BMC Ophthalmology

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Assessment of anterior scleral thickness in Turkish open angle glaucoma patients: an anterior segment optical coherence tomography study

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Abstract

Background To compare anterior scleral thickness (AST) in Turkish patients with open-angle glaucoma (primary open-angle glaucoma (POAG) and pseudoexfoliation glaucoma (PEG)) with healthy controls.

Methods This prospective study involved 41 patients with PEG, 69 patients with POAG, and 46 healthy controls. We obtained spectral domain anterior segment optical coherence tomography (AS-OCT) images from the nasal and temporal quadrants and made AST measurements of 1 mm (AST), 2 mm (AST2), 3 mm (AST3), and 4 mm (AST4) posterior to the scleral spur (SS). Schlemm's canal (SC) diameter and area measurements were performed using the ImageJ software. The results were compared statistically.

Results The average ASTs of the groups did not differ significantly ($p > 0.05$ for each). The analysis of the nasal SC diameter revealed a significant decrease in the POAG group in comparison with the PEG group, with no difference observed between the POAG and control groups ($p = 0.038$*). The mean nasal and temporal SC area was significantly smaller in the PEG and POAG groups compared with the control group ($p < 0.001$** and $p < 0.001$**, respectively).

Conclusions There was no significant difference in nasal and temporal AST between groups; however, the SC area was found to be smaller in glaucoma groups compared with healthy controls. The present findings should be supported by further studies.

Keywords Anterior scleral thickness, Anterior segment optical coherence tomography, Primary open-angle glaucoma, Pseudoexfoliation glaucoma, Schlemm's canal

Introduction

The sclera is a structure consisting of collagen fibers, proteoglycans, and glycoproteins, forming 85% of the outer layer of the eye. It plays an important role in balancing intraocular pressure (IOP) [1]. Previous research demonstrates that the sclera is crucial to the pathophysiology of several ocular illnesses [2]. The region between the cornea and sclera contains essential elements that include the trabecular meshwork (TM) and Schlemm's canal (SC), which facilitate the outflow of aqueous fluid [3]. The scleral spur (SS), another angle element that provides structural support to the TM and SC, is a component of the anterior sclera [4, 5]. Posterior scleral thickness (PST) has been used to determine the biomechanical reaction of the optic nerve head and the lamina cribrosa tissues to IOP [6, 7]. According to the current

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theory, the lamina cribrosa and the tissues of the optic nerve head are biomechanically different in eyes with reduced PST, leading to a higher sensitivity to glaucomatous retinal ganglion cell damage [8]. Some researchers provide indirect evidence that AST is associated with PST and lamina cribrosa [9, 10].

The anterior sclera has been the subject of numerous studies in recent years. Results suggest that the anterior sclera is associated with the pathogenesis of diseases such as myopia, central serous chorioretinopathy, and glaucoma [10–12]. The literature mentioning the possible relationship between normotensive glaucoma (NTG) and anterior scleral thickness (AST) indicates that AST is important in the pathogenesis of glaucoma disease [13]. Also, AST is clinically important after glaucoma surgery and drug delivery [14, 15].

Previous studies have examined AST changes in patients with NTG and primary open-angle glaucoma (POAG) [13, 16]. As far as we know, only one study in the literature has evaluated AST in patients with PEG [17]. However, this study compared the results of a PEG group with patients with pseudoexfoliation syndrome (PES) and healthy controls. PES is the major etiology of OAG that may be identified and is associated with a higher possibility of experiencing vision loss, elevated IOP, and fluctuations in IOP throughout the day when compared with POAG [18].

Given that PEG is such a common type of glaucoma, our objective in this study was to examine AST results in patients with PEG, POAG, and healthy controls using anterior segment optical coherence tomography (AS-OCT). Also, to examine the relationship of AST with central corneal thickness (CCT), SC diameter, and area. To our knowledge, there is no study in the literature comparing AST results of patients with PEG and POAG.

