中山大學 中山眼科中心
ZHONGSHAN OPHTHALMIC CENTER, SUN YAT-SEN UNIVERSITY

Contents lists available at Lighthouse Scholar

EYE SCIENCE

journal homepage: journal.gzzoc. com

doi: 10.12419/es24090202
View this article at: https://dx.doi.org/10.12419/es24090202

· Review Article ·

Application of anterior scleral thickness measurement in different ocular conditions using anterior segment optical coherence tomography: a systemic review

Lihui Meng (孟丽慧)[1,2 #], Qianyi Yu (于仟仪)[1,2 #], Jingyuan Yang (杨景元)[1,2], Youxin Chen (陈有信)[1,2]

1. Department of Ophthalmology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China
2. Key Lab of Ocular Fundus Diseases, Chinese Academy of Medical Sciences, Beijing 100730, China

HIGHLIGHTS

· Anterior scleral thickness is affected by age, daily variations, and ocular diseases, making it crucial for assessing eye health.
· AS-OCT provides a non-invasive method to measure anterior scleral thickness as an indicator of ocular health, which is an area with limited systemic reviews and significant research potential.
· AS-OCT may enhance clinical evaluation and research on ocular biomechanics, aiding in disease monitoring and progression understanding.

Abstract: **Purpose:** To conduct a review to systematically evaluate the use of anterior segment optical coherence tomography (AS-OCT) in measuring anterior scleral thickness across diverse ocular conditions and its clinical implications. **Methods:** Literature search was conducted across electronic databases, including PubMed, Scopus, and Embase, to identify relevant studies. The risk of bias was assessed, and the main characteristics of each studies were analyzed. We calculated the overall mean anterior scleral thickness using the data which have measurement at the same locations. **Results:** A total of 32 studies were included that utilized AS-OCT to measure anterior scleral thickness in both healthy subjects and individuals with ocular disorders such as myopia, keratoconus, scleritis, and others. The review found that anterior scleral thickness is significantly influenced by age, diurnal variation, and specific ocular conditions. For example, myopic eyes may exhibit thinner sclera,

Received date: 2024-09-02; **Revised date:** 2024-09-23; **Accepted date:** 2024-10-16; **Published online:** 2024-12-20

# These two authors contributed equally to this work.

Corresponding author: Youxin Chen, E-mail: chenyx@pumch.cn.

Full Text

particularly along certain meridians, while conditions like scleritis showed increased scleral thickness due to inflammation. However, some studies have inconsistent results. Additionally, AS-OCT proved effective in detecting subtle variations in anterior scleral thickness, which could be linked to the progression of ocular diseases. **Conclusions:** Anterior scleral thickness varies considerably depending on age, time of day, and ocular health, making it a valuable parameter in the assessment of eye conditions. AS-OCT's ability to measure these variations non-invasively broadens its application in both clinical practice and research, offering new insights into the biomechanical properties of the sclera and their implications for ocular diseases.

Keywords: anterior scleral thickness; anterior segment optical coherence tomography; ocular disorder; clinical implication

Cite this article as: Meng LH, Yu QY, Yang JY, Chen YX. Application of anterior scleral thickness measurement in different ocular conditions using anterior segment optical coherence tomography: a systemic review. Eye Science, 2024, 1(4): 319-335. doi: 10.12419/es24082801.

INTRODUCTION

The sclera is a crucial component of the eye, forming around 85% of the outer tunic of the human eyeball. It is a connective tissue that consists of irregularly arranged lamellae of collagen fibrils interspersed with proteoglycans and glycoproteins, serving as a protective layer that maintains the shape of the eyeball and provides an attachment point for the extraocular muscles.[1] It can also influence the biomechanical characteristics of many intraocular tissues, such as the cornea. A variety of ocular disorders affect the sclera, such as scleritis, myopia, and central serous chorioretinopathy (CSC).[2-4] The scleral thickness may change with different ocular conditions. Nowadays, limited imaging techniques are available for comprehensively analyzing the whole structure of the sclera. Ultrasound biomicroscopy and anterior segment optical coherence tomography (AS-OCT) can be used to visualize the anterior segment, including the anterior sclera.[5] At present, OCT can also visualize the sclera of the posterior pole in highly myopic eyes.

The advent of AS-OCT has revolutionized the evaluation of anterior ocular structures, including the anterior sclera.[6] AS-OCT offers high-resolution, non-invasive imaging that allows for precise measurement of anterior scleral thickness in vivo. Initially, the AS-OCT was developed for the assessment of the cornea and anterior chamber. AS-OCT has expanded its utility to include detailed visualization of the sclera, providing clinicians with valuable insights into the structural integrity and pathology of the eye. The growing body of research utilizing AS-OCT underscores its importance in advancing our understanding of ocular biomechanics and pathology. Recently, researchers have utilized AS-OCT to investigate the anterior scleral thickness not only in healthy eyes, but also in certain ocular disorders such as keratoconus, myopia, CSC and others.[3-4,7] Given the critical role of the sclera in maintaining the structural integrity of the globe and regulating choroidal venous flow and intraocular pressure, changes in scleral structure can serve as indicators of susceptibility to various ocular diseases.[8-9] These changes are often reflected in scleral thickness measurements. Compared to ultrasound biomicroscopy, AS-OCT, with its superior axial resolution of 10 μm, offers a more effective and precise tool for evaluating these conditions.[4,10]

The purpose of this systematic review is to identify and summarize the current literature regarding to the anterior scleral thickness measurement in different ocular conditions. By systematically evaluating the available evidence, we aim to better understand the anterior scleral changes in certain ocular diseases and to suggest future directions of research.

METHODS

Search strategy

A comprehensive literature search was conducted across electronic databases, including PubMed, Scopus, and Embase, to identify studies on measurement of anterior scleral thickness using AS-OCT across different ocular conditions. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and keywords related to "scleral thickness", "optical coherence tomography" and "anterior segment OCT". The search was limited to articles published in English and included studies from the inception of the databases until January 2024. Bibliographies of selected articles were also reviewed to identify any additional relevant studies.

The inclusion criteria and exclusion criteria

The inclusion criteria were as follows: 1) use of AS-OCT to measure anterior scleral thickness; 2) quantitative measurements of anterior scleral thickness; and 3) full-text available.

The exclusion criteria were as follows: 1) involved animal subjects or cadaveric eyes; 2) used imaging techniques other than AS-OCT; 3) no information about anterior scleral thickness; 3) case reports, reviews, editorials, or conference abstracts without full text.

Data extraction and risk of bias assessment

Data extraction was performed independently by two authors (Lihui Meng and Qianyi Yu) using a standardized data extraction form. The extracted data included study characteristics (author, year of publication, country), population characteristics (age, sex, ocular condition), AS-OCT parameters (device used), outcomes (mean anterior scleral thickness, standard deviation, measurement locations) and main study conclusions. Discrepancies between reviewers were resolved through discussion or consultation with the corresponding author (Youxin Chen).

For risk of bias assessment, we used the Newcastle-Ottawa Scale (NOS) and the JBI Critical Appraisal Checklist for analytical cross-sectional studies to assess (as shown in supplementary file 1 and 2). The NOS included the following items: 1) the representativeness of the sample; 2) risk of bias in the measurement of exposures; 3) risk of bias in the measurement of outcomes; 4) risk of bias due to confounding factors. And the JBI Checklist included eight items including inclusion criteria, study subjects, exposure, objective, confounding factors, strategies to deal with confounding factors, outcome measurement and statistical analysis.

