Schlemm Canal and Trabecular Meshwork Features in Highly Myopic Eyes With Early Intraocular Pressure Elevation After Cataract Surgery

JIAO QI, WENWEN HE, QIANG LU, KEKE ZHANG, YI LU, AND XIANGJIA ZHU

• PURPOSE: **To investigate the morphologic features of the Schlemm canal and trabecular meshwork in highly myopic eyes with early intraocular pressure (IOP) elevation after cataract surgery.**

• DESIGN: **Retrospective case-control study.**

• METHODS: **Eighty-eight highly myopic eyes of 88 patients after uneventful cataract surgery were included, 31 of which had early postoperative IOP elevation and 57 of which did not. The morphologic features of the Schlemm canal and trabecular meshwork, collected with swept-source optical coherence tomography before surgery, were reviewed. Backwards stepwise multiple linear regression was used to investigate the anatomic risk factors for early IOP elevation in highly myopic eyes.**

• RESULTS: **Highly myopic eyes with early postoperative IOP elevation had smaller Schlemm canal vertical diameter and area, as well as smaller trabecular meshwork thickness and width, in each quadrant than the non-elevation group. There was no significant difference in Schlemm canal horizontal diameter between the IOP elevation and non-elevation groups. In the highly myopic eyes, average Schlemm canal vertical diameter, Schlemm canal area, trabecular meshwork thickness, and width were all correlated negatively with the IOP elevation. A multivariate analysis showed that average Schlemm canal vertical diameter ($\beta = -0.262$, $P = .004$) and trabecular meshwork thickness ($\beta = -0.173$, $P < .001$) were significantly associated with early transient IOP elevation in highly myopic cataract eyes.**

• CONCLUSIONS: **A smaller vertical diameter of Schlemm canal and a thinner trabecular meshwork are 2 anatomic risk factors for early IOP elevation after cataract surgery in highly myopic eyes. (Am J Ophthalmol 2020;216:193–200. © 2020 Elsevier Inc. All rights reserved.)**

THE INCIDENCE OF HIGH MYOPIA IS INCREASING dramatically, especially in Asian countries.[1,2] Early and severe cataract is a common complication of high myopia.[3–6] Therefore, the demand for phacoemulsification is increasing. Cataract surgeons have noted that high myopia may be a risk factor for early intraocular pressure (IOP) elevation after uneventful cataract surgery, which occurs less often with age-related cataract.[7]

Alterations in the morphology of the Schlemm canal and trabecular meshwork, which are the principal sites of aqueous humor outflow resistance, may be important causes of this phenomenon.[8,9] Previous studies have shown that highly myopic eyes have larger Schlemm canal diameter and area, as well as thinner trabecular meshwork thickness compared with emmetropic eyes.[10] However, it remains unclear why only some highly myopic eyes develop early IOP elevation after cataract surgery and others do not.

Therefore, the purpose of this study was to compare the morphologic features of the Schlemm canal and trabecular meshwork in highly myopic cataract (HMC) eyes with and without early IOP elevation after cataract surgery, using swept-source optical coherence tomography (OCT).

METHODS

THIS RETROSPECTIVE CASE-CONTROL STUDY WAS approved by the Institutional Review Board of the Eye and Ear, Nose, and Throat (ENT) Hospital of Fudan University, Shanghai, China. The study adhered to the guidelines of the Declaration of Helsinki. Written informed consents for their medical records to be used for research purposes were obtained from all participants. This study was registered at www.clinicaltrials.gov (accession number NCT02182921).