Materials and methods

This prospective study was conducted in the ophthalmology clinic of Sultan Abdülhamid Han Training and Research Hospital. The study was conducted in compliance with the Declaration of Helsinki and received approval from the ethics committee of Haydarpaşa Numune Training and Research Hospital (HNEAH-KAEK 2023/KK/111).

The study included 41 patients in the PEG group, 69 patients in the POAG group, and 46 healthy controls. Patients were recruited between July and October of 2023. Patients diagnosed with POAG included those with an open anterior chamber angle on gonioscopic examination, untreated IOP > 21 mm Hg in Goldmann applanation tonometry, glaucomatous changes in the optic disc, retinal nerve fiber thinning consistent with glaucoma, and/or glaucomatous visual field defects on Humphrey automatic perimetry. The PEG group included patients with pseudoexfoliation material in the anterior capsule of the lens, iris surface, or pupillary membrane on slit lamp biomicroscopic examination, drug-free IOP greater than 21 mm Hg, glaucomatous changes in the optic disc, findings consistent with glaucoma on repeated Humphrey automated perimetry tests and/or retinal nerve fiber analysis, and an open angle on gonioscopy. The control group was selected based on IOP < 21 mm Hg, a normal optic disc, no symptoms, and no history of ocular disease. Patients in the glaucoma group were under topical prostaglandin analog antiglaucomatous treatment for at least 1 year.

Spherical refractive error (SRE) was ± 6D and cylindrical refractive error (CRE) was < 1D in all groups. The best corrected visual acuity (BCVA) was a minimum of 0.6 or above, according to the Snellen chart. All patients underwent axial length (AL) measurements (IOL Master 500, Carl Zeiss Meditec, Dublin, CA). Patients with a history of ocular surgery or trauma, except for uncomplicated cataract surgery, pterygium or pingecula, rigid scleral contact lens wearers, those aged under 18 years, pregnant women, and patients with chronic diseases such as diabetes mellitus or essential hypertension were excluded from the study.

The AST and SC images were obtained using an EDI-OCT anterior segment instrument (Spectralis, Heidelberg Engineering, Heidelberg, Germany). To minimize the impact of diurnal variation, OCT images were acquired between 10:00 a.m. and 2:00 p.m. by the same experienced technician. The nasal and temporal corneoscleral sections were evaluated using a Heidelberg Spectralis AS-OCT. We used the 'EDI' mode and 'Automated Real Time' tracking using frame averaging, with each cross-sectional image representing the average of 50 B-scans, to improve the image signal-to-noise ratio. The patients were directed to focus on the fixation light to maximize visualization of the nasal and temporal bulbar conjunctiva. Episcleral vessels were used to identify the anterior scleral border. The posterior scleral border was defined as the line separating the hyperreflective sclera from the hyporeflective ciliary muscle. The vertical measurement of the AST was taken 1 mm (AST1), 2 mm (AST2), 3 mm (AST3), and 4 mm (AST4) posterior to the scleral spur (Fig. 1). SC was recognized as a black translucent space that presented an elliptic or elliptical shape along its horizontal axis, in close alignment with the TM. SC diameter and area measurements were made manually using the ImageJ program (Fig. 2). Manual SC diameter measurements and area were conducted only on images in which the structure was completely visible. Two experienced ophthalmologists, who were blinded to the study, took measurements to eliminate bias. Each

