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ORIGINAL PAPER

Short-term change in higher-order aberrations after mitomycin-C-augmented trabeculectomy

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Abstract

Purpose To investigate the changes in ocular higher-order aberrations (HOA) after trabeculectomy using mitomycin-C (MMC).

Methods We retrospectively reviewed data for 63 eyes from 63 glaucoma patients who had undergone MMC augmented trabeculectomy. We measured intraocular pressure (IOP), refractive errors, anterior chamber depth (ACD), and HOA before surgery and 1, 2, and 4 weeks postoperatively. The patients were divided into two groups on the basis of preoperative lens status: phakic and pseudophakic group. We used a paired *t* test to compare preoperative and postoperative HOA values. Regression analysis was used to compare higher-order total (HOT) change and factors including ACD and age.

Results For entire eye aberrations, coma-like and total HOT were significantly increased postoperatively at 1 week ($P = 0.029$, $P = 0.005$, respectively), but not after 2 or 4 weeks in the phakic group and were not significant at any time in the pseudophakic group. Corneal HOA were significantly increased postoperatively after 1, 2 weeks, but not after 4 weeks in the phakic group and were not significant in the pseudophakic group. For internal optics aberrations, HOA were significantly increased postoperatively at 1, 2, and 4 weeks in the phakic group, but were not significant at any time in the pseudophakic group. However, HOT aberration change showed no correlation with age, ACD, IOP change in either group.

Conclusion Following trabeculectomy, HOA changes were significantly increased postoperatively at 1, 2 weeks in the phakic group. Therefore, visual complaint-related HOA changes after trabeculectomy may be more profound in phakic patients.

Keywords Trabeculectomy · Higher-order aberrations · Glaucoma · Mitomycin-C

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Introduction

Glaucoma is an optic neuropathy characterized by gradual progressive morphological changes in the optic disk resulting in visual field defects [1]. Trabeculectomy is commonly performed to retard progressive optic nerve damage and visual field defects when maximal tolerated medical therapy or laser therapy is not effective in lowering intraocular pressure (IOP) [2]. Over the past decades, the use of

mitomycin-C (MMC) in trabeculectomy surgery has significantly improved the success rate [3]. MMC delays wound healing by inhibiting fibroblast proliferation [4]. However, delayed wound healing may be associated with delayed hypotony, bleb leakage, bleb infection, and corneal curvature changes [5]. In the early postoperative period, successful trabeculectomy may be associated with complications including choroidal detachment, hypotony maculopathy, corneal decompensation, and corneal astigmatism [6, 7]. Thus, patients may experience a decrease in vision shortly after trabeculectomy with MMC.

Although corneal topographic changes are an often less serious compared to other vision-threatening complications, patients frequently report vision complaint which may be related corneal topographic changes. Kook et al. [8] reported that surgically induced corneal astigmatism following trabeculectomy with MMC existed with-the-rule change up to 3 months followed by an against-the-rule shift. Delbeke et al. [9] have reported that trabeculectomy induced a small but statistically significant shift in astigmatism with-the-rule.

Recent advances in wave front analysis have revealed that ocular surgeries such as refractive surgery and cataract surgery demonstrated changes in the higher-order aberrations (HOA), which were related to postoperative visual function [10, 11]. In a study on glaucoma surgery, Fukuoka et al. [12] demonstrated firstly an effect of trabeculectomy on ocular and corneal HOA, which deserve attention. However, their study included relatively a small number of patients with phakic eyes. In addition, they used a 1-month postoperative follow-up in their study, which may be too long to detect acute changes; the postoperative wound healing process usually takes 2–3 weeks. Hence, we intended to investigate the HOA changes during the early postoperative period (1, 2, 4 weeks) and to analyze the change in HOA for both phakic and pseudophakic eyes.

The purposes of this study were to investigate the short-term change in HOA following trabeculectomy with MMC, and to compare the HOA changes according to lens status.

Methods

Glaucoma patients who underwent trabeculectomy augmented with MMC at the Pusan National University Yangsan Hospital between February 2013 and July 2015 were enrolled. The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki. The Institutional Review Board of the hospital waived approval for this retrospective case control study (IRB No. 05-2015-066).

Indication for surgery was based on the following factors: an IOP level associated with a high probability of glaucoma progression, an IOP level that failed to reach the target IOP value after maximal tolerated medical therapy and/or laser therapy, glaucomatous visual field loss and/or changes in the optic disk indicative of progressive glaucoma-associated damage or an allergy to current medical therapy.

We included only Korean patients with primary open-angle glaucoma, pseudoexfoliation glaucoma, pigment dispersion glaucoma, uveitic glaucoma, and steroid-induced glaucoma, who had received trabeculectomy augmented with MMC. In case both eyes of a subject were eligible, randomly selected eye was included in this study. Whereas, in a previous study by Fukuoka et al. [12], they included only phakic eyes, we enrolled both of phakic and pseudophakic eyes.

The exclusion criteria were a diagnosis of traumatic glaucoma, pediatric glaucoma, moderate cataract (LOCS III grade > 3), best-corrected visual acuity (BCVA) $< 20/40$, spherical refraction $> +5.0$ diopters and > -8.0 diopters or a cylinder correction $> +3.0$ diopters. Patients with a history of ocular surgery (other than uncomplicated cataract surgery), intraocular disease (e.g., diabetic retinopathy or retinal vein occlusion), or neurologic disease (e.g., pituitary tumor) that could cause visual field loss, and patients < 18 years were excluded. Also, patients who had undergone combined trabeculectomy with cataract surgery were excluded in this study.

Trabeculectomy was performed by a single surgeon (J.H.S.) using the following method. The fornix-based conjunctival flap was dissected from the Tenon's capsule and the sclera in the superotemporal or superonasal quadrant. A square-shaped scleral flap with a thickness of a third to a half of the sclera (3.0×3.0 mm) was made. Approximately 3 min

beneath the conjunctiva flap, a sponge soaked in a 0.4 mg/mL MMC solution was applied, and the area was then washed with 10 mL of balanced salt solution. Trabeculectomy was performed using a punch followed by a peripheral iridectomy. Two fixed sutures were used to close the scleral flap using gentle tension. The conjunctiva was closed with a 10-0 nylon suture. For the first 2 weeks after surgery, patients were treated with 1% atropine drops twice daily and 1% prednisolone acetate and 0.5% moxifloxacin hydrochloride 4 times a day. After 2 weeks, the atropine treatment was discontinued and the prednisolone/moxifloxacin treatment was reduced to twice daily at 1 month. Conjunctival suture removal was performed in all patients 2–3 weeks after the surgery. Laser lysis of the scleral sutures or needling with 5-fluorouracil (5-FU) was performed in case of inadequate IOP control, showing a poor filtering bleb.