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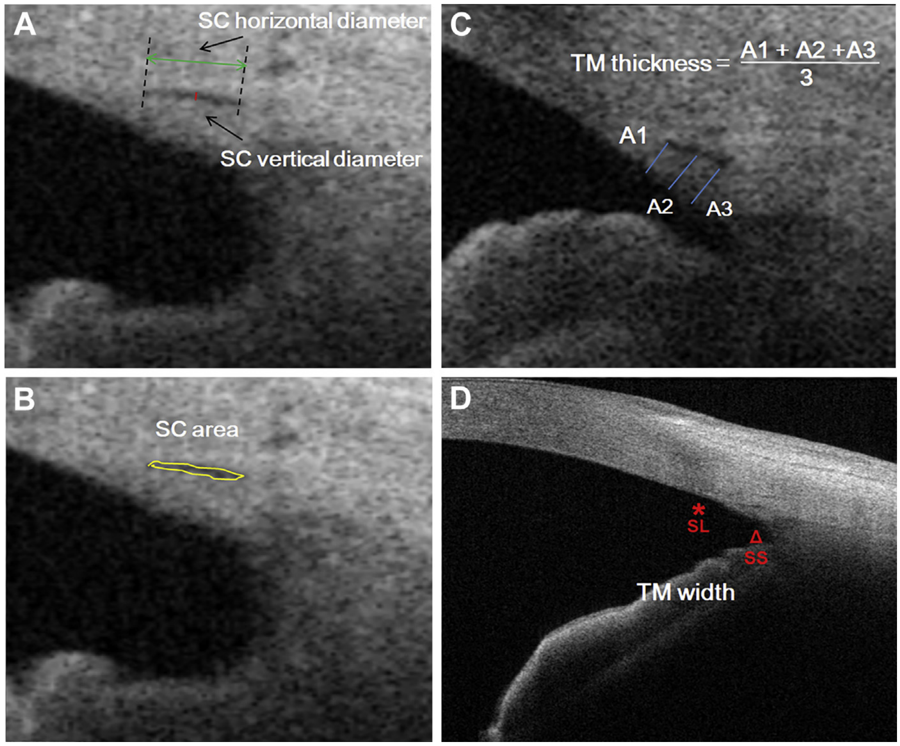

FIGURE 1. Measurement of Schlemm canal (SC) and trabecular meshwork (TM) using swept-source optical coherence tomography. A. SC horizontal diameter was measured from the posterior to the anterior SC endpoint (green line). SC vertical diameter was defined as the distance between the superior and inferior outlines of the Schlemm canal halfway along the Schlemm canal (red line). B. The luminal area of SC was drawn and traced freehand, and the area surrounded by the outline was defined as the SC area (yellow outline). C. TM thickness was defined as the average of the perpendicular distances to the inner layer of TM at the anterior endpoint, midpoint, and posterior endpoints of SC (blue lines). D. TM width was measured from the scleral spur (SS, Δ) to the Schwalbe line (SL, *).

• SUBJECTS: The sample size was calculated based on a power of 90%, a significance level of .05, a paired ratio of 1:2, and a detectable between-group difference in the average trabecular meshwork thickness of 15 μm. The result showed that a minimum sample size of 28 eyes was required for the IOP elevation group and 56 eyes for the control group.

HMC eyes (axial length [AL] ≥26 mm) that had undergone uneventful phacoemulsification and intraocular lens (IOL) implantation between July and December 2018 at the Eye and ENT Hospital of Fudan University were included. The preoperative baseline IOP was <21 mm Hg at 2 continuous visits (time interval: approximately 1 month) in all the included eyes. An early postoperative IOP elevation was defined as IOP ≥25 mm Hg or IOP elevated by ≥8 mm Hg from baseline within 3 days of cataract surgery. ΔIOP was defined as the maximum increase in IOP from the baseline IOP within 3 days of surgery. The exclusion criteria were (1) preoperative IOP ≥21 mm Hg; (2) a history of clinically diagnosed or suspected glaucoma, (3) unclear anterior segment OCT (AS-OCT) images; (4) a history of previous trauma; and (5) severe intraoperative or postoperative complications (eg, posterior capsular rupture, persistent corneal edema, or pupillary capture of the IOL). Finally, 88 HMC eyes of 88 patients (1 eye per patient) were included, 31 of which had suffered early postoperative IOP elevation and 57 of which had not.

