DOI:10.14744/bej.2022.04900
Beyoglu Eye J 2023; 8(1): 38-44

Original Article

Assessment of Choroidal Vascularity in Inactive Thyroid Associated Orbitopathy

Seren Pehlivanoglu, Funda Ebru Aksoy, Gamze Ozturk Karabulut, Ugur Tunc, Korhan Fazil, Ozgur Artunay, Muhittin Taskapili

Department of Ophthalmology, University of Health Sciences Istanbul Beyoglu Eye Training and Research Hospital, Istanbul, Türkiye

Abstract

Objectives: The objectives of the study were to evaluate the vascular and stromal structure of the choroid in patients with inactive thyroid associated orbitopathy (TAO) by measuring choroidal vascularity index (CVI) and choroidal thickness (CT) using enhanced depth imaging (EDI) optical coherence tomography (OCT).

Methods: The choroidal image was taken with EDI mode spectral domain (SD)-OCT. All scans were taken between 9.30 am and 11.30 am to avoid the diurnal variation of CT and CVI. To calculate CVI, macular SD-OCT scans were binarized using the publicly available software ImageJ and luminal area and total choroidal area (TCA) were measured. CVI was calculated as the proportion of LA to TCA. Furthermore, the relation between CVI and axial length, gender, and age was evaluated.

Results: This study included 78 individuals with a mean age of 51.4±7.3 years. Group 1 consisted of 44 patients with inactive stage TAO, and Group 2 consisted of 34 healthy controls. Subfoveal CT was 338.92±73.93 μm in Group 1 and 303.97±40.35 μm in Group 2 (p=0.174). The CVI significantly differed between the two groups, which was higher in group 1 (p=0.000).

Conclusion: Although CT was not different between groups, CVI which is the indicator of the vascular status of the choroid, was higher in patients with TAO in the inactive stage compared with healthy control subjects.

Keywords: Choroidal thickness, choroidal vascularity index, EDI-optical coherence tomography, thyroid-associated ophthalmopathy

Introduction

Thyroid-associated ophthalmopathy (TAO) is an autoimmune inflammatory disease that generally affects adults aged 30–50 years (1). In TAO, thyroid gland autoantibodies induce inflammation that affects the thyroid gland and orbit (2). Thyroid-associated ophthalmopathy consists of two stages, the active and the inactive stage. In the active stage, extraocular muscle and soft-tissue involvement are prominent due to infiltration caused by glycosaminoglycans (GAG), lymphocytes, and immune complexes, while in the inactive stage, inflammatory events subside (3). Beside extraocular muscle and soft-tissue involvement, studies have also shown that retinal and choroidal thicknesses (CTs) are affected in TAO secondary to hemodynamic changes (4-7).

How to cite this article: Pehlivanoglu S, Aksoy FE, Ozturk Karabulut G, Tunc U, Fazil K, Artunay O, et al. Assessment of Choroidal Vascularity in Inactive Thyroid Associated Orbitopathy. Beyoglu Eye J 2023; 8(1): 38-44.

Address for correspondence: Seren Pehlivanoglu, MD. Department of Ophthalmology, University of Health Sciences Istanbul Beyoglu Eye Training and Research Hospital, Istanbul, Türkiye
Phone: +90 212 251 59 00 **E-mail:** srnmert@hotmail.com

Submitted Date: July 01, 2022 **Revised Date:** September 15, 2022 **Accepted Date:** October 09, 2022 **Available Online Date:** March 01, 2023

Beyoglu Eye Training and Research Hospital - Available online at www.beyoglueye.com

Visualization of the choroid has some limitations via fundus fluorescein angiography, indocyanine green angiography, and spectral-domain optical coherence tomography because of the retinal pigment epithelium and opaque sclera (8-10). The development of enhanced depth imaging optical coherence tomography (EDI-OCT) has allowed a better assessment of the choroid in many retina-choroidal diseases (11). EDI-OCT has shown that choroid thickness is increased in TAO in the active stage as a consequence of ocular inflammation (4,5). On the other hand, there are limited studies addressing CT in the inactive stage of TAO. Gul et al. (12) reported that CT was thinner in the inactive stage compared to the active stage. Until recently, CT was the only parameter evaluated with EDI-OCT in several diseases to understand choroidal changes. However, various factors have been shown to affect the CT, including axial length, refractive error, age, and even among individuals of similar age without any eye problem (13-15).