Ocular examinations included BCVA, using logMAR, Goldmann applanation tonometry, anterior segment examination to detect for cataract development, spherical equivalents (SE) measured using automated keratorefractometry (RK-F1, Tokyo, Japan), anterior chamber depth (ACD, Pentacam, Inc., Germany), HOA (iTrace, Tracey Technologies, TEX) preoperatively (baseline), and at 1, 2, and 4 weeks after surgery.

Analysis of the change in postoperative astigmatism is difficult because cylindrical distortion is defined as not only an absolute value but also in terms of direction. Surgical induced astigmatism was determined by vector analysis using the Cravy method [13, 14]. With-the-rule (WTR) is given a plus (+) and against-the-rule (ATR) is given a minus (−).

Measurement of higher-order aberrations

HOA measurements were taken for 4-mm pupils from the center of the cornea in a dark room with an iTrace analyzer (wavefront aberrometer and corneal topographer). The HOA were analyzed quantitatively up to the sixth order using Zernike polynomials. We also calculated the root mean square (RMS) for coma, trefoil, and spherical aberrations; the third, fourth, fifth, and sixth orders; and total combined HOA (third to sixth orders, HOT). RMS of a third-order Zernike coefficient (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3) was considered to represent a coma-like aberration, and a RMS of a fourth-order coefficient (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4) was considered to be a spherical-like aberration.

Data analysis

We compared preoperative and postoperative values using a paired t test. Patients were divided into two groups according to preoperative lens status: a phakic group and a pseudophakic group. As the HOA of crystalline lens and intraocular lens would be different, we divided these groups [15–17]. Continuous data from the two groups was analyzed using an independent t test, while discrete data were analyzed by the Chi-square test. The influence of age, baseline ACD, and IOP changes on absolute pre- and postoperative HOT values were analyzed using linear regression. Statistical analyses were performed using SPSS version 18.0 for window (IBM Corp., Armonk, NY). A P value of less than 0.05 was considered statistically significant.

Results

The study initially included 98 eyes from patients who were eligible for this study. Of these, 11 subjects were excluded because of wave front fixation error, 2 subjects were excluded because of low image quality, 2 subjects were excluded due to development cataract, 5 subjects were excluded due to secondary trabeculectomy due to various complications (hyphema, early bleb failure, etc.), 15 subjects were excluded due to an inadequate follow-up. This left a final total of 63 eyes from 63 patients. Of the 63 eyes, 38 eyes were allocated into the phakic group, and 25 eyes into the pseudophakic group. A total of 19 of the 63 eyes underwent laser suture lysis or needling with 5-FU to adjust the postoperative IOP. Of the 63 eyes, three had mild choroidal detachment after trabeculectomy, which was resolved spontaneously with medication. None of the patient experienced hypotony maculopathy. The postoperative lens opacity remained unchanged after the surgery in all cases.

Demographic and baseline characteristics

The mean age of the patients was 56.8 ± 16.3 years (Table 1). The patients in the phakic group were younger than the patients in the pseudophakic group

Table 1 Demographic data

	Total $n = 63$	Phakic group $n = 38$	Pseudophakic group $n = 25$	P value*
Age (years)	56.8 ± 16.3	52.4 ± 16.9	63.4 ± 13.4	**0.008**
BCVA (logMAR)	0.45 ± 0.37	0.43 ± 0.40	0.47 ± 0.34	0.677
IOP (mmHg)	27.70 ± 9.31	27.82 ± 8.19	27.52 ± 10.97	0.903
ACD (mm)	3.48 ± 0.65	3.19 ± 0.54	4.10 ± 0.40	**< 0.001**
DM history [n (%)]	12 (19.0)	7 (18.4)	5 (20.0)	0.876
HTN history [n (%)]	18 (28.6)	8 (21.1)	10 (40.0)	0.103
POAG [n (%)]	36 (57.1)	19 (50.0)	17 (68.0)	0.158
NTG [n (%)]	1 (1.6)	1 (2.6)	0	0.414
Pseudoexfoliation G [n (%)]	1 (1.6)	1 (2.6)	0	0.414
Uveitic G [n (%)]	18 (28.6)	12 (31.6)	6 (24.0)	0.515
Pigmentary G [n (%)]	2 (3.2)	1 (2.6)	1 (4.0)	0.762
Steroid-induced G [n (%)]	5 (7.9)	4 (10.5)	1 (4.0)	0.348
Spherical equivalents	− 1.09 ± 2.02	− 1.24 ± 1.96	− 0.87 ± 2.13	0.482
Visual field (MD) (dB)	− 18.67 ± 10.02	− 20.34 ± 9.39	− 16.11 ± 10.61	0.119
Visual field (PSD) (dB)	6.97 ± 3.80	7.28 ± 4.06	6.49 ± 3.39	0.430
Baseline HOA				
Entire eye (μm, RMS)				
Coma-like	0.51 ± 0.49	0.49 ± 0.42	0.55 ± 0.58	0.604
Spherical-like	0.26 ± 0.27	0.25 ± 0.25	0.27 ± 0.30	0.794
HOT	0.75 ± 0.73	0.72 ± 0.84	0.80 ± 0.38	0.678
Cornea (μm, RMS)				
Coma-like	0.35 ± 0.50	0.29 ± 0.48	0.48 ± 0.54	0.315
Spherical-like	0.15 ± 0.21	0.13 ± 0.15	0.19 ± 0.30	0.439
HOT	0.40 ± 0.53	0.33 ± 0.49	0.53 ± 0.61	0.324
Internal optics (μm, RMS)				
Coma-like	0.64 ± 0.70	0.44 ± 0.38	1.05 ± 1.00	**0.015**
Spherical-like	0.35 ± 0.48	0.23 ± 0.26	0.60 ± 0.71	**0.031**
HOT	0.75 ± 0.83	0.51 ± 0.44	1.23 ± 1.21	**0.015**

Coma-like: third-order Zernike coefficients (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3); spherical-like: fourth-order Zernike coefficients (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4); higher-order total: magnitude of the third to sixth orders

BCVA best-corrected visual acuity, *IOP* intraocular pressure, *ACD* anterior chamber depth, *DM* diabetes mellitus, *HTN* hypertension, *POAG* primary open-angle glaucoma, *NTG* normal tension glaucoma, *G* glaucoma, *MD* mean deviation, *PSD* pattern standard deviation, *RMS* root mean square, *HOA* higher-order aberrations

