BMC Ophthalmology

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Choroidal profile in patients with inactive thyroid-associated ophthalmopathy

Mahsan Samadi[1], Hamidreza Ghanbari[1], Ali Momeni[1], Elias Khalili Pour[1], Ali Banafsheh Afshan[1], Nima Naghshtabrizi[2], Seyed Mohsen Rafizadeh[1*] and Hamid Riazi Esfahani[1]

Abstract

Background Thyroid associated ophthalmopathy (TAO) is a common autoimmune condition affecting orbital tissues. In this study, we aim to explore the alterations in choroidal vasculature during inactive phases of TAO by assessing choroidal vascularity index (CVI) and subfoveal choroidal thickness (SFCT) in these patients.

Methods In this cross-sectional comparative case series, enhanced-depth imaging optical coherence tomography (EDI-OCT) images were utilized to compare SFCT and CVI between patients with inactive TAO and age- and sex-matched normal individuals. For CVI assessment, foveal scans underwent binarization using the ImageJ software, with calculations based on the ratio of c (LA) to total choroidal area (TCA). Additionally, we investigated the associations between SFCT or CVI and factors such as age, gender, clinical activity score (CAS), proptosis, duration of disease, and margin to reflex distance (MRD).

Results The study included 50 eyes of 37 patients with inactive TAO (mean ± standard deviation (SD) age: 47 ± 11 years) and 282 eyes of 141 healthy individuals (mean ± SD age: 61 ± 11 years). SFCT and CVI were significantly higher in the TAO group compared to the control group (409.5 ± 152.7 µm vs. 249.3 ± 71.2 µm and 0.684 ± 0.037 vs. 0.629 ± 0.038, $p < 0.001$ for both). There was a significant negative association between age and SFCT in both univariate and multivariate analysis ($r = -0.392$, $p = 0.003$ and $\beta = -0.04$, $p < 0.001$, respectively). In multivariate analysis, we also noted a significant negative association between age and CVI ($\beta = -0.09$, $p < 0.001$). Apart from the correlation between MRD2 and SFCT ($r = 0.297$, $p = 0.038$ in univariate analysis and $\beta = 38.15$, $p = 0.028$ in multivariate analysis), no significant associations were observed between CVI or SFCT and clinical parameters in the TAO group ($p > 0.05$).

Conclusions SFCT and CVI were significantly higher in the inactive TAO group compared to healthy controls. Although SFCT was significantly affected by age, no relationship was observed between CVI and physiologicical or disease-related parameters in univariate analysis. These findings accentuate the complexity of choroidal remodeling in TAO and emphasize the multifactorial nature of its pathogenesis. Further investigations are warranted to elucidate the underlying mechanisms driving these observed alterations and their clinical implications in managing individuals with TAO.

Keywords Thyroid-associated ophthalmopathy, Subfoveal choroidal thickness, Choroidal vascularity index, Enhanced depth imaging optical coherence tomography

*Correspondence:
Seyed Mohsen Rafizadeh
mohsen_raf1354@yahoo.com
[1] Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2] Tehran University of Medical Science, Tehran, Iran

Background

Thyroid-associated ophthalmopathy (TAO) is an autoimmune condition involving the orbital tissues by cellular infiltration and inflammation that mostly affects patients with autoimmune thyroid disease including Graves' hyperthyroidism [1, 2]. Upper lid retraction,

proptosis, and strabismus are the most common clinical presentations [3]. Despite its self-limiting course in the majority of patients, TAO can lead to vision-threatening complications, such as dysthyroid optic neuropathy and corneal breakdown due to exposure keratopathy [4].