The choroid has both vascular and stromal components. The choroidal vascularity index (CVI) is a new OCT parameter that indicates the vascular status of the choroid and is defined as the ratio of the luminal area (LA) to the total choroidal area (TCA) (16). There are many published studies that have reported CVI measured with EDI-OCT, which might be more informative than CT measurement alone in retina-choroidal diseases (16,17).

In this study, we aimed to evaluate the vascular and stromal structure of the choroid in patients with inactive TAO by measuring CVI and CT and thus may obtain more information about the pathogenesis of ocular involvement of the thyroid.

Methods

Study Design and Subjects

This cross-sectional study included 78 adult patients who were recruited from the Department of Ophthalmic Plastic and Reconstructive Surgery. A detailed evaluation, including data on demographics and systemic and ocular history, was noted for all patients. Written informed consent was obtained from all patients. The study followed the tenets of the Declaration of Helsinki and was approved by the University of Health Sciences Hamidiye Scientific Research Ethics Committee (register number 21/11).

The patients' diagnosis of TAO was based on the criteria of the European Group on Graves' Orbitopathy (EUGOGO) Consensus Statement (18,19). According to EUGOGO classification, all patients have mild Graves ophthalmopathy, that is, lid retraction <2 mm, mild soft tissue involvement, exophthalmos <3 mm, no diplopia or transient diplopia, and exposure keratopathy responsive to lubrication. Furthermore, thyroid-associated ophthalmopathy activity was defined using the clinical activity score (CAS) (20). In this study, all the patients who have normal thyroid function tests and with CAS s below 3 for 6 months were included in the study. On the other hand, in patients in the active stage of TAO with CAS ≥3, the presence of a difference in proptosis of more than 2 mm between the eyes, optic neuropathy, corneal ulcers, and any restrictions in the ductions, and those under current or previously systemic corticosteroid therapy or with a history of orbital surgery or radiation treatment were considered not eligible for this study. In addition, patients with high blood pressure (systolic pressure >140 mmHg or diastolic pressure >90 mmHg), cardiovascular disease, and diabetes, refractive error more than ±6 diopters and had EDI-OCT with poor image quality, which might affect the choroidal measurements, were also excluded.

Only one eye was selected in eligible patients with inactive TAO. If the involvement was unilateral, the involved eye was included, whereas, in the case of bilaterality, the selection of the eye to be examined was random. In the healthy control group, right eye was included in the study.

An ophthalmological evaluation consisted of the measurement of best-corrected visual acuity (BCVA), intraocular pressure measurement with a Goldmann applanation tonometer, a slit-lamp biomicroscopic examination of the anterior segment, and dilated fundus examination for all the participants. Axial length measurements were taken with IOL Master optical biometry (Zeiss Meditec AG, Jena, Germany). The same examiner, who was skilled at Hertel exophthalmometry, measured the proptosis.

Imaging of the choroid was performed after pupil dilation with 1% topical tropicamide (Tropamid Fort 1%, Bilim Pharmaceuticals, Istanbul, Turkey), using the EDI mode of OCT-imaging device (Spectralis Heidelberg HRA + OCT, Heidelberg Engineering, Germany).

EDI-OCT and CVI

The choroidal image was taken with EDI mode SD-OCT. All scans were taken between 9.30 am and 11.30 am to avoid the diurnal variation of CT (21). In addition, patients' blood pressure was checked before scanning as the highly vascularized choroid might be affected. The imaging protocol was comprised of 49 horizontal 9 mm raster B-scans centered at the fovea per volume scan of 30° Å~ 30°. Signal strength ≥7 was used for analysis. Subfoveal CT was measured manually at the fovea using the caliper tool in the software, as the vertical distance between the hyperreflective line of Bruch's membrane and the hyper-reflective line of the choroido-scleral interface. To calculate CVI, macular SD-OCT scans were binarized using the publicly available software ImageJ 1.51s (National Institutes of Health,