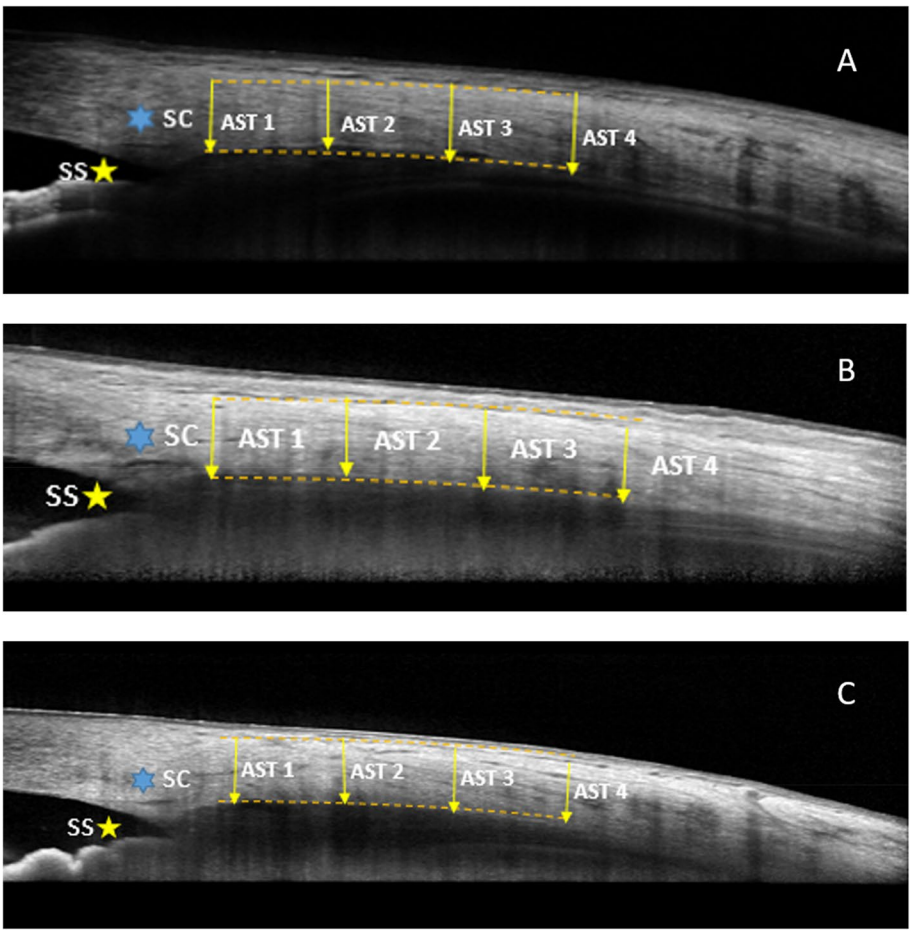

Fig. 1 Evaluation of Anterior Scleral Thickness with Anterior Segment Optical Coherence Tomography. **A** Pseduoexfoliation glaucoma. **B** Primary-open angle glaucoma. **C** Control. SS: Scleral Spur. SC: Schlemm's canal. AST1: Anterior Scleral Thickness 1 mm posterior to the scleral spur. AST2: Anterior Scleral Thickness 2 mm posterior to the scleral spur. AST3: Anterior Scleral Thickness 3 mm posterior to the scleral spur. AST4: Anterior Scleral Thickness 4 mm posterior to the scleral spur