Data synthesis

We did not perform any meta-analysis because of the heterogeneity of these studies. In our study, heterogeneity primarily arose from differences in the sample characteristics (such as age, gender, and comorbidities), variations in study equipment (different AS-OCT devices), and inconsistencies in measurement locations. Additionally, the analytical techniques employed in the included studies varied, which could have influenced the comparability of results. Given these factors, the variability between studies was substantial, and a meta-analysis would not have been appropriate. We summarized anterior scleral thickness in different ocular conditions in different studies and their main findings. Besides, we selected studies which have same location measurement in healthy eyes and CSC subjects, calculating the overall mean values ($\mu_{overall}$) and SD ($\sigma_{overall}$) via the following formulas:

$$\mu_{\text{overall}} = \frac{\sum_{i=1}^{n}(N_i \times \mu_i)}{\sum_{i=1}^{n} N_i}$$

N_i is the sample size of subgroup i.

μ_i is the mean value of subgroup i.

n is the total number of subgroups.

$$\sigma_{\text{overall}} = \sqrt{\sigma^2_{\text{overall}}}$$

σi is the sample size of subgroup i.

$$\sigma^2_{\text{overall}} = \frac{\sum_{i=1}^{n}\left[N_i \times \left(\sigma_i^2 + (\mu_i - \mu_{\text{overall}})^2\right)\right]}{\sum_{i=1}^{n} N_i}$$

RESULTS

The screening process was presented in Figure 1. We initially identified 745 potentially publictions related to the anterior scleral thickness using AS-OCT. After removing the duplicates and reviewing the titles and abstracts, 78 full-text articles were assessed for eligibility. Eventually, 32 studies were included in this systematic review.

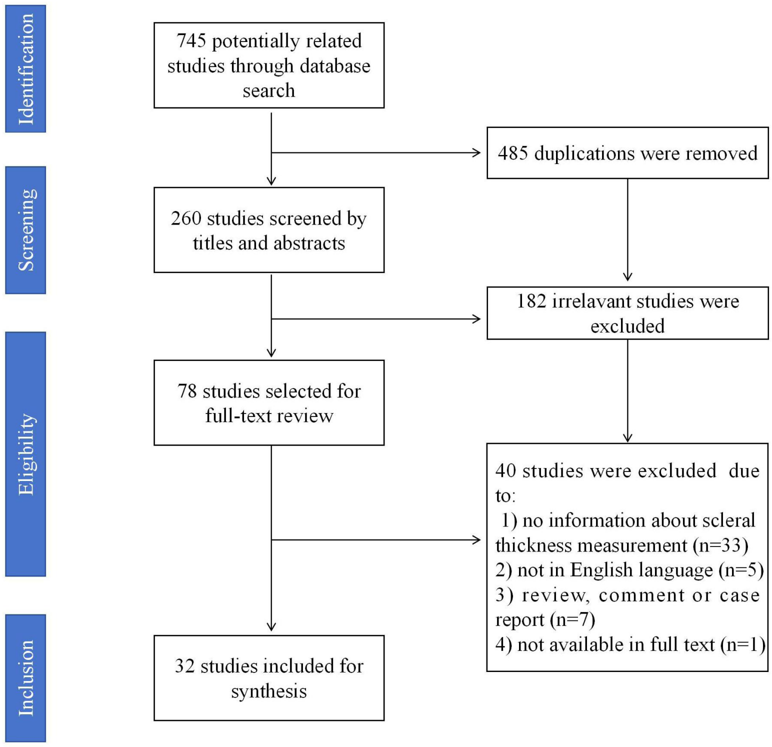

Figure 1 Screening process of the included studies.

Main characteristics of included studies

Except healthy subjects, this review included 11 different types of ocular disorders or conditions, including myopia, keratoconus, exotropia, retinal vein occlusion, CSC, scleritis or episcleritis, glaucoma, fuchs endothelial dystrophy, nanophthalmos, cycloplegia and intravitreal injections. Researchers investigated the associations between anterior scleral thickness with age, measurement locations, diurnal variations, different disorders and local therapies (Table 1).

Risk of bias assessment

As shown in Supplementary file 1 and 2, two evaluation scales, the NOS and the JBI Critical Appraisal Checklist for analytical cross-sectional studies were comprehensively considered. The detailed quality evaluation results can be seen in Supplementary file 1 and 2.

Anterior scleral thickness in healthy eyes

Based on the literature, it is evident that anterior scleral thickness was significantly associated with age, measurement locations and diurnal changes. Ebneter found a significant association of increasing anterior scleral thickness with age ($p<0.0001$, Pearson $r=0.704$). Besides, they found that the thickness varies significantly between quadrants ($p<0.0001$), with the mean anterior scleral thickness (2 mm from the scleral spur) of 571 μm, 511 μm, 475 μm, and 463 μm in the inferonasal, inferotemporal, superotemporal and superonasal quadrant respectively.[11] Buckhurst reported that significant variations in anterior scleral thickness were associated with meridian and distance from scleral spur. In their study, Meridian superionasal sclera was the thinnest (662±57)μm and inferior area was the thickest (806±60) μm. And anterior scleral thickness at 1 mm (682±48) μm was the thinnest and at 6 mm (818±49 μm) the thickest ($P<0.001$).[12] Teuw et al found that the mean anterior scleral thickness of the inferior quadrant was the largest (596±64) μm, followed by the nasal (567±76) μm, temporal (516±67) μm and superior (467±52) μm quadrants ($P<0.001$). Besides, they found that averaged anterior scleral thickness increased 0.96 μm per year.[13] We summarized the results of seven studies (21.88%) which have same measurement locations and calculated the overall mean anterior scleral thickness

Table 1 Summary of main characteristics of incuded studies.