Bethesda, MD, United States of America [USA]), with a semi-automated technique (16). First, the EDI-OCT image was opened with ImageJ, and the polygon tool was used to assess the region of interest (ROI) across the entire length of the OCT scan. The upper boundary of the ROI was traced along the basal margin retina pigment epithelium and the lower boundary along the choroidoscleral border to define the TCA. The image was converted to eight bits, and auto local thresholding (Niblack method) was performed to this binarized image (16). Second, to allow a selection of dark pixels, as defined the LA, the image was again converted into red, green, and blue color. The LA was calculated as the sum of dark pixel areas. In the binarized image, bright pixels were defined as stromal area (SA), which was computed from the subtraction of LA from TCA of the ROI. CVI, an indicator of choroidal vascular status, was calculated as the ratio between LA and TCA (Fig. 1).

Data Analysis

Categorical variables were presented as numbers, while numerical variables were expressed as the mean and standard deviation. The Kolmogorov–Smirnov test was used to assess the normal distribution of data. The outcomes were compared using appropriate tests. Independent-samples t-test was performed for the stromal area, and the Mann–Whitney U test was performed for TCA, LA, CT, and CVI. Multiple linear regression analysis was performed to determine factors related to alterations in the CVI. The Statistical Package for the Social Sciences (SPSS) version 22 (SPSS, Chicago, IL, USA) was used for data analysis, in which $p<0.05$ was considered to indicate statistical significance.

Results

This study included 78 individuals (75.6% woman, 24.4% man) with a mean age of 51.4±7.3 years. Group 1 consisted of 44 patients (56.4%) diagnosed with thyroid-associated orbitopathy who were in the inactive stage, and Group 2 consisted of 34 (43.6%) healthy control individuals in this study. There was no statistically significant difference between Group 1 and Group 2 in terms of the mean age, gender, and BCVA (p=0.19, p=0.45, and p=0.36, respectively) (Table 1). The mean axial length, which was 23.1±0.8 mm in Group 1

Table 1. Demographic and clinical characteristics of the participants

Characteristics	Group 1	Group 2	p
Gender, number (%)			0.45*
Women	34 (77.3)	25 (73.5)	
Men	10 (22.7)	9 (26.4)	
Age (years)			0.19
Mean±SD	50.38±6.82	52.88±7.89	
Min-max	34–66	35–62	
BCVA (Snellen)			0.36
Mean±SD	0.87±0.10	0.94±0.09	
Min-Max	0.7–1.0	0.7–1.0	
IOP (mmHg)			0.456
Mean±SD	14.76±1.53	15.02±1.48	
Min-Max	12–18	12–19	

*Chi-square, Independent-samples t-test. Max: Maximum, Min: Minimum, BCVA: Best corrected visual acuity, IOP: Intra ocular pressure.