• SURGICAL TECHNIQUE: Uneventful phacoemulsification with in-the-bag implantation of a foldable, hydrophilic, acrylic posterior chamber IOL (Rayner Intraocular Lenses, Hove, UK) was performed through a clear corneal incision of 2.6 mm. DisCoVisc (Alcon Laboratories, Fort Worth, Texas, USA) was used in all eyes and removed thoroughly upon completion of surgery. All incisions were hydrated and no stitch was used in any eyes. Relevant surgical parameters were recorded. TobraDex (tobramycin/dexamethasone eye ointment; Alcon Laboratories, Vilvoorde, Belgium) was instilled into all treated eyes at the end of surgery. The routine postoperative medications, including Cravit eye drops (levofloxacin; Santen Pharmaceutical, Japan) and prednisolone acetate (Allergen Pharmaceutical Ireland, Westport, County Mayo, Ireland), were administered 4 times daily for 2 weeks, and pranopulin (Pranoprofen; Senju Pharmaceutical, Osaka, Japan) was administered 4 times daily for 1 month to all patients from the first day after surgery. Mikelan eye drops (carteolol hydrochloride;

TABLE. Baseline Characteristics of All Participants

	Non-elevation (57 Eyes)	IOP Elevation (31 Eyes)	*P* Value
Age, years	63.6 ± 8.1	61.1 ± 7.9	.164
Sex, male/female	26/31	19/12	.160
Eye laterality, right/left	27/30	15/16	.927
AL, mm	29.14 ± 2.16	29.18 ± 2.25	.945
CCT, μm	534.1 ± 38.3	548.1 ± 33.2	.091
ACD, mm	3.46 ± 0.32	3.37 ± 0.39	.264
Baseline IOP, mm Hg	15.2 ± 2.9	15.8 ± 2.6	.292
Average ΔIOP, mm Hg	2.2 ± 2.9	14.3 ± 4.4	.000[a]
Fluid usage, mL	91.54 ± 32.07	93.90 ± 33.79	.747
Aspiration time, s	172.05 ± 69.60	176.35 ± 82.95	.797

ACD = anterior chamber depth; AL = axial length; CCT = central corneal thickness; IOP = intraocular pressure; ΔIOP = maximum IOP elevation from baseline IOP within 3 days after surgery.
[a]Statistically significant ($P < .05$).

Otsuka Pharmaceutical, Tokyo, Japan) were used twice daily by patients with postoperative IOP ≥25 mm Hg and <30 mm Hg; Azarga eye drops (brinzolamide-timolol fixed-combination; Alcon Laboratories) were used twice daily by patients with postoperative IOP ≥30 mm Hg and <35 mm Hg until IOP had decreased to 21 mm Hg or lower. When IOP exceeded 35 mm Hg, D-mannitol was administered via an intravenous drip.

• **ROUTINE OPHTHALMIC EXAMINATIONS:** All the eyes underwent routine preoperative ophthalmologic examinations, including assessment of visual acuity, Goldmann applanation tonometry (Haag-Streit, Bern, Switzerland), funduscopy, B-scan ultrasonography, IOLMaster 700 (Carl Zeiss AG, Oberkochen, Germany), and central corneal thickness (CCT) and anterior chamber depth (ACD) measurement with corneal topography (Pentacam HR; Oculus Optikgeräte GmbH, Wetzlar, Germany).

Postoperative follow-ups, including assessment of visual acuity, funduscopy, and tonometry, were conducted at 1 and 3 days after surgery. Tonometry was performed at 9-10 AM during each follow-up to ensure the consistency. The measurement of IOP was performed by a clinician who was masked to the preoperative AS-OCT data. Each device was operated by a single examiner.

• **OPTICAL COHERENCE TOMOGRAPHY DATA ACQUISITION AND PROCESSING:** The Schlemm canal and trabecular meshwork were scanned with AS-OCT (Tomey SS-1000 CASIA; Tomey, Nagoya, Japan) before cataract surgery by 1 specialized technician. AS-OCT is specifically designed to image the anterior segment, and uses a wavelength of 1,310 nm, a scan speed of 30,000 A-scans per second, and an axial resolution of ≤10 μm.[11] Images were captured in the dark. Seated subjects were told to stare at 1 of 4 peripheral fixation lights to ensure that the iridocorneal angle was centered in the instrument's field of view. The scans were performed independently in the temporal, nasal, superior, and inferior quadrants in the 3-dimensional-angle high-definition model (a raster of 64 B-scans each with 512 A-scans over 8 mm). The scan of each site was repeated 3 times, and the image with the best quality at each position was selected for the final analysis.[12]