	Publication year	Nationality	Disease	Sample size	Age(years)	Gender (M:F)	Study design	OCT device	Study findings
Zinkernagel et al	2015	Switzerland	Repeated Intravitreal Injections	35 (70 eyes)	76 (range 61-87)^	15:20	Retrospective interventional cross-sectional study	SD-AS OCT (Heidelberg)	Intravitreal injections may lead to thinner sclera when applied repeatedly in the same quadrant.
Pekel et al	2015	Turkey	High Myopia	62 (62 eyes)	(30.5±13.2) vs(30.9±10.6)*	20:42	Cross-sectional comparative study	SD-AS OCT (Heidelberg)	The thickness of anterior wall structures of myopia patientsis not statistically different with healthy controls.
Schlatter et al	2015	Switzerland	Keratoconus	55 (62 eyes)	(30.8±8.5) vs(30.7±6.3)	42:13	Comparative case-control study	SD-AS OCT (Heidelberg)	The anterior scleral stroma thickness in keratoconus patients is similar to that in healthy controls.
Ebneter et al	2015	Switzerland	No	53 (53 eyes)	48.6 (median: 47, range 18-92)	25:28	Observational case series	SD-AS OCT (Heidelberg)	The anterior scleral thickness increases with age and varies significantly between quadrants.
Buckhurst et al	2015	United Kingdom	No	74 (74 eyes)	27.7±5.3	28:46	Cross-sectional study	Visante AS-OCT (Zeiss)	Significant variations in AST occur depending on meridian and distance from the SS.
Read et al	2016	Australia	No	19 (19 eyes)	21.5±2.3	9:10	Longitudinal study	SD-AS OCT (Heidelberg)	This study provides the first evidence of diurnal variations occurring in the thickness of the anterior sclera and conjunctiva.
Woodman-Pieterse et al	2018	Australia	Myopia and emmetropes	40 (40 eyes)	21±2	20:20	Longitudinal study	SD-AS OCT (Heidelberg)	There is significant thinning of the anterior sclera during accommodation. These changes were more prominent in myopes.
Ha et al	2019	Korea	Exotropia	76 (76 eyes)	11.6±6.6	30:46	Retrospective chart review	Cirrus high-definition OCT (Zeiss)	The scleral thickness at1.0-0.5 mm anterior to OMR insertion site was thicker that than at the OMR insertion site.
Adiyeke et al	2020	Turkey	CRVO	67 (134 eyes)	(62.2±11.6) vs(57.9±13.8)	32:35	Case-control study	SD-AS OCT (Heidelberg)	Thicknesses of sclera and lamina cribrosa are increased in the CRVO, which may play a role in the pathogenesis of the disease.
Dhakal et al	2020	India	Myopia	95 (95 eyes)	23.7±3.9	37:58	Cross-sectional study	SS-AS OCT (Topcon)	The relative significant thinning of the anterior sclera along the inferior meridian with increasing degree of myopia compared with the other three meridians.
Kaya et al	2020	Turkey	Systemic Lupus Erythematosus	91 (91 eyes)	(37.9±12.5) vs(38.45±13.76)	12:79	Cross-sectional study	SD-AS OCT (Heidelberg)	Scleral thickness is thicker in SLE patients compared to healthy controls.
Imanaga et al	2021	Japan	Central Serous Chorioretinopathy	87 (100 eyes)	(48.0±10.7) vs(49.0±7.9)	67:20	Retrospective comparative study	SD-AS OCT (Heidelberg)	Scleral thickness is greater in CSC eyes than in control, and thick sclera may have a role in the pathogenesis of CSC.

Table 1 (continue)

	Publication year	Nationality	Disease	Sample size	Age(years)	Gender (M:F)	Study design	OCT device	Study findings
Hau et al	2021	Singapore	Scleritis or Episcleritis	37 (37 eyes)	(42±10.0) vs(40±8.7)	19:18	Prospective study	AS OCT (Optovue)	The degree of vascularity and tissue thickness were different between episcleritis, scleritis and controls.
Sung et al	2021	Korea	Myopia	79 (79 eyes)	27.03±2.70	51:28	Cross-sectional study	SD-AS OCT (Heidelberg)	Scleral thicknesses are influenced significantly by axial length, central corneal thickness, intraocular pressure, and Bruch's membrane opening area in myopic eyes.
Niyazmand et al	2021	Australia	Myopia	45 (45 eyes)	24.8±4.6	20:25	Cross-sectional study	SD-AS OCT (Heidelberg)	The biomechanical forces acting on the eye led to nasal anterior scleral thickening and forward movement of the nasal scleral surface.
Lee et al	2021	Korea	Central Serous Chorioretinopathy	30 (30 eyes)	(50.27±14.42) vs(54.73±11.82)	24:6	Prospective case control study	SD-AS OCT (Heidelberg)	Scleral thickness of the study group were significantly greater than those of the control group. Choroidal thickness was positively correlated with scleral thickness.
Park et al	2021	Korea	Primary Open Angle Glaucoma	54 (54 eyes)	51.35±13.27	NA	Prospective observational study	SD-AS OCT (Heidelberg)	There were no significant changes in AST after using the DTFC drugs, the AST showed a significant reduction after using PG analogues. These might be related with the increased uveoscleral outflow.
Fernández-Vigo et al	2021	Spain	No	596 (596 eyes)	42.6±17.2	258:338	Cross-sectional study	SS-AS OCT (Topcon)	The CTT dimensions were then correlated with age, sex, refractive error and AST.
Imanaga et al	2022	Japan	Central Serous Chorioretinopathy	158 (158 eyes)	(50.2±10.9) vs(55.1±12.7)	130:28	Retrospective cross-sectional study	SD-AS OCT (Heidelberg)	A thick choroid and thick sclera appeared to be related to the presence of LOF in CSC.
Wang et al	2022	Canada	Repeated Intravitreal Injections	79 (158 eyes)	73 (range 34–94)	30:49	Cross-sectional study	NA	Compared to injecting naive eyes, multiple intravitreal injections at the repeated scleral quadrant results in scleral thinning.
Burguera-Giménez et al	2022	Spain	No	50 (50 eyes)	29.02±9.58	14:36	Cross-sectional prospective nonrandomized study	Casia 2 (AS SS-OCT; Tomey)	Scleral thickness is associated with the biomechanical corneal response metrics. Significant meridional variances in scleral thickness occur and prove that AST is associated with AL, CCT and IOP.
Li et al	2023	China	High Myopia	76 (76 eyes)	(34.8±13.3) vs(39.1±12.5)	32:44	Cross-sectional study	Casia SS-1000 (AS SS-OCT; Tomey)	AST and SS length were not significantly different between high myopia and control groups.

Table 1 (continue)

	Publication year	Nationality	Disease	Sample size	Age(years)	Gender (M:F)	Study design	OCT device	Study findings
Zhou et al	2023	China	Myopia	93 (93 eyes)	30.2±8.8	37:56	Cross-sectional study	CIRRUS HD-OCT 5000 (Zeiss)	The AST is negatively correlated with AL and positively correlated with age. Compared with emmetropic eyes, the AST is thinner in highly myopic eyes.
Mohapatra et al	2022	India	Central Serous Chorioretinopathy	100 (100 eyes)	(39.72±8.4) vs(36.16±8.4)	92:8	Prospective case-control study	CIRRUS HD-OCT 5000 (Zeiss)	There is a significant increase in posterior scleral thickness in patients with CSCR while AST is not affected.
Korkmaz et al	2023	Turkey	Fuchs endothelial dystrophy	62 (62 eyes)	(62.5±13.2) vs(64±8.1)	10:52	Prospective cross-sectional study	SS-AS OCT (Topcon)	In patients with FED, scleral thickness was significantly higher.
Aichi et al	2023	Japan	Central Serous Chorioretinopathy	115 (230 eyes)	50.7±12.1	99:16	Retrospective comparative study	SD-AS OCT (Heidelberg)	The affected and fellow eyes showed no significant difference in scleral thickness.
Fernández-Vigo et al	2023	Spain	No	113 (113 eyes)	(38.7±12.3) vs(41.8±11.7)	50:63	Cross-sectional study	SS-AS OCT (Topcon)	CTT and AST measurements were thicker in the temporal quadrant of Hispanic patients compared to Caucasians.
Yildiz et al	2023	Turkey	Keratoconus	71 (71 eyes)	(25.3±4.9) vs(26.5±2.3)	45:26	Cross-sectional study	SS-AS OCT (Topcon)	Structural features of the cornea, sclera, and lamina cribrosa with similar collagen content may be similarly affected in patients with keratoconus.
Fernández-Vigo et al	2023	Spain	Nanophthalmos	58 (106 eyes)	NA	NA	Cross-sectional comparative study	SD-AS OCT (Heidelberg) & SS-AS OCT (Zeiss)	Significant anatomical differences are found in nanophthalmic eyes, but no relevant differences in the AST were observed.
Korkmaz et al	2023	Turkey	Cycloplegia	25 (25 eyes)	30.6±12.4	8:17	Prospective cross-sectional study	SS-AS OCT (Topcon)	After cycloplegia, there was a significant thinning of AST posterior to SS and a slight increase in AST at the SS.
Burguera-Giménez et al	2023	Spain	Keratoconus	111 (111 eyes)	(32.3±12.0) vs(29.0±9.6)	47:64	Prospective non-randomized case-control study	Casia 2 (AS SS-OCT; Tomey)	KC eyes presented significant thickness variations among eccentricities over the paracentral sclera.
Teeuw et al	2023	Netherland	No	107 (214 eyes)	51.6±18.5	48:59	Comprehensive prospective imaging study	SD-AS OCT (Heidelberg)	The mean AST of the inferior quadrant was the largest, followed by the nasal, temporal and superior quadrants. The averaged scleral thickness increased 0.96μm per age year.