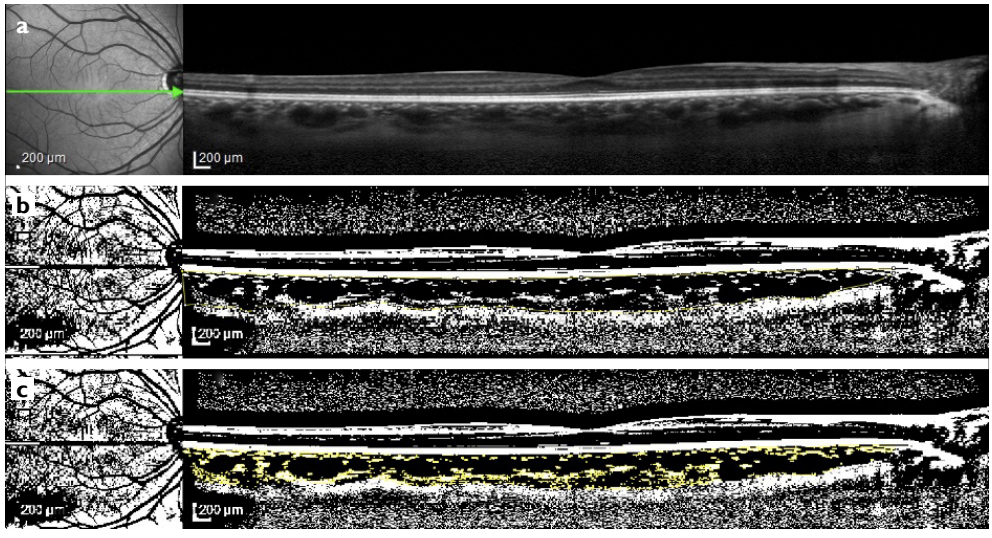

Figure 1. EDI-OCT image of a patient with inactive TAO. Stages of choroidal vascular index calculation using Image J program. **(a)** Raw EDI-OCT image **(b)** the EDI-OCT scans were binarized to determine the total choroidal area (TCA). **(c)** The color threshold tool was used to select the dark pixels, representing the luminal area (yellow lines). CVI was calculated as the ratio of LCA to TCA.

and 22.9±0.7 mm in Group 2, was not significantly different when comparing the groups (p=0.59) (Table 1). In group one, 24 eyes had CAS evaluated as 0, 14 eyes as 1, and 6 eyes as 2. Furthermore, the mean value of Hertel exophthalmometry was 15.93±1.40 mm (range, 14–18 mm) in Group 1. In addition, the mean subfoveal CT was 338.92±73.93 µm (range, 225–525 µm) in Group 1 and 303.97±40.35 µm (range, 162–341 µm) in Group 2. There was no significant difference between the two groups with respect to subfoveal CT (p=0.174). There was no statistical difference in terms of the mean choroidal stromal area measurement between the groups (p=0.645). However, both the means TCA and LA were significantly higher in Group 1 than Group 2 (2.25±0.41 vs. 1.91±0.35 and 1.63±0.35 vs. 1.27±0.23; p=0.001, p=0.000, respectively). The CVI higher in group 1 was significant difference between the groups [p=0.000, Table 2]. According to linear regression analyses, there were no significant correlation of CVI among age, gender, axial length, and hertel value [p=0.068, p=0.058, and p=0.253, and p=0.719, respectively; Table 3].

Table 3. Associations between choroidal vascularity index and clinical parameters in patient group

Parameter	ß	95% CI		p
CVI				
Age (years)	–0.204	–0.329	0.012	0.068
Gender	–0.289	–6.704	–0.936	0.058
Axial length (mm)	–0.123	–2.764	0.740	0.253
Hertel value (mm)	–0.056	–1.637	1.139	0.719

Linear regression analysis P<0.05.

Discussion

We assessed the CVI, an indicator of choroidal vascular status in thyroid-associated patients in the inactive stage. Interestingly, our study showed an increase in the vascular part of the choroid during the inactive stage in thyroid-associated orbitopathy compared to the healthy controls. The LA, which represents the vascular area of the choroid, was higher in the patient's group. On the other hand, there was no significant difference between the patient and healthy groups in terms of stromal area.

In thyroid-associated orbitopathy, the essential mechanism is the infiltration of orbital fat and extraocular muscle with the inflammatory cells, orbital fibroblasts, and the hyaluronan produced by them (3-5). This process causes the orbital structures to expand, and an increase in orbital volume causes orbital venous congestion (5,22). Several technologies, such as Heidelberg retina flowmeter, oculodynamometry, Doppler imaging, ocular blood flow tonometry, dynamic contour tonometry, and optical coherence tomography angiography, have been used to understand the retinal, choroidal, and orbital blood flow changes in patients with TAO (22-25). Studies with color Doppler imaging have shown venous stasis in a superior ophthalmic vein in active TAO patients (22,24). Alimgil et al. (25) mentioned that an increase in intraorbital venous pressure might decrease the arterial filling facility of the choroid and decrease pulse amplitude. Tsai et al. (26) reported that pulsatile ocular blood flow (as an indicator of choroidal blood flow) was significantly lower in patients with Graves' ophthalmopathy than patients without ophthalmopathy. These authors proposed that this decrease in pulsatile ocular blood flow is likely a result of the total effect of elevated venous pressure and increased resistance of choroidal vessels caused by elevated intraorbital pressure. In addition, they reported that the pulsatile ocular blood flow in patients with Graves' ophthalmopathy improved after treatment with systemic steroid use in another study (27). Perez-Lopez et al. (28) performed decompression surgery for patients with a moderate-severe thyroid eye disease (TED). These authors found increased retrobulbar blood flow measurements in TED patients after surgery and explained this change by both decreased orbital pressure and decreased extrinsic vascular compression by decreasing resistance indices in