Schlemm canal horizontal diameter was defined as the distance from the posterior to the anterior endpoint of the Schlemm canal. Schlemm canal vertical diameter was defined as the distance between the superior and inferior outlines of the Schlemm canal halfway along the Schlemm canal.[13] The luminal area of the Schlemm canal was drawn and traced freehand, and the area surrounded by the outline was defined as the Schlemm canal area.[10] The perpendicular distances from the anterior endpoint, midpoint, and posterior endpoint of the Schlemm canal to the inner layer of the trabecular meshwork were calculated, respectively. The average of these 3 measurements was defined as the trabecular meshwork thickness.[14] The trabecular meshwork width was defined as the distance between the scleral spur and the Schwalbe line. The scleral spur was defined as the point between the trabecular meshwork and the ciliary body, which may appear as an inward scleral protrusion.[15] The border between the bright corneal endothelium and the darker trabecular meshwork was defined as the Schwalbe line[13] (Figure 1).

For each image, the parameters of the Schlemm canal and trabecular meshwork in each quadrant were assessed and then quantified manually by 2 independent and well-trained observers using the software built into the apparatus in the high-definition mode. To measure the interobserver reproducibility, the intraclass correlation coefficients (ICC) were calculated.

• **STATISTICAL ANALYSIS:** All analyses were performed with IBM SPSS v22.0 (IBM Corp, Armonk, New York, USA). All continuous data are presented as mean ±