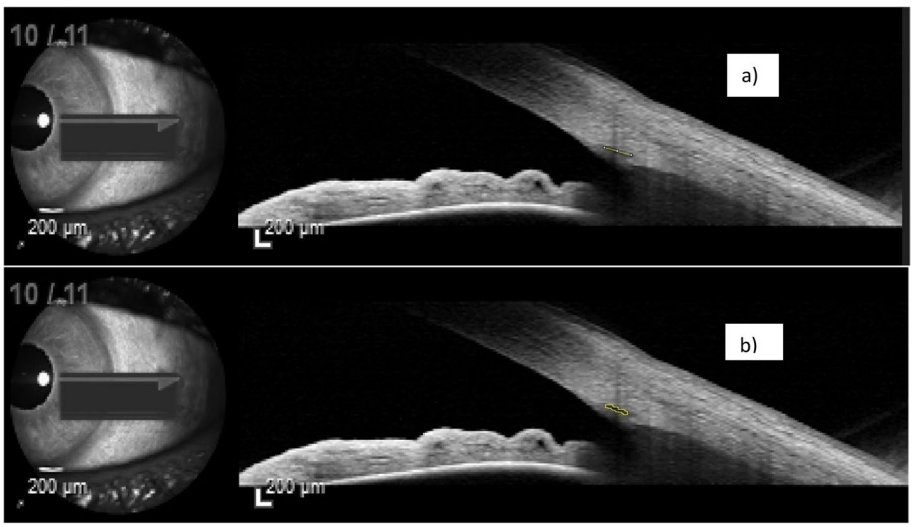

Fig. 2 **a** Schlemm's Canal **(**SC) diameter evaluation with Image-j program. **b** Schlemm's Canal (SC) area evaluation with Image-j program

analyst repeated the measurements three times and recorded the results. The average of the results was used in the statistical analysis. The investigation studied the right eyes of the subjects.

Statistical analysis

Statistical analysis was conducted using the IBM SPSS 26.0 software package. Descriptive statistics (frequency, percentage, median, interquartile range, minimum–maximum values, mean, and standard deviation) of demographic data and all measurements of patients with glaucoma and controls were calculated. In the comparisons of all parameters between groups (POAG, PEG, and controls), analysis of variance (ANOVA) was used for variables that followed a normal distribution, and Spearman correlation analysis was used for non-normally distributed variables. For comparisons between the two groups, the independent sample t-test was used when the data followed a normal distribution. The Mann–Whitney U test was used when evaluating non-normal distributions. In comparisons of nasal and temporal measurements among all groups, the paired sample t-test was used for data that followed a normal distribution, and Wilcoxon's signed-rank test was used for data that did not adhere to a normal distribution. The Shapiro–Wilk test was used to assess the normality of data distribution to determine the appropriate analysis. All statistical analyses were conducted using 95% confidence intervals and a significance level of $p < 0.05$.

Results

The research consisted of 41 patients in the PEG group, 69 patients in the POAG group, and 46 healthy controls. Regarding the distribution of age and sex, there was no significant difference between the groups ($p > 0.05$, respectively) (Table 1). The sociodemographic characteristics of the patients, such as average AL, IOP, CCT, and SRE are summarized in Table 1.

The comparison of the groups in terms of AST revealed no statistically significant differences in AST1, AST2, AST3, and AST4 in the nasal and temporal quadrants ($p > 0.05$ for each). The analysis of the nasal SC diameter revealed a significant decrease in the POAG group in comparison with the PEG group, with no difference observed between the POAG and control groups ($p = 0.038$). No significant variation was observed in the temporal SC diameter between the groups ($p = 0.825$). The mean nasal SC area was significantly smaller in the PEG and POAG groups compared with the control group ($p < 0.001$ and $p < 0.01$, respectively). In the temporal SC area results, the PEG and POAG groups had smaller areas compared with the control group; the PEG group also had smaller temporal SC area results compared with the POAG group ($p < 0.001$, $p = 0.036$, and $p = 0.012$, respectively) (Table 2).

Table 1 Sociodemographic characteristics of participants

	POAG Group ($n = 69$)	PEG Group ($n = 41$)	Control Group ($n = 46$)	*P* value
Age				
Mean ± SD	63.46 ± 5.1	67.98 ± 5.5	65.11 ± 6.3	0.062
(min–max.)	(57–76)	(56–71)	(55–76)	
Gender				
Female (n,%)	38, (55.1%)	18,(43.9%)	21, (45.7%)	0.44
Male (n,%)	31, (44.9%)	23,(56.1%)	25, (54.3%)	
Spherical Refractive Error (SRE) (D)				
Mean ± SD	0.9 ± 2	0.51 ± 1.4	1.08 ± 0.9	0.104
(min–max)	(-4, + 4)	(-4, + 2.75)	(-0.75, + 3.25)	
Intraocular Pressure (IOP) (mmHg)				
Mean ± SD	16.57 ± 2.8	16.27 ± 3.4	15.17 ± 2.1	0.014
(min–max)	(10–24)	(11–26)	(10–21)	*
Central Corneal Thickness(CCT)(µm)				
Mean ± SD	538.77 ± 26.6	524.49 ± 36	533.48 ± 37	0.087
(min–max)	(482–600)	(450–585)	(460–613)	
Axial Length (mm)				
Mean ± SD	23.93 ± 0.68	23.35 ± 0.72	23.47 ± 0.59	0.106
(min–max)	(22.08–25.98)	(22.06–26.02)	(22.32–25.99)	