Table 2. Comparison of choroidal parameters between groups

	Group 1 mean±SD (Min-Max)	Group 2 Mean±SD (Min-Max)	p
LA (mm^2)	1.63±0.36 (0.96–2.38)	1.28±0.23 (0.77–1.63)	0.000*
SA (mm^2)	0.62±0.16 (0.33–1.01)	0.64±0.14 (0.27–0.85)	0.654*
TCA (mm^2)	2.25±0.41 (1.33–3.14)	1.91±0.36 (1.09–2.38)	0.001*
CVI (%)	72.15±6.27 (56.81–86.90)	66.87±2.93 (61.44–75.32)	0.000*
SFCT (µm)	338.92±73.93 (225–525)	303.97±40.36 (162–341)	0.174

LA: Luminal area, SA: Stromal area, TCA: Total choroidal area, CVI: Choroidal vascularity index, SFCT: Subfoveal choroidal thickness. *Mann–Withney, independent samples t-test.

ophthalmic and central retinal arteries. Similarly, Monteiro et al. (24) reported that reduced superior ophthalmic vein flow was normalized after the treatment of active orbitopathy. In all the above-cited studies, elevated venous pressure levels and decreased blood flow were found in active TAO. In contrast, Karabulut et al. (23) did not detect any changes in TED patients whose choroidal perfusion was evaluated indirectly by measuring ocular pulse amplitude in patients with TAO. In addition, they mentioned that there was no correlation between disease activity and ocular pulse amplitude, especially in patients with normal IOP. These authors concluded that although CT was thinner in TAO than in healthy controls, choroidal perfusion did not change, which might be a compensatory mechanism for ocular hemostasis. These findings might be due to the different techniques used for the assessment of choroidal perfusion.

In recent years, EDI-OCT has become the main imaging system to understand choroidal changes in TAO. Many studies have reported that the mean subfoveal CT is increased in patients with active TAO compared to healthy subjects, and that this increase in thickness is directly proportional to disease activity (5,29-31). This increase in CT seen in the active stage has been attributed to orbital venous congestion as a consequence of reduced orbital venous drainage, which was the result of crowded retrobulbar tissue (30,31). Ulas et al. (32) reported that GAG production and accumulation in the connective tissue could be responsible for the increase in CT. However, there are limited studies related to inactive TAO. Fazil et al. (33) compared patients with Graves' disease in the inactive stage with the healthy control subjects and found that CT was slightly higher in patients with Graves' orbitopathy than in healthy subjects, but this did not reach statistical significance. Similarly, Caliskan et al., (31) in their study on 38 patients with Graves ophthalmopathy (14 in the active phase and 24 in the inactive phase), reported that CT was significantly higher in the active group at all the measurement points and, also, there was no significant difference in CT between the inactive group and healthy group at any of the locations. Similarly, current study found that mean CT was not significantly different between inactive TAO patients and healthy controls. Although there was no statistically significant difference in CT between inactive TAO patients and healthy controls, an increase in LA and CVI was detected.

When inflammatory clinical features develop and progress, TAO is in its active phase. Rundle describes an active phase that can last up to 24 months, followed by an inactive phase (34). As noted in previous studies, approximately half of patients with mild-to-moderate TAO resolved spontaneously (34,35). In the current study, the patients were admitted with mild discomfort or difference between the eyes, and their activity scores were below 3 in their examinations. They had not received any treatment before related the TAO. Presumably, these patients somehow went through their active phase for a short time and recovered spontaneously.

CT has been documented to be affected by many confounding factors, such as age and axial length (17). The CVI is the ratio of LA to TCA, which has been used as an indicator to evaluate the vascular status of the choroid (16). The CVI was reported to be unaffected by age, sex, and intraocular pressure in a diabetic population, suggesting CVI as a more reliable and informative parameter for several chorioretinal diseases (17,36,37). In this study, we found no correlation between CVI and patient-related parameters such as age, gender, and axial length.