^Age of all participants; *(Age of patient group)vs(Age of control group); SD-AS OCT Spectral domain anterior segment optical coherence tomography; AST Anterior scleral thickness; SS Scleral spur; OMR Original medial rectus; CRVO Central retinal vein occlusion; CSC Central Serous Chorioretinopathy; SLE Systemic lupus erythematosus DTFC Dorzolamide/timolol fixed combination; PG Prostaglandin; CTT Conjunctival and Tenon's capsule thickness; AL Axial length; IOP Intraocular pressure; LOF Loculation of fluid; FED Fuchs endothelial dystrophy; KC Keratoconus

(Table 2 and Figure 2). In addition, Read et al reported the diurnal variations in the thickness of the anterior sclera. Over a 24-hour period, anterior scleral thickness had a small magnitude thinning close to midday, and a larger magnitude thickening immediately after waking in the morning ($P < 0.01$).[14] And Fernández-Vigo et al found the anterior scleral thickness was higher in the temporal quadrant of Hispanic patients compared to Caucasians, which they thought might be associated with the pathogenesis of different ocular disorders. Anterior scleral thickness values were larger in the temporal quadrant in the Hispanic group (2 mm from the scleral spur: (559.8±80.8) μm and 3 mm from the scleral spur: (591.6±83.0) μm compared to the Caucasian group (520.7±50.1) μm and (558.9±54.7) μm respectively; $P \leq 0.022$).[15] As for different gender, we summarized two studies (6.25%) which reported anterior scleral thickness in male and female subjects respectively (as shown in Table 3). The findings showed that female tended to have thinner anterior scleral thickness than the male subjects, though in different measurement locations.

Anterior scleral thickness in different ocular conditions

Scleritis and episcleritis

Inflammatory conditions like scleritis and episcleritis show significant changes in scleral structure. Hau et al found the degree of vascularity and thickness of sclera and episclera were different between episcleritis, scleritis and controls using AS-OCT or AS-OCTA.[16] AS-OCT may potentially be a useful tool in evaluating patients with scleral inflammation. And several studies have investigated the conjunctival and scleral complex thickness in scleral inflammatory diseases.[2] We did not include them since they had no information about isolated anterior scleral thickness.

Myopia

50% studies proposed that myopic eyes often exhibited thinner sclera when compared to emmetropic and hypertropic eyes. For example, Dhakal et al found that the relative thinning of the anterior sclera along the inferior meridian with increasing myopic degree compared to other meridians ($r=0.27$; $P=0.008$).[17] The anterior scleral thickness can also be influenced by axial length, corneal thickness, intraocular pressure and even Bruch's membrane opening area.[18] This thinning is associated with the elongation of the eye in myopia, contributing to the biomechanical instability of the sclera. However, the other 50% of publications did not find significant differences. For example, Pekel et al. and Li et al. found that the thickness of anterior wall structures of myopic eyes has no statistical difference with healthy eyes.[3,19]

Keratoconus

In keratoconus, anterior scleral thickness tends to be abnormal. Yildiz et al found that structural features of the cornea, sclera, and lamina cribrosa might be similarly affected in patients with keratoconus due to similar collagen content of them.[7] Burguera-Giménez et al reported that keratoconus eyes presented significant thickness variations among eccentricities over the paracentral sclera. The anterior scleral thickness significantly varied with scleral eccentricity over the temporal meridian ($P=0.009$) in healthy controls, whereas in KC eyes, this variation was over the nasal ($P=0.001$), temporal ($P=0.029$) and inferior ($P=0.006$) meridians.[20] However, Schlatter et al reported that the anterior scleral stroma thickness in keratoconus eyes is similar to that in healthy subjects.[20]

Central serous chorioretinopathy

In CSC (Table 4 and Figure 3), 60% of the studies found that anterior scleral thickness was greater than controls and thought that thick sclera might have a role in the pathogenesis of CSC.[4,21] For example, Imanaga et al found that anterior scleral thickness was significantly greater in CSC eyes than in normal control eyes at the superior ((429.4 ± 50.3) μm *vs.* (395.2 ± 55.4) μm; $P = 0.005$), temporal ((447.7±45.7) μm *vs.* (396.5 ± 64.1) μm; $P < 0.001$), inferior ((455.7 ± 81.2) μm *vs.* (437.8 ± 46.9) μm; $P = 0.022$), and nasal ((454.9 ± 44.7) μm *vs.* (416.6 ± 51.2) μm; $P = 0.001$) points.[4] Besides, the anterior scleral thickness may also have a positive association with choroidal thickness. Lee et al found a positive association between subfoveal choroidal thickness and the sub-lateral rectus muscle scleral thickness ($r=0.394$, $P=0.031$).[21] However, Mohapatra et al found that there was a significant increase in posterior scleral thickness in CSC but no significant differences in anterior scleral thickness.[22] Aichi et al also found no

Table 2 Anterior scleral thickness of healthy eyes (included in the calculation).

First author	Publication year	Nationality	Sample size(Healthy)	Age (Healthy)	Gender (M:F, healthy)	OCT device	0mm-SS-T (μm)	1mm-SS-T (μm)	2mm-SS-T (μm)	3mm-SS-T (μm)	0mm-SS-N (μm)	1mm-SS-N (μm)	2mm-SS-N (μm)	3mm-SS-N (μm)
Buckhurst	2015	United Kingdom	74 (74 eyes)	27.7±5.3	28:46	Visante AS-OCT (Zeiss)	731±64	666±57	659±61	673±65	698±63	674±63	690±62	712±57
Adiyeke	2020	Turkey	35 (70 eyes)	57.9±13.8	18:17	SD-AS OCT (Heidelberg)	702.0±30.8	659.0±28.4	649.0±22.2	655.0±24.9	665.3±24.2	651.9±21.7	655.9±26.7	682.8±21.9
Fernández-Vigo	2021	Spain	596 (596 eyes)	42.6±17.2	258:338	SS-AS OCT (Topcon)	556.5±60.7	522.4±65.7	513.3±67.3	548.8±71.9	546.8±63.4	558.4±71.5	574.4±71.6	590.1±76.6
Burguera-Giménez	2022	Spain	50 (50 eyes)	29.02±9.58	14:36	Casia 2 (AS SS-OCT; Tomey)		522±65	497±63	513±71		525±51	531±58	532±65
Li	2023	China	42 (42 eyes)	39.1±12.5	18:24	SS-OCT	767.48±104.28	558.43±87.99	560.29±84.29	589.29±91.62	690.76±68.69	524.98±59.00	554.88±47.07	564.26±55.06
Fernández-Vigo	2023	Spain	53 (53 eyes) Hispanic	38.7±12.3	24:29	SS-AS OCT (Topcon)		536.1±77.9	559.8±80.8	591.6±83.0		589.3±68.3	611.3±78.8	613.0±75.0
			60 (60 eyes) Caucasian	41.8±11.7	26:34	SS-AS OCT (Topcon)		535.5±56.0	520.7±50.1	558.9±54.7		565.8±75.1	577.5±74.5	589.8±76.4
Fernández-Vigo	2023	Spain	30 (60 eyes)	NA	NA	SS-AS OCT (Zeiss)		670±100	704±89	691±118		687±98	740±94	767±120
			30 (60 eyes)	NA	NA	SD-AS OCT (Heidelberg)		691±99	666±87	691±74		682±99	707±84	719±69
Korkmaz	2023	Turkey	25 (25 eyes)	30.6±12.4	8:17	Casia 2 (AS SS-OCT; Tomey)	718.4±40.1	522.5±24.7	527.2±39.9		697.5±46.0	512.3±34.4	529.6±34.2	
Burguera-Giménez	2023	Spain	50 (50 eyes)	29.0±9.6	14:36	SD-AS OCT (Heidelberg)		522±65	497±63	513±71		525±51	531±58	532±65