*P value using the independent t test between phakic group and pseudophakic group; a Chi-square test was used for discrete data

The P value written with bold indicates statistically significant

(52.4 ± 16.9 vs. 63.4 ± 13.3 years, $P = 0.008$). Preoperative ACD in the phakic group was less than in the pseudophakic group (3.19 ± 0.54 mm vs. 4.10 ± 0.40 mm, $P < 0.001$). There were no significant differences in baseline BCVA, preoperative IOP, SE, percentage of underlying disease and glaucoma subtype, or MD and PSD values of visual field examination (all $P > 0.05$). Preoperative HOA (coma-like, spherical-like, HOT) of the entire eye and cornea aberrations were not different between the two groups (all $P > 0.05$). However, the HOAs of internal optics aberrations showed significant differences ($P = 0.015$, $P = 0.031$, $P = 0.015$, respectively).

Changes in BCVA and spherical equivalents

Postoperative BCVA at 1 and 2 weeks was significantly decreased (Table 2) and recovered significantly to 0.54 ± 0.47 logMAR at postoperative 4 weeks. In the phakic group, BCVA decreased significantly from 0.43 ± 0.40 to 0.68 ± 0.48, 0.67 ± 0.51, and 0.59 ± 0.51 at 1, 2, and 4 weeks respectively ($P < 0.001$, $P = 0.001$, $P = 0.006$). In the pseudophakic group, BCVA decreased significantly from 0.47 ± 0.34 to 0.66 ± 0.50 ($P = 0.048$) at 1 week and recovered gradually to 0.47 ± 0.42 at 4 week.

The overall preoperative SE for all patients was − 1.09 ± 2.02 D. The SE showed a significant hyperopic shift at 1 and 2 weeks postoperatively ($P = 0.049$, $P = 0.011$, respectively) and recovered at 4 weeks. In the phakic group, postoperative SE at 1 week showed a hyperopic shift, but this did not achieve statistical significance. At 2 weeks, the SE showed a significant hyperopic shift ($P = 0.024$). Postoperative SE at 4 weeks showed an apparent myopic shift that had recovered to near baseline. However, in the pseudophakic group, the postoperative SE at 1, 2, and 4 weeks was not significantly different from the baseline SE. There were no significant differences in postoperative SE between the two groups.

There were variable changes in surgically induced corneal astigmatism at 1, 2, and 4 week postoperatively. It had changed to WTR astigmatism at 1 and 2 weeks, and to ATR at 4 weeks (Table 3).

Changes in intraocular pressure and anterior chamber depth

Overall preoperative IOP in the patients was 27.70 ± 9.31 mmHg. Postoperative IOP at 1, 2, and 4 weeks showed a significant decrease from the baseline value (Table 4). The postoperative IOP at 1, 2, and 4 weeks was significantly decreased in both groups. There was a significant difference in the IOP between the two groups at 2 weeks (8.94 ± 3.52 vs. 12.82 ± 5.55, $P = 0.003$) but no significant difference at 1 and 4 weeks.

The ACD at postoperative 1 week was significantly less than the preoperative ACD (3.21 ± 0.87 vs. 3.48 ± 0.65 mm, $P = 0.008$). The postoperative ACD at 2 and 4 weeks was increased to preoperative levels. The preoperative ACD and postoperative ACD at 1, 2, and 4 weeks were greater in the pseudophakic group than in the phakic group. In the phakic group, the ACD at postoperative 1 week was significantly less than the preoperative value (2.84 ± 0.76 vs. 3.19 ± 0.54, $P = 0.016$). Postoperative ACD at 4 weeks gradually increased to equivalent to preoperative ACD. However, in the pseudophakic group, postoperative ACD at 1, 2, and 4 weeks did not significantly differ from the preoperative value.

Table 2 Changes in best-corrected visual acuity (BCVA) and spherical equivalents (SE)

	Total $n = 63$	P value*	Phakic group $n = 38$	P value*	Pseudophakic group $n = 25$	P value*	P value†
BCVA (logMAR)							
Baseline	0.45 ± 0.37		0.43 ± 0.40		0.47 ± 0.34		0.677
Post 1 week	0.67 ± 0.48	**< 0.001**	0.68 ± 0.48	**0.001**	0.66 ± 0.50	**0.048**	0.848
Post 2 weeks	0.66 ± 0.52	**< 0.001**	0.67 ± 0.51	**0.001**	0.65 ± 0.54	0.096	0.871
Post 4 weeks	0.54 ± 0.47	0.072	0.59 ± 0.51	**0.006**	0.47 ± 0.42	0.998	0.364
SE							
Baseline	− 1.09 ± 2.02		− 1.24 ± 1.96		− 0.87 ± 2.13		0.482
Post 1 week	− 0.74 ± 2.30	**0.049**	− 0.90 ± 2.38	0.093	− 0.48 ± 2.19	0.312	0.508
Post 2 weeks	− 0.57 ± 1.98	**0.011**	− 0.54 ± 1.43	**0.024**	− 0.61 ± 2.57	0.172	0.894
Post 4 weeks	− 1.06 ± 2.10	0.746	− 1.48 ± 2.16	0.528	− 0.42 ± 1.88	0.985	0.080

*P value using the paired t test between baseline value and postoperative values for each group

†P value using the independent t test between phakic group and pseudophakic group

The P value written with bold indicates statistically significant

Table 3 Calculation of postoperative corneal astigmatic changes (D) and postoperative corneal astigmatic changes (D) with a long vertical meridian using the Cravy method [13]

Variable	1 week	2 weeks	4 weeks
Postoperative corneal astigmatic changes, D	1.26 ± 1.49	1.25 ± 1.05	1.27 ± 1.07
Postoperative corneal astigmatic changes a long vertical meridian, D	0.95 ± 1.50	0.99 ± 1.07	0.83 ± 1.02

D diopters

Table 4 Comparison of changes in intraocular pressure and anterior chamber depth after trabeculectomy between phakic group and pseudophakic group