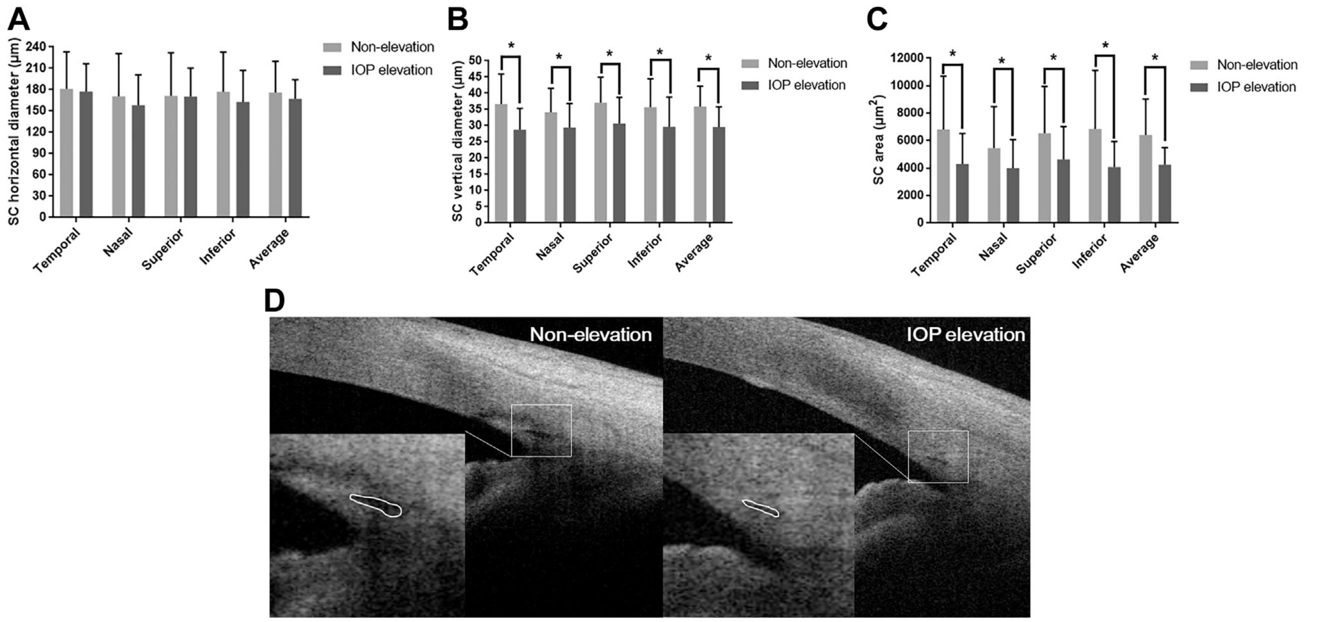

FIGURE 2. Morphologic features of Schlemm canal (SC) on optical coherence tomography. A. No significant differences were detected in the SC horizontal diameters between highly myopic cataract (HMC) eyes with and without postoperative intraocular pressure (IOP) elevation. B. SC vertical diameters in all quadrants and the average value were significantly smaller in HMC eyes with IOP elevation than in those without, *$P < .05$. C. SC areas in all quadrants and the average value were significantly smaller in HMC eyes with IOP elevation than in those without, * $P < .05$. D. Typical illustrations of Schlemm canal in HMC eyes with and without IOP elevation. HMC eyes with IOP elevation had a smaller Schlemm canal vertical diameter than those without.

standard deviation. Categorical data are expressed as frequencies and percentages of each category. Between-group differences were compared with Student *t* test (continuous data) or a χ^2 test (categorical data). The baseline data and the morphologic features of Schlemm canal and trabecular meshwork were compared between HMC eyes with and without early postoperative IOP elevation. Pearson correlation coefficient was used to determine the associations between the morphologic features of Schlemm canal and trabecular meshwork and ΔIOP. Backwards stepwise multiple linear regression was used to identify the anatomic risk factors for early transient IOP elevation after cataract surgery in HMC eyes. The receiver operating characteristic curve (ROC) analysis was used to determine the cut-off value and area under curve (AUC) of identified risk factors for predicting postoperative IOP elevation in HMC eyes. The ideal cut-off value corresponds to the maximal value of the Youden index (Y), which was calculated by Y = sensitivity + specificity − 1. *P* values of <.05 were considered statistically significant.

RESULTS

• BASELINE CHARACTERISTICS OF HIGHLY MYOPIC CATARACT EYES WITH AND WITHOUT POSTOPERATIVE INTRAOCULAR PRESSURE ELEVATION: The baseline characteristics of the HMC eyes with and without postoperative IOP elevation are presented in the Table. There were no statistically significant differences between the 2 groups in age, sex, eye laterality, AL, CCT, ACD, baseline IOP, fluid usage, or aspiration time (Student *t* test for age, AL, CCT, ACD, baseline IOP, fluid usage, and aspiration time; χ^2 test for sex and eye laterality; all $P > .05$). The average ΔIOP was 14.3 ± 4.4 mm Hg in the IOP elevation group and 2.2 ± 2.9 mm Hg in the non-elevation group (Student *t* test, $P < .001$).

• MORPHOLOGIC FEATURES OF SCHLEMM CANAL AND TRABECULAR MESHWORK IN HIGHLY MYOPIC CATARACT EYES WITH INTRAOCULAR PRESSURE ELEVATION: The measurements of Schlemm canal and trabecular meshwork parameters by 2 independent observers showed excellent repeatability and reproducibility (ICC analysis, all $P <$ .05; Supplemental Table; Supplemental Material available at AJO.com).

There were no significant differences in Schlemm canal horizontal diameter of each quadrant or the average value between the IOP elevation and non-elevation groups of HMC eyes (Student *t* test, all $P > .05$; Figure 2A). Figure 2B shows that the Schlemm canal vertical diameter in all quadrants and the average value were smaller in the IOP elevation group than in the non-elevation group (Student *t* test, all $P < .05$). Figure 2C shows that the Schlemm canal area in all quadrants and the average value were