^1 mm-SS-T: Anterior scleral thickness at a temporal distance of 1mm from the scleral spur
1 mm-SS-N: Anterior scleral thickness at a nasal distance of 1mm from the scleral spur

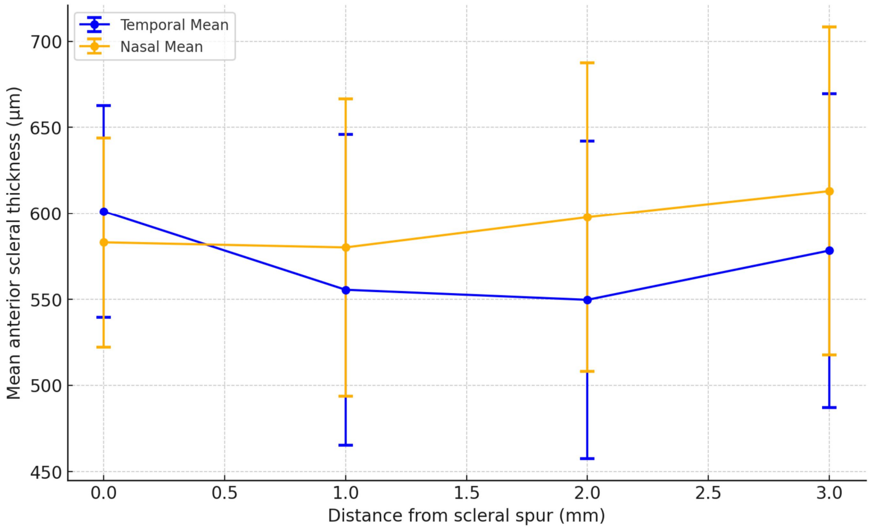

Figure 2 The overall mean temporal/nasal anterior scleral thickness in healthy eyes

Table 3 Anterior scleral thickness of eyes in two gender

First author	Publication year	Nationality	Disease	Sample size	Age	Gender	0~6mm-SS-S (μm)	0~6mm-SS-T (μm)	0~6mm-SS-I (μm)	0~6mm-SS-N (μm)	0~6mm-SS-4q (μm)	0~2mm-LB-4q (μm)
Zhou	2023	China	Myopia	93 (93 eyes)	30.2±8.8	Male (*n*=37)	495±42	603±48	575±62	569±67	559±50	
						Female (*n*=56)	489±34	589±46	573±59	562±55	552±38	
Teeuw	2023	Netherland	No	107 (214 eyes)	51.6±18.5	Male (*n*=48)						552±57
						Female (*n*=59)						524±44

0~6 mm-SS-S: Average anterior scleral thickness at a superior distance of 0~6 mm from the scleral spur.
0~6 mm-SS-T: Average anterior scleral thickness at a temporal distance of 0~6 mm from the scleral spur.
0~6 mm-SS-I: Average anterior scleral thickness at a inferior distance of 0~6 mm from the scleral spur.
0~6 mm-SS-N: Average anterior scleral thickness at a nasal distance of 0~6 mm from the scleral spur.
0~6 mm-SS-4q: Average anterior scleral thickness of 4 quadrants at a distance of 0~6 mm from the scleral spur.
0~2 mm-LB-4q: Average anterior scleral thickness of 4 quadrants at a distance of 0~2 mm from the limbus.

significant differences between CSC and controls.[23]

Other ocular conditions

Some local therapies of the eye may lead to scleral changes. For example, intravitreal injections may lead to thinner sclera if repeating in the same quadrant.[24-25] Zinkernagel et al.[25] reported that eyes with more than 30 injections had thinner average anterior scleral thickness in the inferotemporal quadrant (568.46±66) μm than the fellow eye ((590.6±75) μm, P=0.003). Wang et al. [24] reported that injected eyes had a mean anterior scleral thickness of (588±95) μm *vs.* (618±85) μm in fellow naïve eyes (P<0.001). The anterior scleral thickness showed a significant reduction after using Prostaglandin analogues (P<0.05), which might be associated with the increase uveoscleral outflow.[26] And Korkmaz found that after cycloplegia, there was a significant thinning of anterior scleral thickness posterior to scleral spur in nasal and temporal quadrants (P<0.05) and a slight increase in anterior scleral thickness at the scleral spur but no significant differences.[27]

In retinal vascular diseases, such as retinal vein occlusion, Adiyeke et al.[28] found that thickness of sclera in CRVO eyes were significantly increased at scleral spur in all quadrants ($P<0.05$). Also, in other corneal diseases, such as Fuchs endothelial dystrophy, sclera was significantly thicker at 6 mm posterior to the scleral spur in all quadrants ($P<0.05$).[29]

Noteworthy, AS-OCT has been applied in some systemic diseases' researches. For example, Kaya et al. investigated the anterior scleral thickness in patients with systemic lupus erythematosus (SLE), and found that in SLE patients, the anterior sclera thickness is thicker at all distances compared with controls ($P<0.05$).[30] This broadens the application scope of AS-OCT.

DISCUSSION

In this systematic review, we provided a comprehensive overview of the current understanding of anterior scleral thickness across various ocular conditions using AS-OCT. These studies collectively examined 11 ocular disorders as well as healthy eyes. Variations in anterior scleral thickness can indicate the presence and progression of ocular conditions. For instance, thinner sclera in myopic eyes suggests biomechanical alterations, while increased thickness in conditions like active scleritis may reflects inflammatory responses. Additionally, age and diurnal variations further impact scleral measurements, offering insights into their dynamic nature. The precision of AS-OCT in detecting these subtle changes enhances its utility in monitoring ocular health, potentially aiding early diagnosis and tracking disease progression in clinical settings. The findings underscore the importance of anterior scleral thickness to be a potential biomarker in ocular health.

