine), characteristics of migraine in these populations (attack frequency, intensity, and disease duration), and sociodemographic factors. In addition, technical differences in OCT and OCTA devices and protocols may contribute to inconsistent findings.

This study has several limitations. The relatively small sample size and recruitment from only two research centers may increase the risk of type II errors. Its cross-sectional design precludes causal inferences between retinal or choroidal changes and migraine. Moreover, some statistically significant correlations–many with low correlation coefficients–between disease duration and OCT parameters could be subject to cumulative type I error. Conversely, a major strength of this study is the use of a Swept-Source OCT device, which employs a near-infrared light source (~1,050-nm) that enables deeper tissue penetration and improved visualization of retinal and choroidal layers–a key advantage for examining migraine patients. The device also automatically generates thickness maps based on the ETDRS grid divided into nine sectors, allowing for precise, topographically guided analysis and enhancing the accuracy and reproducibility of the measurements.

In conclusion, compared with controls, individuals with migraine exhibited a significant reduction in choroidal thickness. Longer disease duration was associated with thinner total macula, GCC, and choroidal layers. Furthermore, pRNFL thickness was inversely correlated with migraine-related disability.

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