POAG Primary open-angle glaucoma, *PEG* Pseudoexfoliation glaucoma

Table 2 Results of the anterior scleral thickness (AST) measurements at 1,2,3, and 4 mm from the scleral spur and Schlemm's Canal (SC) diameter,area in the temporal and nasal quadrants

	POAG Group ($n=69$)	PEG Group ($n=41$)	Control Group ($n=46$)	*P* value
Nasal Quadrant AST1 (µm)				
Mean ± SD	555.19 ± 69.7	558 ± 56.4	554.37 ± 58.4	0.918
Nasal Quadrant AST2 (µm)				
Mean ± SD	594.14 ± 69.31	605.83 ± 75.9	579.76 ± 58.6	0.314
Nasal Quadrant AST3 (µm)				
Mean ± SD	623.24 ± 72.1	628.43 ± 73.7	597.98 ± 70.7	0.079
Nasal Quadrant AST4 (µm)				
Mean ± SD	634.47 ± 77.8	647.53 ± 82.7	615.95 ± 85.1	0.243
Temporal Quadrant AST1 (µm)				
Mean ± SD	550.59 ± 64.3	543.17 ± 50.2	565.68 ± 54.1	0.057
Temporal Quadrant AST2 (µm)				
Mean ± SD	542.88 ± 62.7	546.5 ± 53.3	549.15 ± 51.2	0.683
Temporal Quadrant AST3 (µm)				
Mean ± SD	575.98 ± 67	576.4 ± 52.8	583.61 ± 65.1	0.465
Temporal Quadrant AST4 (µm)				
Mean ± SD	602.1 ± 68.2	597.77 ± 51.3	615.22 ± 61.7	0.45
Nasal Quadrant SC diameter (µm)				
Mean ± SD	293.26 ± 63.5	328.36 ± 76.5	302.71 ± 54.4	**0.038***
Nasal Quadrant SC area (μm^2)				
Mean ± SD	8009.8 ± 2808.4	7231.74 ± 2382.1	10,421.52 ± 2602.4	**0.0001****
Temporal Quadrant SC diameter (µm)				
Mean ± SD	289.3 ± 64.8	294.57 ± 79.4	294.46 ± 63.1	0.825
Temporal Quadrant SC area (μm^2)				
Mean ± SD	8289.12 ± 2805.6	6760.62 ± 2432.4	9777.87 ± 3294	**0.0003****

POAG Primary open-angle glaucoma, *PEG* Pseudoexfoliation glaucoma

No statistically significant correlation was observed between AST and CCT, SC diameter, or area in any of the groups ($p > 0.05$ for each) (Tables 3, 4, and 5).

Discussion

This is the first study to compare the AST of patients with POAG and PEG. In addition, comparisons were made between the groups in terms of SC diameter and area, and the relationship of AST with CCT, SC diameter,

Table 3 Correlation analysis between the anterior scleral thickness (AST) and central corneal thickness (CCT), Schlemm's Canal (SC) diameter, and area of the Psueoexfoliation glaucoma (PEG) Group. (Spearman Correlation Analysis)