	Total $n = 63$	*P* value*	Phakic group $n = 38$	*P* value*	Pseudophakic group $n = 25$	*P* value*	*P* value†
IOP (mmHg)							
Baseline	27.70 ± 9.31		27.82 ± 8.19		27.52 ± 10.97		0.903
Post 1 week	9.23 ± 4.52	**< 0.001**	9.30 ± 4.65	**< 0.001**	9.96 ± 4.36	**< 0.001**	0.297
Post 2 weeks	10.52 ± 4.81	**< 0.001**	8.94 ± 3.52	**< 0.001**	12.82 ± 5.55	**< 0.001**	**0.003**
Post 4 weeks	12.02 ± 5.90	**< 0.001**	11.49 ± 5.54	**< 0.001**	12.86 ± 6.47	**< 0.001**	0.395
ACD (mm)							
Baseline	3.48 ± 0.65		3.19 ± 0.54		4.10 ± 0.40		*< 0.001*
Post 1 week	3.21 ± 0.87	**0.008**	2.84 ± 0.76	**0.016**	3.95 ± 0.55	0.331	*< 0.001*
Post 2 weeks	3.39 ± 0.78	0.334	3.02 ± 0.61	0.090	4.19 ± 0.39	0.638	*< 0.001*
Post 4 weeks	3.35 ± 0.70	0.051	3.03 ± 0.51	0.258	4.03 ± 0.53	0.722	*< 0.001*

**P* value using the paired *t* test between the baseline values and postoperative values for each groups

†*P* value using the independent *t* test between phakic group and pseudophakic group

The *P* value written with bold indicates statistically significant

Changes in higher-order aberrations after trabeculectomy

Figure 1 shows iTrace wavefront aberrometer images from a patient preoperatively and at postoperative 1 week.

Entire eye aberrations

The preoperative coma-like, spherical-like, and HOT RMS were 0.51 ± 0.49, 0.26 ± 0.27, 0.75 ± 0.65 μm, respectively (Table 5, Fig. 2). Coma-like RMS after 1 week was significantly increased to 0.79 ± 1.11 μm ($P = 0.029$). HOT RMS values at 1 and 2 weeks were significantly increased to 1.21 ± 1.20 and 1.10 ± 1.10 μm ($P = 0.013$ and $P = 0.021$, respectively). No significant changes were found in terms of other aberrations.

In phakic group, preoperative coma-like, spherical-like, and HOT RMS were 0.49 ± 0.42, 0.25 ± 0.25, 0.72 ± 0.84 μm (Table 6), 1 week after surgery, coma-like and HOT RMS was significantly increased in the phakic group to 0.88 ± 1.25 and 1.23 ± 1.39 μm ($P = 0.029$, $P = 0.005$, Fig. 3A). However, there were no significant changes in postoperative coma-like, spherical-like, or HOT RMS in the pseudophakic group at 1, 2, or 4 weeks (Fig. 3B). A comparison of the HOA aberrations between the phakic and pseudophakic groups showed no significance (Table 6).

Corneal aberrations

Postoperative coma-like, spherical-like, and HOT RMS were not significantly changed at 1, 2, or 4 weeks (Table 5, Fig. 2).

In phakic group, preoperative coma-like, spherical-like, and HOT RMS were 0.29 ± 0.48, 0.13 ± 0.15, and 0.33 ± 0.49 μm (Table 6). Coma-like RMS was significantly increased to 0.48 ± 0.78 and

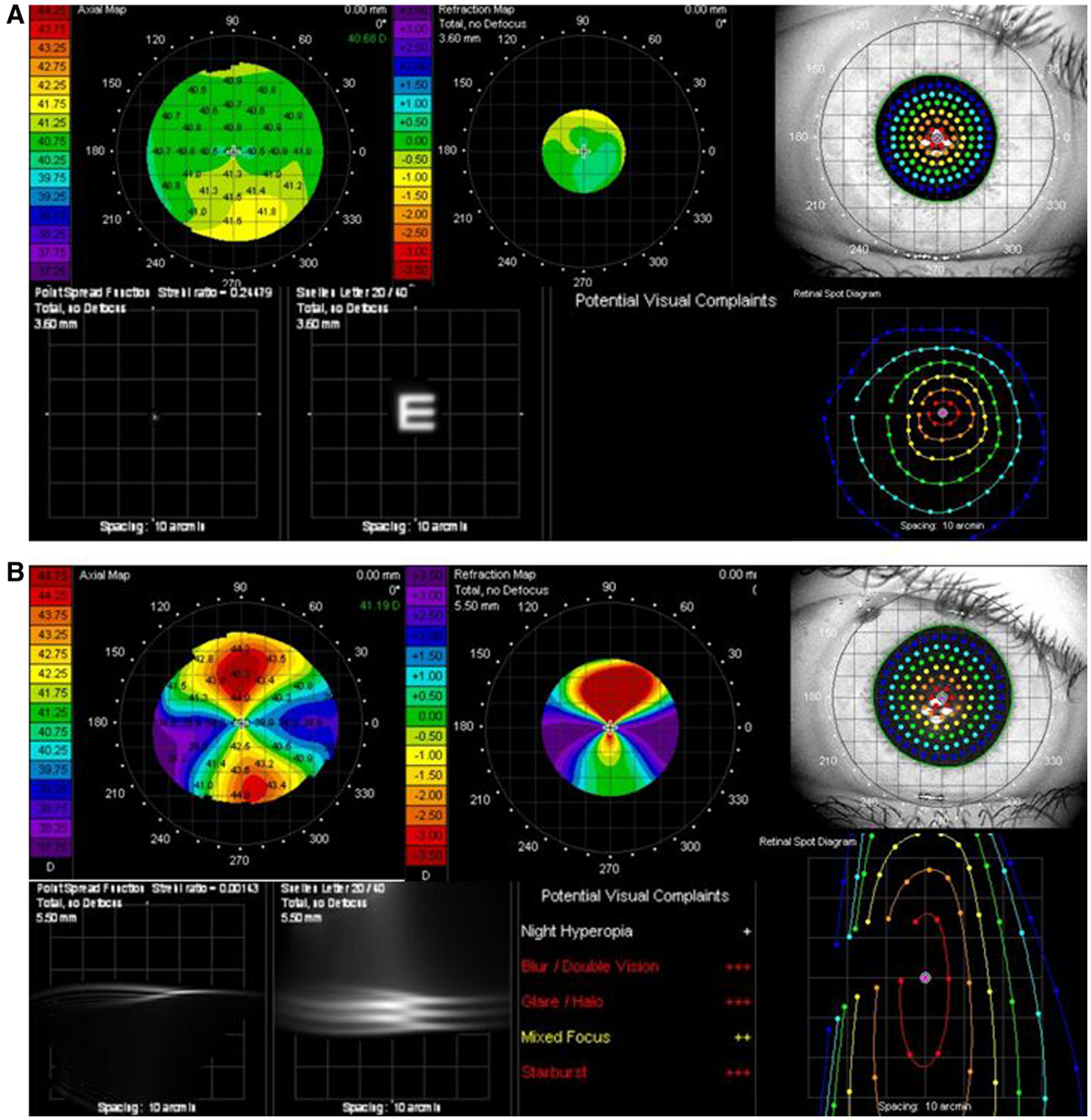

Fig. 1 Corneal topography, iTrace wave front aberrometer, and corneal topographer at baseline **A** and 1 week after trabeculectomy **B** for a 36-year-old man with a phakic eye. Wavefront maps were markedly changed after trabeculectomy. Top left, axial map and refraction map of corneal topography shown with-the-rule change after surgery; bottom left, a stimulated retinal images of postoperative Landolt E distorted above baseline; bottom center, postoperative potential visual complaints were blurring/double vision/glare/halo; bottom right, postoperative retinal spot diagram elongated vertically