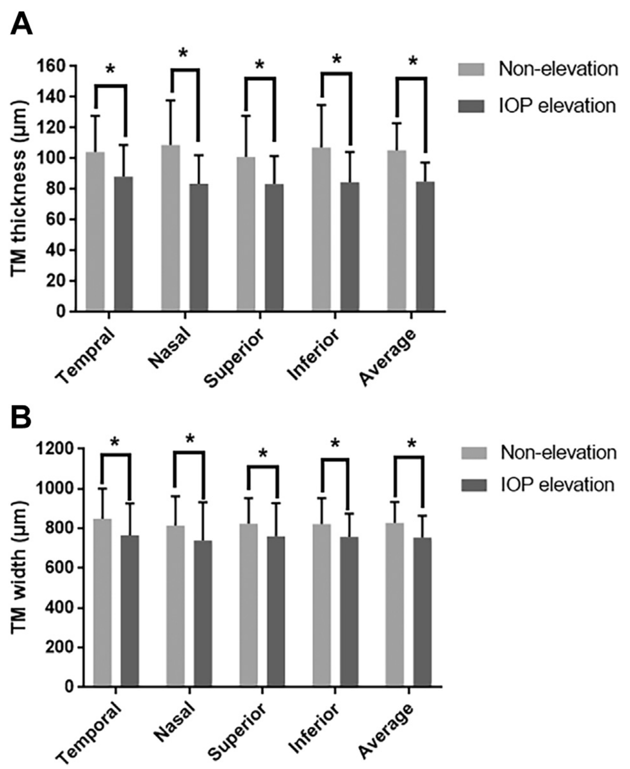

FIGURE 3. Morphologic features of trabecular meshwork (TM) on optical coherence tomography. A. TM thicknesses in all quadrants and the average value were significantly thinner in highly myopic cataract (HMC) eyes with intraocular pressure (IOP) elevation than in those without, * $P < .05$, B. TM widths in all quadrants and the average value were significantly smaller in HMC eyes with IOP elevation than in those without, * $P < .05$.

smaller in the IOP elevation group than in the non-elevation group of HMC eyes (Student *t* test, all $P < .05$). Figure 2D shows typical OCT images of the Schlemm canal in HMC eyes with and without postoperative IOP elevation.

The trabecular meshwork thickness in HMC eyes is shown in Figure 3A. The trabecular meshwork was significantly thinner in the IOP elevation group than in the non-elevation group of HMC eyes (Student *t* test, all $P < .05$). Meanwhile, the trabecular meshwork width in all quadrants and the average value were also smaller in the IOP elevation group than in the non-elevation group (Student *t* test, all $P < .05$; Figure 3B).

• **ANATOMIC RISK FACTORS FOR POSTOPERATIVE INTRAOCULAR PRESSURE ELEVATION IN HIGHLY MYOPIC CATARACT EYES:** ΔIOP correlated negatively with the average Schlemm canal vertical diameter (Pearson correlation coefficient, $r = -0.436$, $P < .001$; Figure 4A), average Schlemm canal area (Pearson correlation coefficient, $r = -0.394$, $P < .001$; Figure 4B), average trabecular meshwork thickness (Pearson correlation coefficient, $r = -0.573$, $P < .001$; Figure 4C), and average trabecular meshwork width (Pearson correlation coefficient, $r = -0.251$, $P = .018$; Figure 4D) in the entire population. Looking at the 2 groups separately, ΔIOP were only negatively correlated with the average Schlemm canal vertical diameter (Pearson correlation coefficient, $r = -0.432$, $P = .015$; Figure 4E) and the average trabecular meshwork thickness (Pearson correlation coefficient, $r = -0.433$, $P = .015$; Figure 4F) in the IOP elevation group, while no such correlations were found in the non-elevation group (Pearson correlation coefficient, all $P > .05$).

A backwards stepwise multiple linear regression analysis, which included age, sex, eye laterality, AL, ACD, CCT, baseline IOP, average Schlemm canal horizontal and vertical diameter, average trabecular meshwork thickness, and width as potential predictive factors, demonstrated that average Schlemm canal vertical diameter ($\beta = -0.262$, $P = .004$) and average trabecular meshwork thickness ($\beta = -0.173$, $P < .001$) were associated with ΔIOP in HMC eyes.

ROC analyses identified that the average Schlemm canal vertical diameter to predict the IOP elevation after cataract surgery in HMC eyes was 32.6 μm and the AUC was 0.765, and the cut-off value and AUC for the average trabecular meshwork thickness were 89.1 μm and 0.825, respectively.