The choroid is a highly vascularized structure that plays a critical role in retinal blood supply. Existing literature indicates that the choroidal thickness (CT) can be influenced by various ocular and systemic conditions, including TAO [5–7]. Thyroid disease can lead to alterations in CT due to hemodynamic changes. Some believe that the congestion in the ophthalmic vein is the cause of a thicker choroid in TAO [8–10]. The Infiltration of the choroid with the inflammatory cells and subsequent alteration of vascular permeability, leading to increased leakage, might be another factor contributing to the increased CT during active stages of the disease [11]. Additionally, Ulas et al. [12] concluded that increased production and accumulation of glycosaminoglycans in the connective tissue may also be another probable mechanism for a thicker choroid in TAO patients. While CT has primarily served as a measure for assessing choroidal changes in different diseases, several studies have shown that it is influenced by factors such as gender, age, axial length, refractive error, intraocular pressure (IOP), and diurnal fluctuations [13, 14]. To address this issue, Agrawal et al. introduced choroidal vascularity index (CVI), which is calculated as the proportion of the choroidal luminal area (LA) to the total choroidal area (TCA) [14, 15] by binarizing the images obtained from enhanced depth imaging-optical coherence tomography (EDI-OCT). This novel imaging parameter is indicative of choroidal vascular status and unlike CT, remains unaffected by other factors [14].

While emerging evidence suggests that CT and CVI are generally increased in active TAO, data on choroidal alterations in inactive TAO are limited [16]. In this study, we aim to compare the choroidal vasculature in patients with inactive TAO with a normal age- and sex- matched population using CVI and CT. In addition, we assessed the relationship between CVI and CT with duration of disease and clinical features using Clinical Activity Score (CAS), exophthalmometric value, and margin to reflex distance (MRD). While previous studies have primarily focused on choroidal changes during the active phases of thyroid-associated ophthalmopathy (TAO), our study uniquely investigates the choroidal vascularity index (CVI) and subfoveal choroidal thickness (SFCT) specifically in patients with inactive TAO. This focus allows us to explore potential lingering vascular alterations that may influence long-term management strategies for patients with TAO.

Materials and methods

Study design

This cross-sectional comparative study was conducted at the Oculoplastic Department of Tehran University of Medical Sciences, Farabi Eye Hospital between January 2022 and March 2023. It was registered and approved by the Farabi Eye Hospital Institutional Review Board and Ethics Committee (IR.TUMS.FARABIH.REC.1401.017) and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

Subjects

TAO diagnosis was based on at least one of the suggestive clinical features, including proptosis, upper lid retraction, restrictive strabismus, eyelid swelling and erythema, chemosis, and caruncle edema that were confirmed with endocrinologic findings or radiologic evidence on orbital computerized tomography scan (CT-scan). Disease activity was assessed by CAS, which assigns one point to each of the following items: spontaneous orbital pain, gaze-evoked orbital pain, eyelid erythema, eyelid swelling, conjunctival redness, chemosis, and caruncle inflammation. CAS ≥ 3 indicates active disease [17]. Patients with inactive TAO (CAS < 3) and euthyroid state for at least 6 months were included in this study. The Control group comprised age- and gender- matched normal healthy individuals who attended our hospital for annual check-up. All participants had a spherical equivalent (SE) ranging between -6 and $+6$. Exclusion criteria included the presence of systemic conditions such as systemic corticosteroid therapy, uncontrolled diabetes, and hypertension, as well as a prior history of dysthyroid optic neuropathy or any significant ocular disease that could affect choroidal structure such as glaucoma, uveitis, diabetic retinopathy, retinal vascular disease, age-related macular degeneration (AMD), documented ocular or orbital tumor, and previous orbital, vitreoretinal, and glaucoma surgery. Unclear OCT images that interfered with CVI evaluation were also excluded.

All participants received a comprehensive ophthalmic examination, including refraction and best-corrected visual acuity (BCVA) assessment, slit-lamp examination, and dilated fundus examination. Eyelid retraction was assessed by measurement of the MRD. Proptosis was additionally evaluated by a skilled ophthalmologist (SM.R) using a Hertel exophthalmometer. In order to explore the potential impact of proptosis on choroidal metrics, we divided participants with inactive TAO into two groups based on their Hertel exophthalmometry readings. The threshold of 24 mm was selected as it represents the median value of the ranged measurements within our study population. This approach allows for a

balanced comparison between the two groups with similar sample sizes, minimizing the potential for bias that may arise from arbitrary cut-off points. Additionally, using the median as a threshold is a common practice in clinical research to facilitate the interpretation of results while maintaining statistical robustness.