PEG Group ($n=41$)		Nasal Quadrant AST1	Nasal Quadrant AST2	Nasal Quadrant AST3	Nasal Quadrant AST4	Temporal Quadrant AST1	Temporal Quadrant AST2	Temporal Quadrant AST3	Temporal Quadrant AST4
CCT	**r**	0.141	0.038	-0.191	-0.153	-0.060	-0.074	-0.128	-0.130
	p	0.381	0.813	0.231	0.347	0.715	0.649	0.444	0.485
Nasal SC diameter	**r**	0.026	-0.158	-0.247	-0.178				
	p	0.873	0.323	0.119	0.272				
Nasal SC area	**r**	-0.047	-0.194	-0.233	-0.148				
	p	0.769	0.224	0.142	0.363				
Temporal SC diameter	**r**					-0.060	-0.079	-0.011	0.040
	p					0.712	0.629	0.948	0.832
Temporal SC area	**r**					0.085	0.051	0.053	0.160
	p					0.602	0.756	0.752	0.391

r correlation coefficient

Table 4 Correlation analysis between the anterior scleral thickness (AST) and central corneal thickness (CCT), Schlemm's Canal (SC) diameter, and area of the Primary open-angle glaucoma (POAG) Group. (Spearman Correlation Analysis)

POAG Group ($n=69$)		Nasal Quadrant AST1	Nasal Quadrant AST2	Nasal Quadrant AST3	Nasal Quadrant AST4	Temporal Quadrant AST1	Temporal Quadrant AST2	Temporal Quadrant AST3	Temporal Quadrant AST4
CCT	r	0.166	0.083	0.088	0.205	0.138	0.092	-0.006	0.030
	p	0.174	0.496	0.470	0.101	0.257	0.454	0.959	0.815
Nasal SC diameter	r	0.168	0.089	0.087 0.483	0.146 0.253				
	p	0.174	0.474						
Nasal SC area	r	-0.100	-0.068	-0.008	-0.005				
	p	0.419	0.586	0.946	0.972				
Temporal SC diameter	r					0.049	0.034	0.103 0.412	0.202
	p					0.695	0.786		0.116
Temporal SC area	r					0.150	0.192	0.187	0.194
	p					0.229	0.122	0.132	0.131

r correlation coefficient

Table 5 Correlation analysis between the anterior scleral thickness (AST) and central corneal thickness (CCT), Schlemm's canal (SC) diameter, and area of the Control Group. (Spearman Correlation Analysis)

Control Group ($n=46$)		Nasal Quadrant AST1	Nasal Quadrant AST2	Nasal Quadrant AST3	Nasal Quadrant AST4	Temporal Quadrant AST1	Temporal Quadrant AST2	Temporal Quadrant AST3	Temporal Quadrant AST4
CCT	r	0.190	0.082	0.082	-0.008	-0.015	-0.028	-0.038	0.070
	p	0.207	0.588	0.587	0.959	0.920	0.852	0.801	0.658
Nasal SC diameter	r	0.221	0.241	0.181	0.040 0.797				
	p	0.145	0.111	0.234					
Nasal SC area	r	0.049 0.751	0.037	0.086	0.085				
	p		0.810	0.572	0.582				
Temporal SC diameter	r					0.138	-0.014	-0.090	-0.114
	p					0.360	0.925	0.554	0.466
Temporal SC area	r					-0.074	-0.191	-0.195	-0.203
	p					0.625	0.203	0.195	0.193

r correlation coefficient

and area was analyzed. There was no significant difference in nasal and temporal AST between the groups; however, the SC area was smaller in the glaucoma groups compared with the healthy controls. In the correlation analysis between the groups, no significant relation was observed between AST and CCT, SC diameter, and SC area.

The sclera constitutes 85% of the outer layer of the eye and may be affected by the biomechanical response to IOP [1]. Although many studies are showing that CCT and PST are strong predictors of glaucoma development, our knowledge of the relationship between AST and glaucoma is limited [6, 7, 19]. In an AS-OCT study in Korean patients with OAG, the AST of patients with NTG was thinner than that of patients with POAG and controls, but no significant difference was found between patients with POAG and the control group. However, the study only measured AST in the temporal quadrant [13]. Yan et al. revealed a significantly thinner AST in patients with POAG compared with a control group [16]. In a study conducted on patients with high myopia, Kudsieh et al. observed a significantly thinner AST in patients with high myopia with glaucoma compared with those without glaucoma. This study also evaluated the temporal AST [20]. However, Alpoğan et al., who also evaluated the images taken from the temporal and nasal quadrants, observed no significant difference between PES and PEG groups in terms of AST [17]. The findings of Alpoğan et al. are supported by our investigation. In this current study, no statistically significant difference was seen between AST measured in the nasal and temporal quadrants in patients with PEG, POAG, and controls. Additional research using a larger sample size has the potential to provide supporting results.