DISCUSSION

HIGH MYOPIA IS A MAJOR CAUSE OF POOR VISION AND blindness worldwide. Many anatomic abnormalities are seen in eyes with high myopia, including a thinner sclera and choroid,[16,17] making these eyes more susceptible to severe comorbidities, such as glaucoma and chorioretinopathy.[18,19]

High myopia may be a risk factor for early IOP elevation after uneventful cataract surgery. Morphologic investigations of Schlemm canal and trabecular meshwork in highly myopic eyes have been performed with AS-OCT and have shown that these eyes have a thinner trabecular meshwork and a larger Schlemm canal diameter and area than emmetropic eyes.[10] However, it remained unclear why only some highly myopic eyes develop postoperative IOP elevation and others with similar axial length do not.

Anatomic differences in the drainage passage may explain this discrepancy. To avoid early postoperative elevated IOP after cataract surgery, normal aqueous outflow channel functions are necessary in dealing with the retained viscoelastics or lens materials and the inflammation induced by the disruption of the blood-aqueous barrier.[20] The morphologic features of the Schlemm canal and trabecular meshwork, the principal sites of aqueous outflow, warrant close attention. AS-OCT is a noncontact imaging device that rapidly produces high-resolution

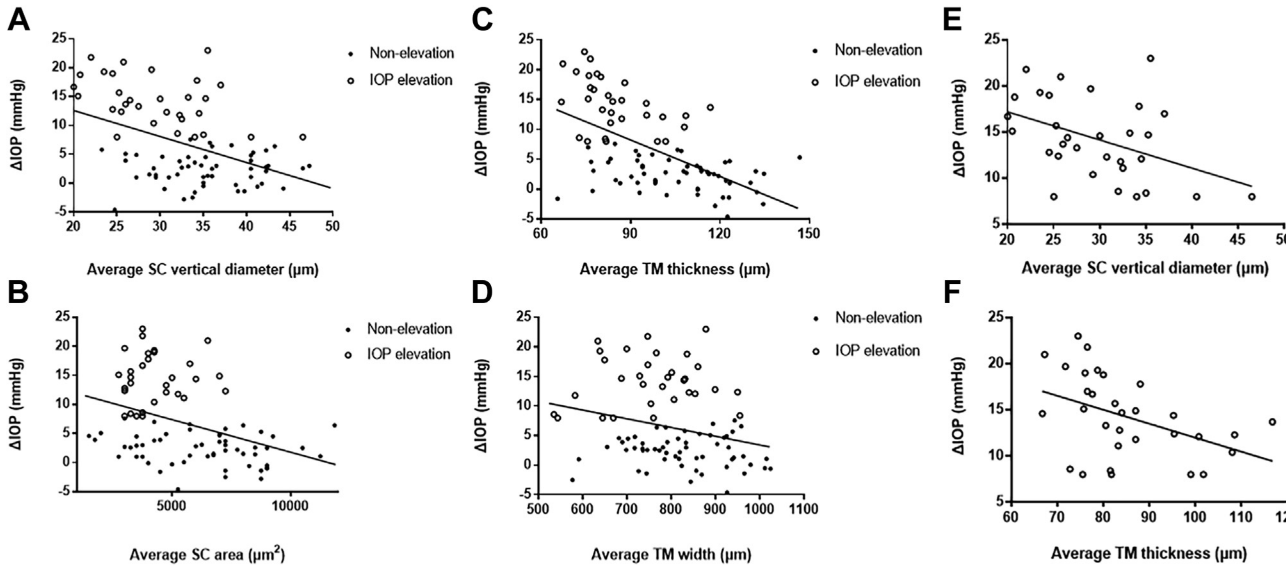

FIGURE 4. Correlation analysis of anterior segmental characteristics and the intraocular pressure elevation within 3 days of surgery (ΔIOP). A. ΔIOP correlated negatively with the average Schlemm canal (SC) vertical diameter in the entire population ($r = -0.436$, $P < .001$), B. ΔIOP correlated negatively with the average SC area in the entire population ($r = -0.394$, $P < .001$), C. ΔIOP correlated negatively with the average trabecular meshwork (TM) thickness in the entire population ($r = -0.573$, $P < .001$), D. ΔIOP correlated negatively with the average TM width in the entire population ($r = -0.251$, $P = .018$), E. ΔIOP correlated negatively with the average SC vertical diameter in the IOP elevation group ($r = -0.399$, $P = .026$), F. ΔIOP correlated negatively with the average TM thickness in the IOP elevation group ($r = -0.554$, $P < .001$).

images and quantitative measurements of the anterior segment.[21–23] Therefore, this device may be useful for evaluating the angle differences in highly myopic eyes that do and do not experience postoperative IOP elevation.