Image acquisition and processing

To assess choroidal structure, EDI-OCT images were captured using the Spectral-domain (SD) OCT instrument (Heidelberg Engineering, Heidelberg, Germany). Equally-spaced raster B-scans at 8 mm ×12 mm were acquired, and the scan passing through the fovea was considered for image analysis. All scans were captured between 9:00 and 12:00 to minimize the influence of circadian fluctuations. Scans with blinking or motion artifact and poor signal strength were excluded. Subfoveal choroidal thickness (SFCT) was measured using built-in calipers in the OCT software, representing the vertical distance between the outer edge of Bruch's membrane-RPE complex and the innermost border of the choroidoscleral junction. All the segmentations were manually performed by two skilled observers and refined by an experienced retina specialist (H.RE) in the case of disagreement.

Binarization of the image

Image binarization for calculating CVI was conducted following the protocol previously reported by Sonoda et.al. [18]. Distinguishable subfoveal choroidal images were identified by two independent graders for further analysis. The boundaries for the region of interest (ROI) were defined as the basal edge of the RPE for the upper margin and the choroidoscleral border for the lower margin. The edge of the optic nerve head (ONH) served as the nasal margin, while the temporal margin was set 7.5 mm temporal to the edge of ONH. These distances were established using the autoadjust function within the OCT instrument.

To differentiate the vascular area from the interstitium, choroidal images were converted to binary format using a modified Niblack method [18]. All selected OCT images were exported to FIJI (version 1.51 h; National Institutes of Health, Bethesda, Maryland) which is an expanded version of ImageJ software available at http://imagej.nih.gov/Fiji/. Subsequently, the choroidal area was delineated using the ROI manager. The software's oval selection tool from the toolbar was employed to randomly select three choroidal vessels, each with lumens greater than 100 µm. The noise in the OCT images was minimized by setting the average brightness as the minimum value. The image was further processed by converting it to 8 bits and adjusting it using the auto local threshold of Niblack. Subsequently, the binarized image was converted to red–green–blue (RGB) format, and the threshold tool was applied to determine the luminal area. Automatic calculation of the total choroidal area (TCA), luminal area (LA), and stromal area (SA) was done by adding the data related to the distance of each pixel. The choroidal stroma was characterized by light pixels, whereas the luminal area was defined by dark pixels. Eventually, the CVI was determined by dividing LA by TCA.

The inter-rater reliability of SFCT and CVI measurements was examined by applying the absolute agreement model of the inter-class correlation coefficient (ICC) on twenty EDI-OCT images, segmented initially by two independent graders. The ICCs (with 95% confidence intervals) were 0.988 (0.970–0.995) for SFCT measurements and 0.969 (0.918–0.988) for CVI measurements.

Statistical analysis

To characterize the data, continuous variables were described using mean, median, standard deviation, and range, while categorical variables were expressed as frequency and percentage. Kolmogorov–Smirnov test was used to assess the normality of data. Given the likely correlation of the parameters between two eyes, we used Generalized Estimating Equation (GEE) for comparing outcomes between groups. In the TAO group, we utilized the Spearman's rank correlation coefficient test for univariate analysis and a linear regression model for multivariate analysis to examine the association between clinical parameters (proptosis, MRD, CAS, and duration of the symptoms) with CVI and choroidal thickness. A P-value below 0.05 was considered for statistical significance. We performed all statistical analysis using IBM SPSS Statistics (Version 27).

Results

Among 332 eyes included in this study, 50 eyes of 37 subjects were diagnosed with inactive TAO and 282 eyes of 141 healthy individuals served as the control group. The mean ± standard deviation (SD) age was 47 ± 11 years (range 24–64 years) and 61 ± 11 years (range 32–87 years) for the TAO and control groups, respectively. The characteristics of the participants are demonstrated in Table 1. No statistically significant differences were observed between the two groups in terms of age, gender, spherical equivalent, and visual acuity (VA) ($p > 0.05$) (Table 1).