Eighty-three to 96% of the aqueous humor is transferred to the collector ducts using the conventional pathway of the trabecular meshwork and SC [21]. Due to the importance of SC in the pathogenesis and treatment of glaucoma, SC imaging with AS-OCT and SC diameter and area measurements have been investigated [22, 23].

In the study by Huang et al., according to the SC diameter and area data given by the enface reconstruction of AS-OCT, the SC diameter of patients with POAG was found to be significantly shorter and the SC area was found to be significantly smaller compared with controls [24]. In a study performed by İmamoğlu et al. on patients with PEG, SC diameters were observed to be shorter, and the SC area was reported to be smaller in the temporal quadrants of patients with PEG in comparison with the control group [22]. Our investigation found no statistically significant variation in the average diameter of the SC from the temporal quadrant between the groups; however, when the mean nasal SC diameter was analyzed, the SC diameter of the POAG group was significantly shorter than the PEG group. Regarding the SC area results, nasal SC area averages were smaller in both the POAG and PEG groups compared with the healthy controls. According to the temporal quadrant SC area results, patients with PEG had significantly smaller SC areas than patients with POAG, and patients with POAG-PEG had smaller SC areas than controls. Our results support other studies in the literature and demonstrate the effect of resistance in SC on the pathogenesis of OAG.

Yan et al. found no significant correlation between AST and SC diameter and area in the POAG group; however, they observed a significant correlation between AST0 (AST measurement at the SS level) and SC area in the control group [16]. Yoo et al. found a significant relationship between CCT and AST in the NTG group but there was no correlation in the POAG and control groups [13]. In the UBM study conducted by Mohamed-Noor et al. with ocular hypertension, NTG, POAG, and control groups, a correlation was observed between CCT and AST only in the NTG group, but no correlation was observed in the ocular hypertension, POAG, or control groups [10]. We observed no significant correlation between CCT, SC diameter, SC area, and AST in any of the groups in the present study (POAG, PEG, and control), which supported these results.

This study has limitations. First, our study includes only Turkish patients. According to a previous study, AST showed ethnic differences [9]. Hence, various ethnic groups may have different outcomes. Secondly, only horizontal quadrants were used for AST measurements because it might be necessary to apply pressure to the eyelids to view vertical quadrants. Accordingly, we have no data on the results of the vertical quadrants.

Conclusion

As a result, there was no significant difference in nasal and temporal AST between groups; however, the SC area was smaller in glaucoma groups compared with the healthy controls. This is important for the outcomes of possible future glaucoma surgeries. There was no significant correlation was found between AST and CCT, SC diameter, and area. Further studies, including larger patient series and different ethnic groups, are required to evaluate the role of AST in the pathogenesis of glaucoma and the relationship between AST and anterior chamber angle elements.

Acknowledgements
Not applicable.

Authors' contributions
I.M.T. designed the study, collected data, wrote the main text, prepared figure and tables and reviewed the manuscript. M.S. collected data, wrote the main text and reviewed the manuscript.

Funding
The authors of the submitted work received no financial support from any organization.

Data availability
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The investigation was approved by the Human Research Ethics Committee of Haydarpasa Numune Training and Research Hospital (HNEAH-KAEK 2023/KK/111) and conducted in accordance with the Helsinki Declaration. Before including any subjects, we obtained informed permission from all of them.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 14 December 2024 Accepted: 13 February 2025
Published online: 21 February 2025

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