In the present study, using AS-OCT, we found that a smaller Schlemm canal vertical diameter and a thinner trabecular meshwork were associated with elevated IOP after cataract surgery in highly myopic eyes, suggesting that highly myopic eyes with these anatomic features are less capable of dealing with aqueous drainage during the early postoperative period, when the angle is obstructed by the sudden increase in surgically derived remnants. The abnormalities of the Schlemm canal and trabecular meshwork detected in HMC eyes with IOP elevation are similar to those found in eyes with primary open-angle glaucoma (POAG).[24,25] Therefore, the similar changes in the angle structure discovered in eyes with POAG and HMC eyes with IOP elevation may also help to clarify why highly myopic patients are more susceptible to open-angle glaucoma.

Yan and associates[25] have reported that trabecular meshwork thickness correlated negatively with IOP in POAG subjects. Therefore, we speculate that the thinner trabecular meshwork in HMC eyes reduces their ability to regulate IOP. Cells in the trabecular meshwork are known to be able to avidly phagocytose particulate material and debris, to keep the drainage channels unobstructed.[26] The thinner trabecular meshwork in HMC eyes may have fewer trabecular meshwork cells capable of phagocytosis. Therefore, during the early period after cataract surgery, the thinner trabecular meshwork cannot phagocytose the retained viscoelastic and lens materials, ultimately leading to transient IOP elevation. Several reasons may contribute to the thinning of the trabecular meshwork in HMC eyes. First, the elongation of axial length in high myopia causes thinning of the sclera, which may also lead to thinning of the trabecular meshwork. Second, in our previous study, we showed that the levels of some inflammatory cytokines are significantly altered in the aqueous humor of highly myopic eyes, including monocyte chemoattractant protein-1, a major proinflammatory chemokine.[27] This proinflammatory microenvironment may cause the trabecular meshwork to be remodeled in highly myopic eyes.

The Schlemm canal is also an important site of aqueous outflow resistance, because IOP is regulated by the aqueous outflow through the trabecular meshwork, draining into the Schlemm canal, and finally empties into the scleral veins. A smaller Schlemm canal vertical diameter and area were detected in highly myopic eyes with IOP elevation, suggesting that the narrow Schlemm canal in these eyes may be less functional. The narrowing of the Schlemm canal may result from the reduced biomechanical properties of HMC eyes, which cause the Schlemm canal to be weak and deformable. Several previous studies have demonstrated that corneal biomechanical properties in highly myopic eyes were changed, such as lower corneal stiffness and greater maximal deformation amplitude.[28–30]

Therefore, the biomechanical properties of the Schlemm canal may be altered in a similar way in HMC eyes. Subjects with high myopia show many changes in their collagen fiber, such as reduced collagen and glycosaminoglycan synthesis, a predominantly laminar arrangement of the collagen fiber bundles and a loss of fiber cross-links, which may increase the plasticity of the collagen fibers and reduce the stability of their cross-links, ultimately causing the Schlemm canal to be weak and deformable.[31–33]

One limitation of the study was the potential selection bias on subject enrollment, as AS-OCT was not a regular examination before cataract surgery currently, and not all the HMC patients underwent this examination. Given this, our findings are still preliminary and inconclusive. In the future, we will further conduct a properly designed prospective study in which every highly myopic patient presenting for cataract surgery is imaged by AS-OCT.

In conclusion, using swept-source OCT, we found that a smaller vertical diameter of the Schlemm canal and a thinner trabecular meshwork in HMC eyes may contribute to early transient IOP elevation after uneventful cataract surgery. Therefore, preoperative assessment of these structures with AS-OCT may be important for HMC patients to ensure sufficient communications with patients, timely medications, and better clinical outcomes.

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