The SFCT was significantly higher in TAO group (409.5 ± 152.7 µm, range: 173 to 1024.7 µm) than in control group (249.3 ± 71.2 µm, range: 100 to 463 µm) ($p < 0.001$). Moreover, we found a significant difference in CVI comparing TAO and control group (0.684 ± 0.037, range: 0.624 to 0.790 and 0.629 ± 0.038, range:

Table 1 Comparison of demographic and clinical parameters between two groups

		Group		*P* value
		TAO	Control	
Gender	Male	19 (38.0%)	114 (40.4%)	0.994
	Female	31 (62.0%)	168 (59.6%)	
Age	Mean ± SD (years)	47 ± 11	61 ± 11	0.326
	Median (range)	50 (24 to 64)	62 (32 to 87)	
VA (Log MAR)	Mean ± SD	0.1 ± 0.22	0.16 ± 0.2	0.087
	Median (range)	0 (0 to 1)	0.15 (0 to 1)	
SE	Mean ± SD	− 2.25 ± 2.14	− 0.82 ± 2.21	0.648
	Median (range)	− 1.75 (− 6 to − 0.75)	− 0.75 (− 5.25 to 6)	
Exophthalmometry	Mean ± SD (mm)	24.2 ± 2.6	-	
	Median (range)	24 (18 to 30)	-	
MRD1	Mean ± SD (mm)	6.5 ± 2.6	-	
	Median (range)	7 (1 to 11)	-	
MRD2	Mean ± SD (mm)	6.7 ± 1.3	-	
	Median (range)	7 (5 to 10)	-	
CAS	0	25 (50.0%)	-	
	1	17 (34.0%)	-	
	2	8 (16.0%)	-	
Duration of disease	Mean ± SD (months)	53 ± 78	-	
	Median (range)	24 (6 to 300)	-	

TAO Thyroid-associated ophthalmopathy, *VA* Visual acuity, *SE* Spherical equivalent, *MRD* Margin to reflex distance

CAS Clinical activity score, $P < 0.05$ indicates significance

0.512 to 0.786, respectively) ($p < 0.001$). After adjusting for demographic factors (age, sex, and VA), GEE analysis revealed the same results ($p < 0.001$ for SFCT and CVI) (Table 2).

In univariate analysis, SFCT was negatively correlated with age (r = − 0.392, $p = 0.003$). There was no significant correlation between CVI and age, sex, or SFCT ($p = 0.582$, $p = 0.705$, and $p = 0.650$, respectively) (Table 3). We measured CAS, proptosis, MRD 1, MRD 2, and duration of disease in TAO group (Table 1). Spearman's rho analysis was conducted to find out the probable correlation between these clinical parameters and CVI or SFCT. Only MRD2 showed a statistically significant positive correlation with SFCT (ρ = 0.297, $p = 0.038$). No significant association was observed between either SFCT or CVI and the other clinical factors (Table 3).

We also performed multivariate analysis to further explore the associations between the clinical parameters and SFCT or CVI. There was a significant negative correlation between both SFCT and CVI with age (β = − 4.04 for SFCT and β = − 0.09 for CVI, $p < 0.001$ for both). Additionally, SFCT was found to be significantly correlated with CVI and MRD2 (β = 5.97, $p < 0.001$ and β = 38.15, $p = 0.028$, respectively). We found no correlations between the other clinical factors with SFCT and CVI (Table 4).

To further investigate the relationships between proptosis and CVI and SFCT, we divided participants

Table 2 Comparison of subfoveal choroidal thickness and choroidal vascularity index between two groups

		Group		P1	P2
		TAO	Control		
CVI	Mean ± SD (%)	0.684 ± 0.037	0.629 ± 0.038	< 0.001*	< 0.001*
	Median (range)	0.675 (0.62 to 0.79)	0.627 (0.512 to 0.786)		
SFCT	Mean ± SD (μm)	409.5 ± 152.7	249.3 ± 71.2	< 0.001*	< 0.001*
	Median (range)	374 (173 to 1024.7)	248 (100 to 463)		

TAO Thyroid-associated ophthalmopathy, *CVI* Choroidal vascularity index, *SFCT* Subfoveal choroidal thickness, P1: *p* value without adjustment, P2: *p* value after adjustment for age, sex, and VA, asterisk indicates significance