Agrawal et al. (38) evaluated subfoveal CVI in a sample of 345 healthy eyes of the same ethnicity, with a mean age of 61 years. These authors mentioned that the evaluation of a single scan passing through the fovea is representative of the whole posterior pole choroidal vascularity and the mean CVI calculated subfoveal with a width of 1500 μm was 65.61%±2.33%. Similarly, in our study, the mean CVI (%) was 66.87±2.93 in the healthy control group.

It has been postulated that choroidal vasodilatation and vascular engorgement might be a nonspecific response to inflammation (17). Agrawal et al. (16) evaluated CVI in patients with posterior uveitis and panuveitis and found an increased CVI in these patients. Increased CVI has also been found in many inflammatory diseases affecting the choroid, such as Vogt-Koyanagi-Harada and multiple evanescent white dot syndrome (39,40).

In the current knowledge, during the inactive period, there is no increase in muscle thickness and intraorbital congestion that affect the choroidal blood flow (33-35). Thus, we do not expect a change in choroidal blood flow, but contrary, according to our findings, the increased CVI seen in this study might be due to presence of inflammatory process even in the inactive stages.

Furthermore, we did not find any correlation between CVI and Hertel value of the patients. This result might be related that it could be no obvious proptosis in inactive TAO.

Our study has some limitations. First, this was a cross-sectional study. Thus, we could not evaluate the correlation of changes of clinical activate score and choroidal vascular status or CT. Multiple studies have reported that CT is positively correlated with the CAS grade (4,30). Other studies report that CAS and CT are not correlated (3,26,28). Since we include patients with low CAS (<3), we could not evaluate the relationship between CAS and CT. Furthermore, the small sample size was another limitation for this study.

Conclusion

In this study, although CT was not different between groups, CVI, which is the indicator of the vascular status of the choroid, was higher in patients with TAO in the inactive stage compared with healthy control subjects. The choroidal vascular index can be used as a marker in choroid blood flow monitoring, where measuring the proportions of choroidal vasculature components gives better information about choroidal changes in patients with inactive TAO. The increased CVI found in this study might indicate that vascular changes and the subtle inflammatory process begin even in the inactive stage of the disease. Regular and uninterrupted follow-up of patients in the inactivated stage may allow the inflammatory process to be brought under control before it peaks. Large, comparative, long follow-up studies are now needed comparing patients in the active and inactive stages of TAO.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences Hamidiye Scientific Research Ethics Committee (date: 08.01.2021, no: 21/11).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Conception: S.P., F.E.A.; Design – S.P., F.E.A.; Supervision – U.T., M.T., F.E.A.; Resource – U.T., G.O.K.; Materials – U.T., K.F.; Data Collection and/or Processing – S.P., G.O.K., K.F.; Analysis and/or Interpretation – S.P., G.O.K., O.A.; Literature Search – O.A., M.T., K.F.; Writing – S.P., G.O.K.; Critical Reviews – O.A., M.T.