It is regarded that the anterior scleral thickness is positively with age. This might be due to age-related changes in scleral collagen and biomechanics.[11,13] The observed regional variations in anterior scleral thickness, such as the thicker inferior quadrant compared to other quadrants, suggested that these variations could be linked to the different mechanical stresses exerted on the sclera by ocular movements and external forces.[13] The diurnal variations reported by Read et al indicated that the sclera was not static throughout the day, which might be due to physiological changes in ocular blood flow, intraocular pressure and other metrics fluctuating with the circadian rhythm.[14] The ethnic differences revealed by Fernández-Vigo et al., with Hispanic patients showing higher temporal quadrant thickness compared to Caucasians,

Table 4 Anterior scleral thickness of eyes with central serious chorioretinopathy (included in the calculation)

First author	Publication year	Nationality	Disease	Sample size (CSC)	Age (CSC)	Gender (M:F, CSC)	6mm-SS-S (μm)	6mm-SS-T (μm)	6mm-SS-I (μm)	6mm-SS-N (μm)
Imanaga	2021	Japan	Central Serous Chorioretinopathy	40 (47 eyes)	48.0± 10.7	33:7	429.4± 50.3	447.7± 45.7	455.7± 81.2	454.9± 44.7
Imanaga	2022	Japan	Central Serous Chorioretinopathy (loculation of fluid (LOF))	98 (98 eyes)	NA	86:12	426.2± 63.0	445.7± 55.9	459.2± 62.3	445.4± 59.3
			Central Serous Chorioretinopathy (non-loculation of fluid (non-LOF))	60 (60 eyes)	NA	44:16	395.1± 52.1	414.9± 47.4	428.8± 49.6	414.3± 55.9
Aichi	2023	Japan	Central Serous Chorioretinopathy	115 (230 eyes)	46.4± 18.3	54:46	410.3± 58.4	434.3± 52.9	447.9± 59.5	434.9± 59.1

CSC: Central Serous Chorioretinopathy.
6mm-SS-S: Anterior scleral thickness at a superior distance of 6 mm from the scleral spur.
6mm-SS-T: Anterior scleral thickness at a temporal distance of 6 mm from the scleral spur.
6mm-SS-I: Anterior scleral thickness at a inferior distance of 6 mm from the scleral spur.
6mm-SS-N: Anterior scleral thickness at a nasal distance of 6 mm from the scleral spur.

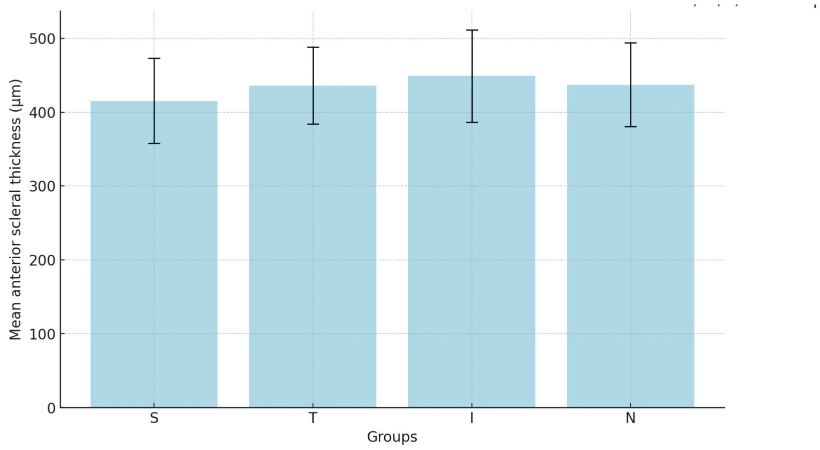

Figure 3 The overall mean anterior scleral thickness in different meridians in CSC eyes

suggest that genetic or environmental factors may also influence scleral structure.[31] This finding may explain the phenomenon to some extent that different ethics have quite different epidemiology in certain ocular disorders. Males had thicker anterior scleral thickness compared to females, but the significance of this phenomenon is not known and could perhaps represent an anthropological difference between two genders.[2]

The sclera has tight associations with other ocular structures, such as the cornea, choroid and ciliary muscle. The anterior scleral thickness is associated with the biomechanical corneal response metrics. Although the measurement profiles did not differ between keratoconus and control groups in some studies, the inferior–superior asymmetry differences demonstrated scleral changes over the vertical meridian in keratoconus, which need further investigation.[7,20,32] According to Korkmaz study, inhibition of forward–inward movement of the ciliary body by cycloplegia can affect anterior scleral thickness via causing a change in the mechanical force of the ciliary muscle on the sclera.[27] In CSC, the association between choroidal changes and anterior scleral thickness has been observed.[21]

The association between myopia and reduced anterior scleral thickness is well-documented in the reviewed studies. The thinning of the sclera, particularly along certain meridians, reflects the biomechanical alterations associated with axial elongation in myopic eyes. This thinning compromises the structural integrity of the sclera, potentially exacerbating myopic progression and increasing the risk of myopia-related complications.[33] However, the inconsistencies reported by Pekel et al. suggest that anterior scleral thickness changes in myopia may not be uniform and could depend on additional factors such as the degree of myopia, axial length, and individual variations in scleral composition.[3,34]

In inflammatory conditions like scleritis and episcleritis, the significant thickening of the sclera observed in the reviewed studies underscores the utility of AS-OCT in diagnosing and monitoring these conditions. AS-OCT was instrumental in identifying necrosis and scleral nodules in subclinical cases, and different subtypes of scleritis indicate different pathogenesis. Moreover, complete resolution of scleral inflammation can be followed by OCT.[35] The ability of AS-OCT to detect subtle changes in scleral structure makes it a valuable tool in distinguishing between different types of scleral inflammation and in assessing the effectiveness of therapeutic interventions.

The findings related to CSC suggest a potential role for increased anterior scleral thickness in the pathogenesis of the disease, possibly due to its association with choroidal thickness. However, the lack of consensus, as seen in the studies by Mohapatra et al. and Aichi et al., indicates that further investigation was required to elucidate the exact relationship between anterior scleral thickness and CSC.[22-23,36] The potential influence of other factors, such as intraocular pressure and choroidal circulation, should also be considered in future studies.

The impact of local therapies, such as intravitreal injections and the use of prostaglandin analogues, cycloplegia on anterior scleral thickness further broadens the clinical relevance of anterior scleral thickness measurements. The observed thinning of the sclera following repeated injections or chronic medication use suggests that these interventions may have unintended effects on scleral integrity, which could influence treatment outcomes, particularly in patients requiring long-term therapy. This may remind clinicians to monitor anterior scleral thickness in patients undergoing such treatments to prevent adverse effects.

The variations in anterior scleral thickness observed in conditions like retinal vein occlusion, Fuchs endothelial dystrophy, and systemic diseases like SLE suggest that scleral changes are not confined to ocular pathologies but may also reflect systemic health. The thicker sclera in SLE patients, as reported by Kaya et al., implies that systemic inflammatory or autoimmune processes could impact scleral structure, providing a potential link between systemic health and ocular manifestations.[30] This finding opens new avenues for research into the role of anterior scleral thickness as a marker for systemic disease.