Table 3 Univariate analysis showing the associations between subfoveal choroidal thickness and choroidal vascularity index and patient-related parameters in TAO group

	Univariate analysis			
	SFCT		CVI	
Parameter	r	*P*	r	*P*
Age[a]	− 0.392	0.003*	0.076	0.582
Gender[a]	0.177	0.196	− 0.052	0.705
CVI[a]	− 0.063	0.65	-	-
Proptosis[b]	− 0.088	0.541	0.165	0.253
MRD1[b]	0.156	0.284	0.124	0.397
MRD2[b]	0.297	0.038*	0.171	0.24
CAS[b]	− 0.039	0.787	− 0.168	0.244
Disease duration[b]	− 0.288	0.103	0.108	0.548

SFCT Subfoveal choroidal thickness, *CVI* Choroidal vascularity index, *MRD* Margin to reflex distance, *CAS* Clinical activity score, asterisk indicate statistical significance

[a] correlation based on Pearson

[b] correlation based on Spearman's Rho

with inactive TAO into two groups based on their Hertel exophthalmometry readings. Group 1 consisted of 28 patients with Hertel values of 24 mm or lower, while group 2 included 22 individuals with Hertel values of more than 24 mm. we selected 24 mm based on the median of the measured values. There were no statistically significant differences between the two groups regarding SFCT and CVI ($p = 0.707$, $p = 0.585$, respectively). The results of the age-adjusted analysis demonstrated that there were no significant differences in SFCT and CVI between two groups ($p = 0.663$, $p = 0.434$, respectively). (Table 5).

Discussion

In this study, we assessed the choroidal vascular status in patients with inactive TAO. We noted that SFCT and CVI values were higher in inactivate TAO patients compared to healthy control individuals. Despite these significant findings, the clinical relevance of the increased SFCT and CVI in inactive TAO remains unclear. Further

Table 4 Multivariate analysis showing the associations between subfoveal choroidal thickness and choroidal vascularity index and patient-related parameters in TAO group

	Multivariate analysis			
	SFCT		CVI	
Parameter	β (95% CI)	*P*	β (95% CI)	*P*
Age	− 4.04 (− 4.88, − 3.21)	< 0.001*	− 0.09 (− 0.13, − 0.05)	< 0.001*
Gender	− 11.52 (− 32.56, − 3.21)	< 0.28	0.2 (− 0.73, 1.14)	0.67
CVI	5.97 (3.59, 8.36)	< 0.001*	-	-
Proptosis	1.83 (− 17.94, 21.62)	0.85	0.37 (− 0.11, 0.86)	0.12
MRD1	11.86 (− 5.14, 28.87)	0.166	0.21 (− 0.21, 0.64)	0.32
MRD2	38.15 (4.24, 72.06)	0.028*	0.47 (− 0.4, 1.36)	0.28
CAS	29.24 (− 30.19, 88.69)	0.327	− 0.74 (− 2.25, 0.76)	0.33
Disease duration	− 0.45 (− 1.26, 0.35)	0.26	− 0.004 (− 0.02, 0.01)	0.62

SFCT Subfoveal choroidal thickness, *CVI* Choroidal vascularity index, *MRD* Margin to reflex distance, *CAS* Clinical activity score, asterisk indicate statistical significance

Table 5 Associations between subfoveal choroidal thickness and choroidal vascularity index and subgroup exophthalmometric values

		Hertel Exophthalmometry		Unadjusted *p*	Adjusted *p*[*]
		< = 24 mm	> 24 mm		
CVI	Mean ± SD (%)	0.6811 ± 0.0379	0.6894 ± 0.0378	0.585	0.434
	Median (range)	0.6755 (0.624 to 0.79)	0.68 (0.6392 to 0.77)		
SFCT	Mean ± SD (μm)	396 ± 96	382 ± 114	0.707	0.663
	Median (range)	387 (173 to 563)	372 (182 to 692)		

CVI Choroidal vascularity index, *SFCT* Subfoveal choroidal thickness, $p < 0.05$ indicates significance

[*] Adjusted for age

studies are needed to establish the implications of these changes for patient management and outcomes. In univariate analysis, we found a negative association between age and SFCT. Moreover, we investigated the CVI and SFCT associations with clinical parameters including CAS, MRD, proptosis, and duration of disease in TAO group. However, except for a positive correlation between MRD2 and SFCT, both univariate and multivariate analysis revealed no significant relationships.