References

1. Gharib S, Moazezi Z, Bayani MA. Prevalence and severity of ocular involvement in Graves' disease according to sex and age: A clinical study from Babol, Iran. Caspian J Intern Med 2018;9:178–83.
2. Smith TJ, Hegedüs L. Graves' disease. N Engl J Med 2016;375:1552–65. [CrossRef]
3. Verity DH, Rose GE. Acute thyroid eye disease (TED): Principles of medical and surgical management. Eye (Lond) 2013;27:308–19. [CrossRef]
4. Yildirim G, Sahli E, Alp MN. Evaluation of the effect of proptosis on choroidal thickness in Graves' ophthalmopathy. Turk J Ophthalmol 2020;50:221–7. [CrossRef]
5. Ozkan B, Kocer CA, Altintas O, Karabas L, Acar AZ, Yuksel N, et al. Choroidal changes observed with enhanced depth imaging optical coherence tomography in patients with mild Graves orbitopathy. Eye (Lond) 2016;30:917–24. [CrossRef]
6. Wu Y, Tu Y, Wu C, Bao L, Wang J, Lu F, et al. Reduced macular inner retinal thickness and microvascular density in the early stage of patients with dysthyroid optic neuropathy. Eye Vis 2020;7:16. [CrossRef]
7. Sayın O, Yeter V, Arıtürk N. Optic disc, macula, and retinal nerve fiber layer measurements obtained by OCT in thyroid-associated ophthalmopathy. J Ophthalmol 2016;2016:9452687.
8. Brown JS, Flitcroft DI, Ying GS, Francis EL, Schmid GF, Quinn GE, et al. In vivo human choroidal thickness measurements: Evidence for diurnal fluctuations. Invest Ophthalmol Vis Sci 2009;50:5–12. [CrossRef]
9. Mrejen S, Spaide RF. Optical coherence tomography: İmaging of the choroid and beyond. Surv Ophthalmol 2013;58:387–429.
10. Branchini LA, Adhi M, Regatieri CV, Nandakumar N, Liu JJ, Laver N, et al. Analysis of choroidal morphologic features and vasculature in healthy eyes using spectral-domain optical coherence tomography. Ophthalmology 2013;120:1901–8. [CrossRef]
11. Hamzah F, Shinojima A, Mori R, Yuzawa M. Choroidal thickness measurement by enhanced depth imaging and swept-source optical coherence tomography in central serous chorioretinopathy. BMC Ophthalmol 2014;14:145. [CrossRef]
12. Gul A, Basural E, Ozturk HE. Comparison of choroidal thickness in patients with active and stable thyroid eye disease. Arq Bras Oftalmol 2019;82:124–8. [CrossRef]
13. Usui S, Ikuno Y, Akiba M, Maruko I, Sekiryu T, Nishida K, et al. Circadian changes in subfoveal choroidal thickness and the relationship with circulatory factors in healthy subjects. Invest Ophthalmol Vis Sci 2012;53:2300–7. [CrossRef]
14. Chakraborty R, Read SA, Collins MJ. Diurnal variations in axial length, choroidal thickness, intraocular pressure, and ocular biometrics. Invest Ophthalmol Vis Sci 2011;52:5121–9. [CrossRef]
15. Li XQ, Larsen M, Munch IC. Subfoveal choroidal thickness in relation to sex and axial length in 93 Danish university students. Invest Ophthalmol Vis Sci 2011;52:8438–41. [CrossRef]
16. Agrawal R, Salman M, Tan KA, Karampelas M, Sim DA, Keane PA, et al. Choroidal vascularity ındex (CVI)--a novel optical coherence tomography parameter for monitoring patients with panuveitis? PLoS One 2016;11:e0146344. [CrossRef]
17. Iovino C, Pellegrini M, Bernabei F, Borrelli E, Sacconi R, Govetto A, et al. Choroidal vascularity index: An ın-depth analysis of this novel optical coherence tomography parameter. J Clin Med 2020;9:595. [CrossRef]
18. Bartalena L, Baldeschi L, Dickinson AJ, Eckstein A, Kendall-Taylor P, Marcocci C, et al. Consensus statement of the European group on Graves' orbitopathy (EUGOGO) on management of Graves' orbitopathy. Thyroid 2008;18:333–46. [CrossRef]
19. Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, et al. The 2016 European thyroid association/European Group on Graves' orbitopathy guidelines for the management of Graves' orbitopathy. Eur Thyroid J 2016;5:9–26. [CrossRef]
20. Mourits MP, Koornneef L, Wiersinga WM, Prummel MF, Berghout A, van der Gaag R. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: A novel approach. Br J Ophthalmol 1989;73:639–44. [CrossRef]
21. Singh SR, Rasheed MA, Goud A, Sahoo NK, Vupparaboina KK,