0.49 ± 0.80 μm at 1 and 2 weeks ($P = 0.035$, $P = 0.021$, Fig. 3A). In addition, spherical-like RMS was significantly increased to 0.22 ± 0.31 and 0.23 ± 0.27 μm at 1 and 2 weeks ($P = 0.031$, $P = 0.022$). HOT RMS was significantly increased to 0.53 ± 0.84 and 0.55 ± 0.84 μm at 1 and 2 weeks ($P = 0.041$, $P = 0.019$). However, in the pseudophakic group, all the HOAs did not show significant any changes after 1, 2, or 4 weeks (Fig. 3B). There were no differences in the HOA aberrations between the phakic and pseudophakic groups (Table 6).

Table 5 Changes in higher-order aberrations in all patients after trabeculectomy

	Total $n = 63$					
	Coma-like	*P* value*	Spherical-like	*P* value†	Higher-order total	*P* value‡
Entire eye (μm, RMS)						
Baseline	0.51 ± 0.49		0.26 ± 0.27		0.75 ± 0.65	
Post 1 week	0.79 ± 1.11	**0.037**	0.48 ± 0.98	0.063	1.21 ± 1.20	**0.013**
Post 2 weeks	0.59 ± 0.58	0.337	0.36 ± 0.52	0.053	1.10 ± 1.10	**0.021**
Post 4 weeks	0.56 ± 0.73	0.546	0.25 ± 0.25	0.956	0.96 ± 1.16	0.166
Cornea (μm, RMS)						
Baseline	0.35 ± 0.50		0.15 ± 0.21		0.40 ± 0.53	
Post 1 week	0.44 ± 0.67	0.359	0.18 ± 0.27	0.579	0.48 ± 0.72	0.410
Post 2 weeks	0.44 ± 0.67	0.302	0.19 ± 0.24	0.447	0.49 ± 0.70	0.330
Post 4 weeks	0.42 ± 0.61	0.486	0.22 ± 0.42	0.373	0.48 ± 0.73	0.471
Internal optics (μm, RMS)						
Baseline	0.64 ± 0.70		0.35 ± 0.48		0.75 ± 0.83	
Post 1 week	0.85 ± 0.85	0.181	0.59 ± 0.71	0.061	1.05 ± 1.10	0.126
Post 2 weeks	0.69 ± 0.70	0.784	0.46 ± 0.51	0.420	0.84 ± 0.86	0.668
Post 4 weeks	0.71 ± 0.74	0.711	0.39 ± 0.54	0.830	0.82 ± 0.89	0.723

Coma-like: third-order Zernike coefficients (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3); spherical-like: fourth-order Zernike coefficients (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4); higher-order total: magnitude of the third to sixth orders

The paired *t* test was used for comparison of preoperative and postoperative HOA for the enrolled patients, < 0.05 was significant

RMS root mean square

**P* value coma-like

†*P* value spherical-like

‡*P* value higher-order total

The *P* value written with bold indicates statistically significant

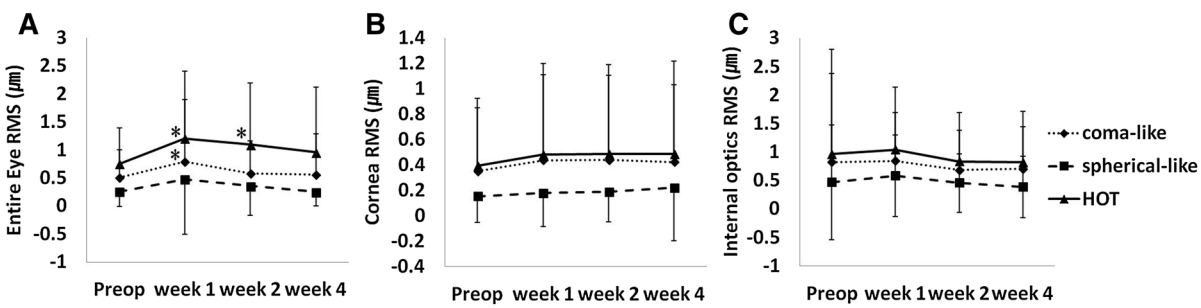

Fig. 2 Changes in coma-like aberration, spherical-like aberration, and higher-order total aberration (HOT) for all patients after trabeculectomy. **A** Entire eye aberrations, HOT aberration was significantly increased at 1, 2 weeks ($P = 0.013$, $P = 0.021$, respectively) and coma-like aberration was significantly increased at 1 week ($P = 0.037$). **B** Corneal aberrations, coma-like, spherical-like, and HOT were not significantly changed at 1, 2, or 4 weeks. **C** Internal optics aberrations, all high-order aberrations showed no significant change at 1, 2, or 4 weeks. Coma-like: third-order Zernike coefficients (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3); spherical-like: fourth-order Zernike coefficients (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4); higher-order total: magnitude of the third to sixth orders, RMS (root mean square) *P* value using the paired t test for comparison of preoperative and postoperative HOA of enrolled patients, "*" indicates statistical significance

Table 6 Comparison of higher-order aberrations between phakic group and pseudophakic group after trabeculectomy