In recent years, several imaging methods have been established to investigate choroidal changes in various pathological conditions [19–21]. Among these methods, EDI-OCT has emerged as the leading imaging modality due to its feasibility and non-invasive approach in assessing choroidal structure. In recent literature, its application in measuring CT and CVI has become a routine method of quantitatively assessing choroid status in various pathologies, including diabetic retinopathy, glaucoma, AMD, and TAO [22–26].

Several studies have shown an increased SFCT in TAO. The thickening of the choroid may be attributed to reduced orbital venous drainage during the active stages of the disease [8, 9]. However, there is no consensus regarding choroidal changes during the inactive phase of TAO in the literature [9, 27]. Ceylanoglu et al. [11] compared 56 patients with inactive TAO to 64 age- and sex-matched healthy individuals and reported a significant increase in SFCT SFCT inactive TAO patients compared to the healthy controls. Consistent with their findings, we found a statistically significant higher SFCT in the inactivate TAO group compared to the control group in the current study. However, Caliskan et al. [9] reported significantly increased CT in active TAO patients but no significant difference was found when comparing the inactive TAO group with healthy controls in terms of SFCT. Similarly, Pehlivanoglu et al. [28] and Fazil et al. [27] reported that there was no significant difference in SFCT between inactive TAO patients and healthy group. These conflicting results could be attributed to the heterogenicity of the study populations, since CT is influenced by various factors including age, gender, axial length, IOP, and diurnal fluctuations, making it susceptible to the confounding effects of these variables [13, 14]. These discrepancies may arise from differences in patient populations, measurement techniques, and age-related factors, which could significantly influence the outcomes. A thorough understanding of these variables is essential for interpreting the results accurately.

Recent literature has further elucidated the choroidal changes associated with thyroid-associated ophthalmopathy (TAO). For instance, a systematic review by Ioana et al. highlighted that subfoveal choroidal thickness (SFCT) is consistently higher in active TAO, correlating positively with the clinical activity score (CAS) and proptosis, suggesting its role as a marker of disease activity [29]. Moreover, Ermiş et al. found that choroidal vascularity index (CVI) and choroidal thickness were significantly increased in patients with inactive thyroid eye disease (iTED), indicating persistent vascular changes even when clinical symptoms are quiescent [30]. Furthermore, Unlu et al. noted that vascular changes in the peripapillary choroidal area persist in both active and inactive phases of thyroid orbitopathy, which may reflect underlying chronic alterations in choroidal structure [31]. These findings underscore the complexity and potential clinical implications of choroidal remodeling in TAO.

The Development of the binarization technique for interpreting OCT images by Agrawal et al. [14] led to the introduction of the CVI for describing the status of choroidal vasculature. The Choroid consists of vascular and stromal components, and CVI is calculated as the proportion of choroidal vasculature to total choroidal area. Higher values of CVI imply an increase in either the diameter or the number of the choroidal blood vessels. In contrast to CT, recent literature has shown that CVI is less affected by physiological factors, suggesting it as a more reliable parameter in evaluating choroidal vasculature in various chorioretinal diseases [32, 33].

The CVI was first investigated in TAO by Yeter et al. [34]. They reported that TAO induced an almost equal increase in stromal and luminal choroidal area, resulting in no significant difference in CVI between the TAO and control groups. Since then, several studies have evaluated alterations of CVI in TAO patients. In consistent to Yeter et al. findings, these studies noted significantly higher CVI in TAO patients than healthy controls [9, 11, 28, 35, 36]. This increase in CVI could be explained by considering the inflammatory response in TAO and the subsequent dilation and congestion of the choroidal blood vessels [32]. Ceyanoglu et al. [11] and Pehlivanoglu et al. [28] investigated CVI in inactive TAO and reported significantly higher values of CVI in the TAO group than in the control group. Similarly, in our study CVI was found to be significantly increased in inactive TAO patients compared with healthy age- and sex- matched controls. There is a hypothesis suggesting that choroidal vasodilation and vascular engorgement could be a generalized reaction to inflammation [27, 32]. Based on current understanding, muscle thickness and intraorbital congestion do not typically increase during the inactive TAO period, thus having no impact on choroidal blood flow [28]. Therefore, Increased CVI in these patients may suggest the presence of subclinical inflammation in clinically inactive TAO.