Strengths of our systematic review include that this topic was the first time to report. And we followed the strict protocol in the synthesis process. However, there was significant variability in the standards used across studies, particularly in relation to diagnostic tools and measurement techniques. For example, AS-OCT equipment from different manufacturers can yield slightly varying results due to differences in resolution, scanning protocols, or imaging software. Additionally, measurement techniques are often not uniformly applied across studies, which can lead to inconsistencies in the data. Standardization of these tools and methods would not only enhance the accuracy and consistency of measurements but also facilitate better comparability across studies. Establishing standardized protocols for AS-OCT imaging, measurement analysis, and reporting could significantly improve the reproducibility of research findings and lead to more robust conclusions in future studies. Our analysis was limited due to the high risk of bias and heterogeneity of included studies, which preclude the further statistical analysis and pooling data for meta-analysis. Specifically, variations in patient characteristics (e.g., age, gender, comorbidities and ethnicities) and study equipment (e.g., SD-OCT vs. SS-OCT) could introduce bias or lead to divergent findings. To better understand the robustness of the conclusions, it would be useful to evaluate how such heterogeneity might affect the outcomes with large sample size in the future.

To advance future research in this area, several critical steps should be taken to tackle the deficiencies identified in the current literature. These steps include 1) measuring same locations in cohort studies; 2) conducting research in a large sample size and maximizing the representativeness; 3) use design such as matching, and analytic strategies (multivariable adjustment, propensity score matching, or inverse probability weighting) to control for potential confounding factors; 4) conducting subgroup analyses or sensitivity tests to assess the consistency of results across different settings or groups; 5) promoting well-designed studies to investigate anterior scleral thickness in different age group, gender group and different ocular conditions.

In conclusion, this systematic review underscores the significant role of anterior scleral thickness in ocular health and disease, as well as the growing importance of AS-OCT in clinical practice. Continued research into anterior scleral thickness, with a focus on standardization, longitudinal analysis, and multimodal imaging, will further advance our understanding of scleral biomechanics and its implications for ocular and systemic health.

Correction notice

None

Acknowledgement

None

Author Contributions

(I) Conception and design: Lihui Meng and Qianyi Yu
(II) Administrative support: Jingyuan Yang and Youxin Chen
(III) Provision of study materials or patients: All authors
(IV) Collection and assembly of data: Lihui Meng and Qianyi Yu
(V) Data analysis and interpretation: Lihui Meng and Qianyi Yu
(VI) Manuscript writing: All authors

(VII) Final approval of manuscript: All authors

Funding

This work was supported by the National Postdoctoral Researcher Funding Program, National Natural Science Foundation of China (82271112).

Conflict of Interests

None of the authors has any conflicts of interest to disclose. All authors have declared in the completed the ICMJE uniform disclosure form.

Patient consent for publication

None

Ethical Statement

None

Provenance and Peer Review

This article was a standard submission to our journal. The article has undergone peer review with our anonymous review system.

Data Sharing Statement

None

References

1. Boote C, Sigal IA, Grytz R, et al. Scleral structure and biomechanics. Prog Retin Eye Res. 2020, 74: 100773. DOI: 10.1016/j.preteyeres.2019.100773.
2. Kommula H, Murthy SI, Loomba A, et al. Scleral thickness in normal Indian eyes measured using spectral domain anterior segment optical coherence tomography. Indian J Ophthalmol. 2023, 71(5): 1833-1836. DOI: 10.4103/ijo.IJO_2046_22.
3. Pekel G, Yağcı R, Acer S, et al. Comparison of corneal layers and anterior sclera in emmetropic and myopic eyes. Cornea. 2015, 34(7): 786-790. DOI: 10.1097/ICO.0000000000000422.
4. Imanaga N, Terao N, Nakamine S, et al. Scleral thickness in central serous chorioretinopathy. Ophthalmol Retina. 2021, 5(3): 285-291. DOI: 10.1016/j.oret.2020.07.011.
5. Nolan W. Anterior segment imaging: ultrasound biomicroscopy and anterior segment optical coherence tomography. Curr Opin Ophthalmol. 2008, 19(2): 115-121. DOI: 10.1097/ICU.0b013e3282f40bba.
6. Lim SH. Clinical applications of anterior segment optical coherence tomography. J Ophthalmol. 2015, 2015: 605729. DOI: 10.1155/2015/605729.
7. Yıldız MB, Bolaç R. Is keratoconus more than just a corneal disease? Cornea. 2024, 43(3): 360-364. DOI: 10.1097/ICO.0000000000003366.
8. Gogola A, Jan NJ, Brazile B, et al. Spatial patterns and age-related changes of the collagen crimp in the human cornea and sclera. Invest Ophthalmol Vis Sci. 2018, 59(7): 2987-2998. DOI: 10.1167/iovs.17-23474.
9. Zhou N, Yang L, Xu X, et al. Uveal effusion syndrome: clinical characteristics, outcome of surgical treatment, and histopathological examination of the sclera. Front Med. 2022, 9: 785444. DOI: 10.3389/fmed.2022.785444.
10. Fernández-Vigo JI, Shi H, Burgos-Blasco B, et al. Anterior scleral thickness dimensions by swept-source optical coherence tomography. Clin Exp Optom. 2022, 105(1): 13-19. DOI: 10.1080/08164622.2021.1924629.
11. Ebneter A, Häner NU, Zinkernagel MS. Metrics of the normal anterior sclera: imaging with optical coherence tomography. Graefes Arch Clin Exp Ophthalmol. 2015, 253(9): 1575-1580. DOI: 10.1007/s00417-015-3072-5.
12. Buckhurst HD, Gilmartin B, Cubbidge RP, et al. Measurement of scleral thickness in humans using anterior segment optical coherent tomography. PLoS One. 2015, 10(7): e0132902. DOI: 10.1371/journal.pone.0132902.
13. Teeuw GJ, Vergouwen DPC, Ramdas WD, et al. Assessment of conjunctival, episcleral and scleral thickness in healthy individuals using anterior segment optical coherence tomography. Acta Ophthalmol. 2024, 102(5): 573-580. DOI: 10.1111/aos.16606.
14. Read SA, Alonso-Caneiro D, Free KA, et al. Diurnal variation of anterior scleral and conjunctival thickness. Ophthalmic Physiol Opt. 2016, 36(3): 279-289. DOI: 10.1111/opo.12288.
15. Fernández-Vigo JI, Fernández-Aragón S, Burgos-Blasco B, et al. Comparison in conjunctival-Tenon’s capsule thickness, anterior scleral thickness and ciliary muscle dimensions between Caucasians and Hispanic by optical

coherence tomography. Int Ophthalmol. 2023, 43(11): 3969-3977. DOI: 10.1007/s10792-023-02798-9.