	Phakic group $n = 38$			Pseudophakic group $n = 25$			P value*	P value†	P value‡
	Coma-like	Spherical-like	Higher-order total	Coma-like	Spherical-like	Higher-order total			
Entire eye (μm, RMS)									
Baseline	0.49 ± 0.42	0.25 ± 0.25	0.72 ± 0.84	0.55 ± 0.58	0.27 ± 0.30	0.80 ± 0.38	0.604	0.794	0.678
Post 1 week	0.88 ± 1.25	0.55 ± 1.19	1.23 ± 1.39	0.67 ± 0.88	0.38 ± 0.52	1.08 ± 0.85	0.872	0.516	0.889
Post 2 weeks	0.60 ± 0.49	0.34 ± 0.37	0.98 ± 0.70	0.57 ± 0.70	0.38 ± 0.70	0.90 ± 1.59	0.516	0.766	0.328
Post 4 weeks	0.65 ± 0.84	0.29 ± 0.25	1.02 ± 1.35	0.42 ± 0.48	0.20 ± 0.25	0.84 ± 0.69	0.227	0.171	0.582
Cornea (μm, RMS)									
Baseline	0.29 ± 0.48	0.13 ± 0.15	0.33 ± 0.49	0.48 ± 0.54	0.19 ± 0.30	0.53 ± 0.61	0.315	0.439	0.324
Post 1 week	0.48 ± 0.78	0.22 ± 0.31	0.53 ± 0.84	0.44 ± 0.36	0.09 ± 0.10	0.45 ± 0.37	0.628	0.198	0.543
Post 2 weeks	0.49 ± 0.80	0.23 ± 0.27	0.55 ± 0.84	0.41 ± 0.17	0.10 ± 0.09	0.42 ± 0.18	0.551	0.141	0.471
Post 4 weeks	0.49 ± 0.73	0.29 ± 0.49	0.58 ± 0.87	0.36 ± 0.13	0.08 ± 0.05	0.38 ± 0.14	0.338	0.192	0.290
Internal optics (μm, RMS)									
Baseline	0.44 ± 0.38	0.23 ± 0.26	0.51 ± 0.44	1.05 ± 1.00	0.60 ± 0.71	1.23 ± 1.21	**0.015**	**0.031**	**0.015**
Post 1 week	0.75 ± 0.75	0.46 ± 0.54	0.89 ± 0.91	1.06 ± 1.05	0.84 ± 0.96	1.37 ± 1.41	0.328	0.150	0.237
Post 2 weeks	0.78 ± 0.72	0.54 ± 0.54	0.96 ± 0.89	0.91 ± 0.64	0.51 ± 0.44	1.15 ± 0.77	0.268	0.268	0.221
Post 4 weeks	0.76 ± 0.73	0.44 ± 0.44	0.87 ± 0.83	0.85 ± 0.78	0.45 ± 0.75	1.05 ± 1.04	0.535	0.535	0.674

Coma-like: third-order Zernike coefficients (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3); spherical-like: fourth-order Zernike coefficients (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4); higher-order total: magnitude of the third to sixth orders

Independent t test was used for HOA between phakic group and pseudophakic group

RMS root mean square

*P value coma-like

†P value spherical-like

‡P value higher-order total

The P value written with bold indicates statistically significant

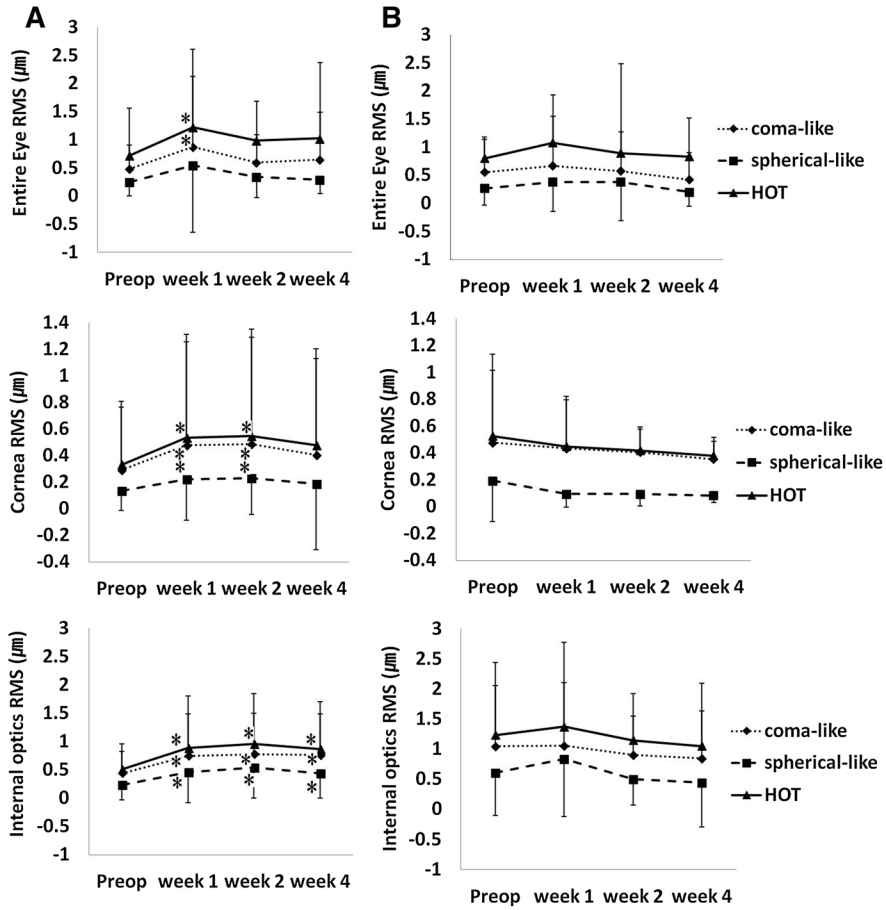

Fig. 3 Changes in coma-like aberration, spherical-like aberration, and higher-order total aberration (HOT) of phakic group and pseudophakic group after trabeculectomy. **A** In phakic group, HOT aberration and coma-like aberration were significantly increased after 1 week ($P = 0.05$, $P = 0.029$, respectively) of entire eye aberration. Of corneal aberrations, HOT aberrations were significantly increased at 1 and 2 weeks ($P = 0.041$, $P = 0.019$, respectively) and coma-like ($P = 0.035$, $P = 0.021$, respectively), spherical-like aberration ($P = 0.031$, $P = 0.022$, respectively) as well. Internal optics aberrations, HOT aberrations were significantly increased at 1, 2, and 4 weeks ($P = 0.048$, $P = 0.009$, $P = 0.049$, respectively) and coma-like ($P = 0.049$, $P = 0.011$, $P = 0.045$, respectively), spherical-like aberrations were also significant ($P = 0.048$, $P = 0.009$, $P = 0.049$, respectively). **B** In pseudophakic group, none of the coma-like, spherical-like, or higher-order total aberrations were significantly changed after trabeculectomy. Coma-like: third-order Zernike coefficients (C_3^{-3}, C_3^{-1}, C_3^1, C_3^3); spherical-like: fourth-order Zernike coefficients (C_4^{-4}, C_4^{-2}, C_4^0, C_4^2, C_4^4); higher-order total: magnitude of the third to sixth orders; RMS (root mean square) P value by paired t test for comparison of preoperative and postoperative HOA of enrolled patients, * statistically significant

Internal optics aberrations

Preoperative coma-like, spherical-like, and HOT RMS were 0.64 ± 0.70, 0.35 ± 0.48, 0.75 ± 0.83 μm, respectively. Postoperative HOAs were not significantly different after 1, 2, and 4 weeks in the study group (Table 5, Fig. 2).