The observed increase in subfoveal choroidal thickness (SFCT) and choroidal vascularity index (CVI) in patients

with inactive thyroid-associated ophthalmopathy (TAO) may be attributed to subclinical inflammation that persists even in the absence of overt clinical signs. Chronic inflammatory processes can lead to vascular remodeling, affecting choroidal architecture. Such changes may result in increased vascular permeability and subsequent alterations in choroidal blood flow. Additionally, the role of glycosaminoglycans and their accumulation in the choroidal stroma may contribute to the observed thickening, as noted in previous studies [12]. These factors highlight the multifactorial nature of choroidal changes in TAO patients, emphasizing the need for further research to elucidate the underlying mechanisms.

We assessed the relationships between CVI and SFCT with physiologic parameters and found a significant negative association between age and CVI in multivariate analysis, as well as between age and SFCT in both univariate and multivariate analysis. This finding is consistent with many other studies [9, 11, 37, 38]. In TAO group, we found a positive association between MRD2 and SFCT. However, no significant correlations were detected between CVI or SFCT and other clinical parameters including proptosis, CAS, MRD1, and duration of disease. Additionally, in subgroup analysis comparing CVI and SFCT between TAO patients with lower than 24 mm and higher than 24 mm exophthalmometric values, no significant difference was noted. In support of our study, Loiudice et al. [36] found no correlation between SFCT or CVI and disease-related parameters such as proptosis and CAS. Contrarily, several studies have reported relationship between either CVI or SFCT and duration of disease, proptosis, and CAS [9, 34, 39, 40]. These inconclusive results suggest that there are many unknown factors affecting choroidal vascular and stromal structures, calling for further investigations in the future.

A limitation of our study is the cross-sectional design, which restricted evaluation of the choroidal vascular changes over time. Furthermore, the relatively small sample size might have limited the statistical power in correlation analysis in our study. Moreover, the most effective method for assessing CVI in both normal and pathological conditions involves a volumetric analysis of choroidal vascularity changes within the macular region. In our present investigation, however, all CVI evaluations were restricted to specific foveal horizontal B-scans. While Agrawal et al. demonstrated that a single scan can adequately represent choroidal vascularity across the entire posterior pole in healthy individuals, it is important to exercise caution when extrapolating our findings to assess changes in choroidal metrics in selected foveal slabs to the entire macular area in patients with TAO [14]. Furthermore, the absence of significant associations between CVI and SFCT with clinical parameters such as proptosis, CAS, and disease duration should be explicitly recognized as a limitation of this study, highlighting the need for more comprehensive investigations to explore these relationships.

Conclusion

In the current study, CVI and SFCT were found to be significantly increased in inactive TAO subjects compared with healthy individuals. We observed a negative correlation between age and both SFCT and CVI. No association was noted between either CVI or SFCT and disease-related parameters including CAS, proptosis, and duration of disease in inactivate TAO group.

Acknowledgements
Not applicable.

Authors' contributions
MS drafted the manuscript. HG, AM, and ABA contributed in data acquisition and analysis regarding the segmentation and processing of the OCT images and CVI calculation. SMR was a major contributor in designing the work and examination of the TAO patients. EKH, HRE and NN contributed in interpreting the data and writing the manuscript. All authors read and approved the final manuscript.

Funding
The authors received no financial support for the research, authorship, and publication of this manuscript.

Data availability
Data is provided within the manuscript and is also available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Our study was registered and approved by the Farabi Eye Hospital Institutional Review Board and Ethics Committee (IR.TUMS.FARABIH.REC.1401.017) and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 2 November 2024 Accepted: 18 April 2025
Published online: 25 April 2025

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