Chhablani J. Diurnal variation in subfoveal and peripapillary choroidal vascularity index in healthy eyes. Indian J Ophthalmol 2019;67:1667–72. [CrossRef]
22. Alp MN, Ozgen A, Can I, Cakar P, Gunalp I. Colour Doppler imaging of the orbital vasculature in Graves' disease with computed tomographic correlation. Br J Ophthalmol 2000;84:1027–30. [CrossRef]
23. Karabulut GO, Fazil K, Ozturker C, Gunaydin ZK, Altan C, Inal A, et al. Do ocular pulse amplitude and choroidal thickness change in patients with thyroid eye disease? Orbit 2019;38:347–52. [CrossRef]
24. Monteiro ML, Moritz RB, Neto HA, Benabou JE. Color Doppler imaging of the superior ophthalmic vein in patients with Graves' orbitopathy before and after treatment of congestive disease. Clinics (Sao Paulo) 2011;66:1329–34.
25. Alimgil ML, Benian O, Esgin H, Erda S. Ocular pulse amplitude in patients with Graves' disease: A preliminary study. Acta Ophthalmol Scand 1999;77:694–6. [CrossRef]
26. Tsai CC, Kau HC, Kao SC, Lin MW, Hsu WM, Liu JH, et al. Pulsatile ocular blood flow in patients with Graves' ophthalmopathy. Eye (Lond) 2005;19:159–62. [CrossRef]
27. Tsai CC, Kau HC, Tsai HH, Kao SC, Hsu WM. Pulsatile ocular blood flow change after treatment with systemic steroid in patients with Graves' ophthalmopathy. Eye (Lond) 2006;20:1025–9. [CrossRef]
28. Perez-Lopez M, Sales-Sanz M, Rebolleda G, Casas-Llera P, Gonzalez-Gordaliza C, Jarrin E, et al. Retrobulbar ocular blood flow changes after orbital decompression in Graves' ophthalmopathy measured by color Doppler imaging. Invest Ophthalmol Vis Sci 2011;52:5612–7. [CrossRef]
29. Lai FH, Iao TW, Ng DS, Young AL, Leung J, Au A, et al. Choroidal thickness in thyroid-associated orbitopathy. Clin Exp Ophthalmol 2019;47:918–24. [CrossRef]
30. Zhu Y, Song Y, Cai Q, Zhou Y, Li JJ. Study on observing the central macular choroidal thickness of thyroid-associated ophthalmopathy patients with spectral-domain optical coherence tomography. Zhonghua Yan Ke Za Zhi 2018;54:688–93.
31. Caliskan S, Acar M, Gurdal C. Choroidal thickness in patients with Graves' ophthalmopathy. Curr Eye Res 2017;42:484–90.
32. Ulas F, Dogan U, Dikbas O, Celebi S, Keles A. Investigation of the choroidal thickness in patients with hypothyroidism. Indian J Ophthalmol 2015;63:244–9. [CrossRef]
33. Fazil K, Karabulut GO, Alkin Z. Evaluation of choroidal thickness and retinal vessel density in patients with inactive Graves' orbitopathy. Photodiagnosis Photodyn Ther 2020;32:101898.
34. Menconi F, Profilo MA, Leo M, Sisti E, Altea MA, Rocchi R, et al. Spontaneous improvement of untreated mild Graves' ophthalmopathy: Rundle's curve revisited. Thyroid 2014;24:60–6.
35. Perros P, Crombie AL, Kendall-Taylor P. Natural history of thyroid associated ophthalmopathy. Clin Endocrinol (Oxf) 1995;42:45–50. [CrossRef]
36. Kim M, Ha MJ, Choi SY, Park YH. Choroidal vascularity index in Type-2 diabetes analyzed by swept-source optical coherence tomography. Sci Rep 2018;8:70. [CrossRef]
37. Wei X, Mishra C, Kannan NB, Holder GE, Khandelwal N, Kim R, et al. Choroidal structural analysis and vascularity index in retinal dystrophies. Acta Ophthalmol 2019;97:e116–21. [CrossRef]
38. Agrawal R, Gupta P, Tan KA, Cheung CM, Wong TY, Cheng CY. Choroidal vascularity index as a measure of vascular status of the choroid: Measurements in healthy eyes from a population-based study. Sci Rep 2016;6:21090. [CrossRef]
39. Pellegrini M, Veronese C, Bernabei F, Lupidi M, Cerquaglia A, Invernizzi A, et al. Choroidal vascular changes in multiple evanescent white dot syndrome. Ocul Immunol Inflamm 2019;29:340–5. [CrossRef]
40. Agrawal R, Li LK, Nakhate V, Khandelwal N, Mahendradas P. Choroidal vascularity ındex in vogt-koyanagi-harada disease: An EDI-OCT derived tool for monitoring disease progression. Transl Vis Sci Technol 2016;5:7. [CrossRef]