16. Hau SC, Devarajan K, Ang M. Anterior segment optical coherence tomography angiography and optical coherence tomography in the evaluation of episcleritis and scleritis. Ocul Immunol Inflamm. 2021, 29(2): 362-369. DOI: 10.1080/09273948.2019.1682617.
17. Dhakal R, Vupparaboina KK, Verkicharla PK. Anterior sclera undergoes thinning with increasing degree of myopia. Invest Ophthalmol Vis Sci. 2020, 61(4): 6. DOI: 10.1167/iovs.61.4.6.
18. Sung MS, Ji YS, Moon HS, et al. Anterior scleral thickness in myopic eyes and its association with ocular parameters. Ophthalmic Res. 2021, 64(4): 567-576. DOI: 10.1159/000512396.
19. Li M, Luo Z, Yan X, et al. The anterior segment biometrics in high myopia eyes. Ophthalmic Res. 2023, 66(1): 75-85. DOI: 10.1159/000526280.
20. Schlatter B, Beck M, Frueh BE, et al. Evaluation of scleral and corneal thickness in keratoconus patients. J Cataract Refract Surg. 2015, 41(5): 1073-1080. DOI: 10.1016/j.jcrs.2014.08.035.
21. Lee YJ, Lee YJ, Lee JY, et al. A pilot study of scleral thickness in central serous chorioretinopathy using anterior segment optical coherence tomography. Sci Rep. 2021, 11(1): 5872. DOI: 10.1038/s41598-021-85229-y.
22. Mohapatra T, Trehan HS, Kurumkattil R, et al. Anterior scleral thickness in patients of central serous chorioretinopathy: a Case-control study. Oman J Ophthalmol. 2022, 16(1): 12-17. DOI: 10.4103/ojo.ojo_3_22.
23. Aichi T, Terao N, Imanaga N, et al. Scleral thickness in the fellow eyes of patients with unilateral central serous chorioretinopathy. Retina. 2023, 43(9): 1573-1578. DOI: 10.1097/IAE.0000000000003850.
24. Wang Y, Wei Sim F, Patrick Wang MA, et al. Changes in scleral thickness following repeated anti-vascular endothelial growth factor injections. J Ophthalmic Vis Res. 2022, 17(2): 196-201. DOI: 10.18502/jovr.v17i2.10790.
25. Zinkernagel MS, Schorno P, Ebneter A, et al. Scleral thinning after repeated intravitreal injections of antivascular endothelial growth factor agents in the same quadrant. Invest Ophthalmol Vis Sci. 2015, 56(3): 1894-1900. DOI: 10.1167/iovs.14-16204.
26. Park JH, Yoo C, Chung HW, et al. Effect of prostaglandin analogues on anterior scleral thickness and corneal thickness in patients with primary open-angle glaucoma. Sci Rep. 2021, 11(1): 11098. DOI: 10.1038/s41598-021-90696-4.
27. Korkmaz I, Esen Baris M, Guven Yilmaz S, et al. Effect of cycloplegia on anterior segment structures and scleral thickness in emmetropic eyes. J Ocul Pharmacol Ther. 2023, 39(10): 699-704. DOI: 10.1089/jop.2023.0039.
28. Adiyeke SK, Kutlu N, Aytogan H, et al. Thicknesses of sclera and lamina cribrosa in patients with central retinal vein occlusion. Retina. 2020, 40(10): 2050-2054. DOI: 10.1097/IAE.0000000000002712.
29. Korkmaz I, Degirmenci C, Selver OB, et al. Evaluation of scleral thickness in patients with Fuchs endothelial dystrophy. Graefes Arch Clin Exp Ophthalmol. 2023, 261(10): 2883-2889. DOI: 10.1007/s00417-023-06107-z.
30. Kaya H, Karasu U, Martin Ç, et al. Measurements of scleral thickness and corneal optic densitometry in patients with systemic lupus erythematosus. Medicine. 2020, 99(31): e21467. DOI: 10.1097/MD.0000000000021467.
31. Fernández-Vigo JI, Shi H, Burgos-Blasco B, et al. Impact of age, sex and refractive error on conjunctival and Tenon's capsule thickness dimensions by swept-source optical coherence tomography in a large population. Int Ophthalmol. 2021, 41(11): 3687-3698. DOI: 10.1007/s10792-021-01928-5.
32. Burguera-Giménez N, Díez-Ajenjo MA, Burguera N, et al. Anterior scleral thickness profile in keratoconus. Life. 2023, 13(11): 2223. DOI: 10.3390/life13112223.
33. Sun Y, Sha Y, Yang J, et al. Collagen is crucial target protein for scleral remodeling and biomechanical change in myopia progression and control. Heliyon. 2024, 10(15): e35313. DOI: 10.1016/j.heliyon.2024.e35313.
34. KhalafAllah MT, Fuchs PA, Nugen F, et al. Heterogenous thinning of peripapillary tissues occurs early during high myopia development in juvenile tree shrews. Exp Eye Res. 2024, 240: 109824. DOI: 10.1016/j.exer.2024.109824.
35. BenAbderrahim K. Optical coherence tomography versus ophthalmic examination findings in the management of anterior scleritis: a prospective study. J Fr Ophtalmol. 2022, 45(1): 40-46. DOI: 10.1016/j.jfo.2021.07.009.
36. Imanaga N, Terao N, Sawaguchi S, et al. Clinical factors related to loculation of fluid in central serous chorioretinopathy. Am J Ophthalmol. 2022, 235: 197-203. DOI: 10.1016/j.ajo.2021.09.009.

Supplementary file 1 Risk of bias assessments for the 32 included studies (NOS)

First author	Publication year	Selection	Comparability	Exposure	Score
Zinkernagel	2015	3	1	3	7
Pekel	2015	3	1	2	6
Schlatter	2015	3	1	3	7
Ebneter	2015	3	1	2	6
Buckhurst	2015	4	1	2	7
Read	2016	2	1	2	5
Woodman-Pieterse	2018	3	1	2	6
Ha	2019	3	1	2	6
Adiyeke	2020	3	1	3	7
Dhakal	2020	3	1	2	6
Kaya	2020	4	1	1	6
Imanaga	2021	4	1	2	7
Hau	2021	2	1	3	6
Sung	2021	4	1	1	6
Niyazmand	2021	2	1	2	5
Lee	2021	2	1	3	6
Park	2021	3	1	3	7
Fernández-Vigo	2021	3	2	2	7
Imanaga	2022	4	2	2	8
Wang	2022	4	1	2	7
Burguera-Giménez	2022	2	1	3	6
Li	2023	4	1	2	7
Zhou	2023	4	1	2	7
Mohapatra	2022	4	1	3	8
Korkmaz	2023	3	1	2	6
Aichi	2023	4	1	3	8
Fernández-Vigo	2023	4	1	2	7
Yildiz	2023	3	1	2	6
Fernández-Vigo	2023	3	1	2	6
Korkmaz	2023	2	1	3	6
Burguera-Giménez	2023	3	1	3	7
Teeuw	2023	4	1	2	7

Supplementary file 2 Risk of bias assessments for the 32 included studies (JBI)

First author	Publication year	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Zinkernagel	2015	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Pekel	2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Schlatter	2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Ebneter	2015	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Buckhurst	2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes

Supplementary file 2 (continue)

First author	Publication year	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Read	2016	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Woodman-Pieterse	2018	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Ha	2019	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Adiyeke	2020	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Dhakal	2020	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Kaya	2020	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Imanaga	2021	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Hau	2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Sung	2021	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Niyazmand	2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Lee	2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Park	2021	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Fernández-Vigo	2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Imanaga	2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wang	2022	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Burguera-Giménez	2022	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Li	2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zhou	2023	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Mohapatra	2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Korkmaz	2023	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Aichi	2023	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Fernández-Vigo	2023	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Yildiz	2023	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Fernández-Vigo	2023	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Korkmaz	2023	Yes	Yes	Yes	Yes	No	Not applicable	Yes	Yes
Burguera-Giménez	2023	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Teeuw	2023	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes

JBI Critical Appraisal Checklist for analytical cross sectional studies:
(1) Were the criteria for inclusion in the sample clearly defined?
(2) Were the study subjects and the setting described in detail?
(3) Was the exposure measured in a valid and reliable way?
(4) Were objective, standard criteria used for measurement of the condition?
(5) Were confounding factors identified?
(6) Were strategies to deal with confounding factors stated?
(7) Were the outcomes measured in a valid and reliable way?
(8) Was appropriate statistical analysis used?