Preoperative coma-like, spherical-like, and HOT RMS were 0.44 ± 0.38, 0.23 ± 0.26, 0.51 ± 0.44 in the phakic group and 1.05 ± 1.00, 0.60 ± 0.71, 1.23 ± 1.21 μm in the pseudophakic group (Table 6). In the phakic group, coma-like RMS was significantly increased to 0.75 ± 0.75, 0.78 ± 0.72, and 0.76 ± 0.73 μm at 1, 2, and 4 weeks ($P = 0.049$, $P = 0.011$, $P = 0.045$, respectively, Fig. 3A). Spherical-like RMS was also significantly increased to 0.46 ± 0.54, 0.54 ± 0.54, and 0.44 ± 0.44 μm at 1, 2, and 4 weeks ($P = 0.048$, $P = 0.009$, $P = 0.049$, respectively). HOT RMS was significantly increased to 0.89 ± 0.91, 0.96 ± 0.89, and 0.87 ± 0.83 μm at

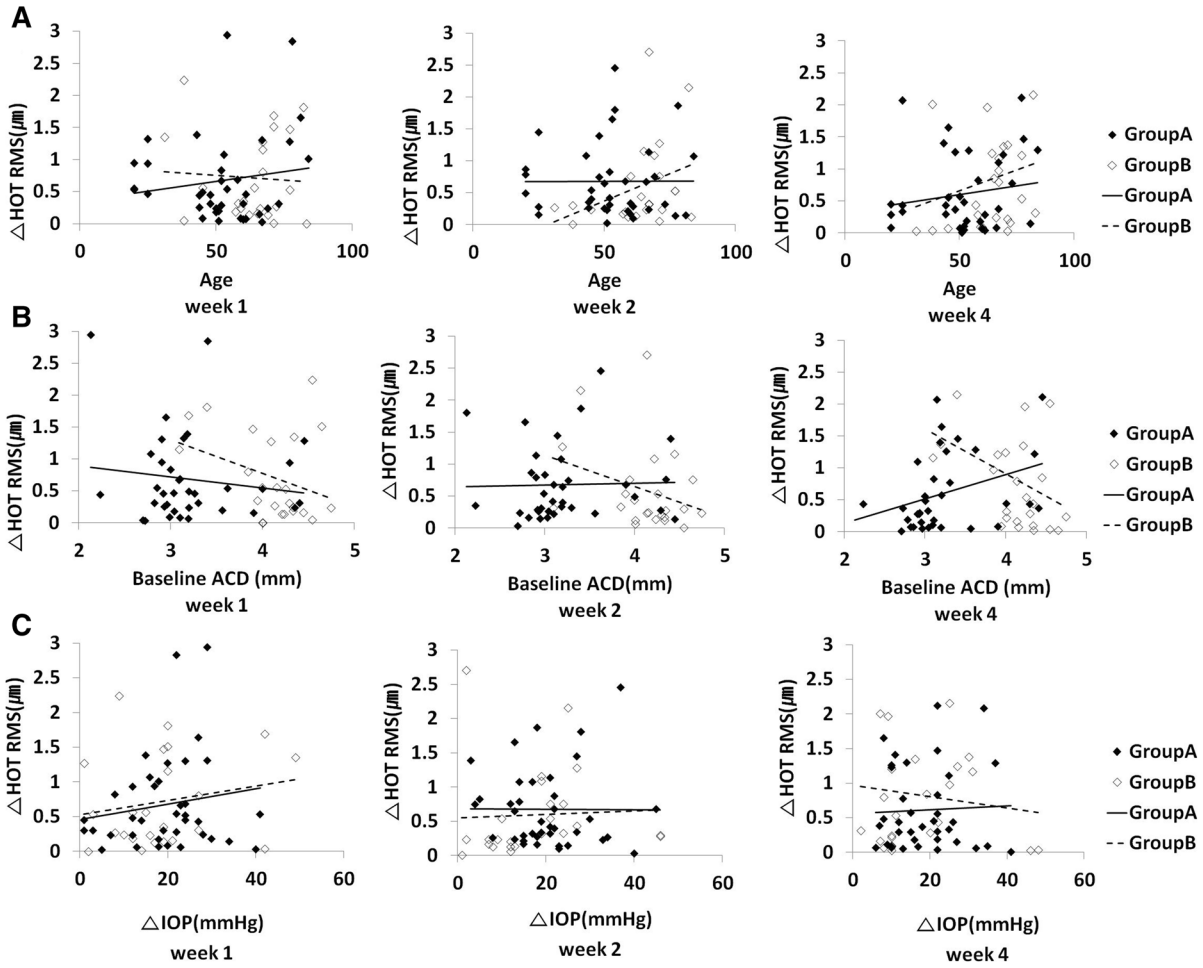

Fig. 4 A linear regression comparison of age, baseline anterior chamber depth (ACD), and IOP differences (ΔIOP) with absolute values of higher-order total differences (Δ HOT) between the preoperative and postoperative stage. **A** Age showed no significant effect on HOT aberration differences at 1, 2 or 4 weeks in group A ($R^2 = 0.023$, 0.001, 0.007), B ($R^2 = 0.001$, 0.079, 0.044) ($Ps > 0.05$). **B** Preoperative ACD showed no significant effect on HOT aberration differences at 1, 2, and 4 weeks in group A ($R^2 = 0.014$, 0.002, 0.009), B ($R^2 = 0.001$, 0.018, 0.149) ($Ps > 0.05$). **C** IOP change showed no show significant effect for HOT aberration differences at 1, 2, and 4 weeks in group A ($R^2 = 0.024$, 0.001, 0.002), B ($R^2 = 0.001$, 0.009, 0.015) ($Ps > 0.05$). HOT, Higher-order total: magnitude of the third to sixth orders, RMS (root mean square); Group A, Phakic eye; Group B, Pseudophakic eye

1, 2, and 4 weeks ($P = 0.048$, $P = 0.009$, $P = 0.050$, respectively). However, in the pseudophakic group, there was no significant change in any HOAs at 1, 2 or 4 weeks (Fig. 3B). There was no significant difference in the HOA aberrations between the phakic and pseudophakic groups (Table 6).

Factors associated with higher-order aberrations

Age had no significant effect on the HOT aberration at 1, 2 or 4 weeks in either group ($Ps > 0.05$, Fig. 4A). Preoperative ACD did not show any significant effect on HOT aberration differences at 1, 2, or 4 weeks in either group. ($Ps > 0.05$, Fig. 4B). The change in IOP showed no significant effect on the difference in the HOT aberrations at 1, 2, or 4 weeks between the groups ($Ps > 0.05$, Fig. 4C).

Discussion

Trabeculectomy is a standard surgical treatment for uncontrolled glaucoma. Recently, minimally invasive glaucoma surgeries are being developed using new

microsurgical devices [18, 19], patients may expect good vision even after glaucoma surgery; however, while trabeculectomy can control the progression of glaucoma, patients can experience blurred vision immediately after surgery. Although the introduction of MMC has revolutionized filtering surgery and improved the success rate of trabeculectomy, it can induce a delay in wound healing that may exacerbate early blurred vision [8, 20].

A number of researchers have investigated changes in astigmatism and visual acuity following trabeculectomy [8, 20–28]. Cunliffe et al. have reported a decrease in BCVA 1 week postoperatively that resulted in a myopic shift due to the change in ACD; after 3 weeks, BCVA was similar to preoperative levels [20, 23]. In our study, hyperopic shift at 1 week were found in phakic group, which may be related with axial length shortening, although the change of ACD were myopic shift of Cunliffe et al.'s study. Dietze et al. [25] reported that postoperative BCVA decreased after 1 week following trabeculectomy because of corneal topographic change, but returned preoperative level within 12 weeks. These results are consistent with our study. We found that postoperative BCVA was significantly decreased from 1 to 4 weeks postsurgery in the phakic group. However, we found a significant decrease in the pseudophakic group only at postoperative 1 week. These results suggest that preoperative lens status might have an influence on early postoperative visual quality. And we guessed that increase in HOA in phakic group may be one of the causes of decreased visual acuity at 1, 2, 4 weeks postoperatively.

In a study on astigmatism, Rosen et al. [21] showed that WTR astigmatism was increased at 3 months after trabeculectomy; they speculated that this was caused by the use of cautery in the surgery. Hugkulstone et al. [22] have proposed that posterior placement of the incision on flap sutures may cause early postoperative WTR astigmatism. According to our study, in the phakic group, SE was significantly decreased 2 weeks postoperatively but showed no consistent change at postoperatively for pseudophakic group. We speculate that it was associated with decrease of ACD and crystalline lens structure in phakic eye. As the degree of percentage change of ACD in phakic group was higher than that in pseudophakic group, crystalline lens thickness in phakic group was thicker than that in pseudophakic group, diopter changes may be prominent in phakic eyes.

We found that ACD was significantly decreased at 1 and 2 weeks in the phakic group as previously reported [8, 20, 23], but the ACD change was not apparent in the pseudophakic group. This result implies that preoperative lens status has an influence on early postoperative ACD, although the in BCVA and HOT aberration were not significantly correlated with ACD changes in either group.

Our study has focused on HOA changes after trabeculectomy with MMC and investigated HOA related factors. Patients were divided into two groups: phakic and pseudophakic. We evaluated three aspects of HOA aberration: entire eyes, cornea, and internal optics. In this study, we have observed that coma-like, spherical-like, and HOT of corneal and internal optics aberration were significantly increased postoperatively at 1 and 2 weeks in the phakic group. However, all the HOA were not significantly increased in the pseudophakic group.

Fukuoka et al. [12] suggested that HOA changes can be caused by anterior displacement of internal optics, decreased axial length, and uncertain mechanism of the lens. In contrast, Sugimoto et al. [29] reported that supraciliochoroidal fluid (SCF) was detected (33%) without choroidal detachment by ultrasound biomicroscopy within the first 2 weeks following trabeculectomy. They speculated that SCF created by iridectomy during trabeculectomy could have changed the position of the lens. These SCF changes may effect on both of crystalline lens and ciliary structure in phakic eye. In addition, we hypothesized that age and preoperative ACD can affect the results of our study. Age and preoperative ACD were different between the two groups in our study, which is consistent with what we would expect; older glaucoma patients undergoing cataract surgery are likely to have a greater ACD. Patients with deeper preoperative ACD have greater reserves than those with shallower preoperative ACD. Fukuoka's study presented changes of HOA in only phakic eye after trabeculectomy and did not show HOA of acute phase within 1 month of posttrabeculectomy. In our study, we classified HOA changes according to lens status; we had focused on short-term changes of HOA after trabeculectomy. Nevertheless, result of our study is similar to the Fukuoka study that ocular (internal

optics) HOA increases in the early postoperative period.

Our study has several limitations. Firstly, the use of topical atropine could be a bias. Hiraoka et al. [30] had shown that topical cycloplegia with topical atropine increased only ocular HOA, not cornea HOA in children. In our study, significant changes in HOA of cornea and internal optics aberrations were found, suggesting that other factors than atropine may effect on HOA changes after trabeculectomy; the use of topical atropine is frequently used to prevent other complications such as malignant glaucoma, choroidal detachment, shallow anterior chamber, corneal-iris adhesion for postoperative period; hence, the effect of topical atropine on HOA may be related with trabeculectomy. Secondly, the follow-up period in our study was too short to analyze changes in HOA after trabeculectomy. Unlike the previous study by Fukuoka et al. that used a 1- and 3-month follow-up, our study focused on short-term changes after trabeculectomy. Further studies are needed with a longer follow period. Thirdly, the change in HOA after phacotrabeculectomy with MMC remains an important issue. To address this problem, further studies should compare findings between a trabeculectomy group and a combined surgery group.

In conclusion, in phakic eyes, coma-like, spherical-like, and HOT were significantly increased postoperatively at 1, 2, and 4 weeks upon internal optics aberration. However, in pseudophakic eyes, coma-like, spherical-like, and HOT were not significantly increased at 1, 2 or 4 weeks for all aberrations. These results suggest that visual complaint-related HOA changes and changes of ACD, SE after trabeculectomy may be more frequent in phakic patients than in pseudophakic patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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