Development of a nomogram for femtosecond laser astigmatic keratotomy for astigmatism after keratoplasty

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PURPOSE: To develop a nomogram for femtosecond laser astigmatic keratotomy (AK) to treat post-keratoplasty astigmatism.

SETTING: Three academic medical centers.

DESIGN: Retrospective interventional case series.

METHODS: A review of post-keratoplasty femtosecond laser AK was performed. Uncorrected (UDVA) and corrected (CDVA) distance visual acuities, manifest refraction, and keratometry were recorded preoperatively and 1, 3, 6, and 12 months postoperatively. The location, length, depth, and diameter of the AK incisions were recorded, and the surgically induced astigmatic correction was related to these variables using regression analysis.

RESULTS: One hundred forty femtosecond laser AK procedures were performed after penetrating keratoplasty (PKP) (n = 129) or deep anterior lamellar keratoplasty (DALK) (n =11), with 89 procedures (80 PKP, 9 DALK) included in the analysis. The mean CDVA improved from 20/59 (0.47 logMAR ± 0.38 [SD]) preoperatively to 20/45 (0.35 ± 0.31 logMAR) postoperatively (P = .013) (n = 46). The mean keratometric astigmatism decreased from 8.26 ± 2.90 diopters (D) preoperatively to 3.62 ± 2.59 D postoperatively (P < .0001) (n = 89). The mean refractive cylinder decreased from 6.77 ± 2.80 D preoperatively to 2.85 ± 2.57 D postoperatively (P < .0001) (n = 69). A nomogram for femtosecond laser AK to treat post-keratoplasty astigmatism was generated using regression analysis.

CONCLUSIONS: Femtosecond laser AK significantly improved UDVA and CDVA and significantly reduced keratometric astigmatism and refractive cylinder after keratoplasty. The nomogram generated should improve the accuracy of post-keratoplasty femtosecond laser AK.

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High corneal astigmatism is a frequently encountered hindrance to visual rehabilitation after cornea transplantation. The degree of corneal astigmatism tolerated after cornea transplantation depends on several factors, including the refractive state of the fellow eye, visual potential, degree of binocularity, contact lens tolerance, and patient expectations.[1] Nonsurgical options for the management of postoperative astigmatism include spectacles, contact lenses, and scleral lenses. However, spectacles might be ineffective if the astigmatism is irregular or of a large magnitude. The success of contact lenses and scleral lenses is dependent on the patient's lifestyle, age, and ability to tolerate the lenses.[2]

After topography-guided selective suture removal, surgical options to reduce astigmatism include, but are not limited to, wound revision, astigmatic keratotomy (AK), astigmatic keratectomy (wedge resection), and photorefractive procedures.[3–8] Arcuate keratotomy, typically performed with freehand techniques or

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mechanized devices such as the Hanna arcitome (Moria), is a generally effective, well-established treatment for astigmatism after corneal transplantation.[5,6,9,10] However, this procedure has poor predictability and a risk for associated complications, such as corneal perforation and wound gape.[4,11,12]

Using a femtosecond laser is an increasingly common means of creating arcuate keratotomies for the treatment of postsurgical and native astigmatism, often at the time of femtosecond laser–assisted cataract surgery.[13–17] The femtosecond laser uses a wavelength in the infrared range to induce a nonthermal photodisruptive ablation based on the generation of a sequence of adjacent cavitation gas bubbles focused in corneal tissue.[13] Femtosecond laser AK provides more precise incision creation than manual or mechanical keratotomy with enhanced reproducibility, safety, and accuracy.[13–19] Femtosecond laser AK has been shown to significantly improve uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) as well as significantly reduce astigmatism in patients after corneal transplantation.[13] A retrospective analysis of eyes that had manual AK and femtosecond laser AK[16] found improvement in UDVA and CDVA in both groups; however, only the femtosecond laser AK group achieved a statistically significant improvement in both UDVA and CDVA.

Several nomograms are available for planning manual AK incisions in native corneas, such as the Hanna nomogram[20] and the Lindstrom nomogram.[21] Abbey et al.[22] proposed a femtosecond laser AK nomogram for the treatment of astigmatism in native corneas based on a modified Lindstrom nomogram. Subsequently, Hurmeric and Yoo[A] proposed a modified version of the previous native corneal nomogram to be used for post-keratoplasty astigmatism. The adaptation of a nomogram created for the treatment of astigmatism in native corneas to one for post-keratoplasty corneas assumes that the grafted corneas and native corneas respond in a similar manner to corneas having incisional surgery. However, this assumption is not valid according to Wilkins et al.,[5] who showed that the effect of AK incisions in post-keratoplasty eyes was proportional to the magnitude of the astigmatism, which is not the case in native corneas. Thus, we describe the development of a nomogram for femtosecond laser AK for the management of post-keratoplasty astigmatism that considers a variety of incision-related factors and the degree of preexisting astigmatism.

PATIENTS AND METHODS

This study followed the tenets of the Declaration of Helsinki. Institutional review board approval was obtained at each participating center.

Patient Identification and Data Collection

This retrospective study was performed at the following 3 centers: Jules Stein Eye Institute, Los Angeles, California, USA; Bascom Palmer Eye Institute, Miami, Florida, USA; and the University of Toronto, Toronto, Ontario, Canada. The charts of all patients who had femtosecond laser AK for the management of post-keratoplasty astigmatism between January 2007 and January 2015 were evaluated for the following information: preoperative UDVA, CDVA, manifest refraction, keratometry, and thinnest corneal pachymetry. In addition, operative parameters, including laser energy and spot separation, as well as the location, arc length, depth, diameter, and angle of each keratotomy incision were recorded. The postoperative UDVA, CDVA, manifest refraction, and keratometry were recorded at 1, 3 and 6 months, and 1 year. Also recorded were postoperative complications and subsequent surgical procedures, including whether the AK incisions were opened. All patients included in the data analysis had all cornea transplant sutures removed at least 100 days before the femtosecond laser AK procedure was performed, and all eyes were followed for a minimum of 1 month after the procedure. Corneal biomechanics are altered in the presence of corneal edema; therefore, eyes in which the thinnest recorded corneal pachymetry was greater than 750 μm were excluded. Data included eyes with previous or combined glaucoma surgery, cataract extraction, or refractive surgery at the time of the corneal transplantation.

Surgical Technique

All AK procedures were performed using the Intralase FS 60 or iFS Advanced femtosecond laser (both Abbott Medical Optics, Inc.). At the Jules Stein Eye Institute and the Bascom Palmer Eye Institute, the arc length of AK incisions was based on preoperative corneal topography using the Hanna nomogram (Table 1).[6] At the University of Toronto, the arc length of the paired incisions, which were centered on the steep axis and placed on the donor side of the cornea, were planned using the following formula: 60-degree paired

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Table 1. Hanna nomogram for astigmatic keratotomy for correction of post-keratoplasty astigmatism.*

Refractive Astigmatism (D)	Optical Zone Diameter (mm)	Incision Depth (% of Corneal Thickness)	Angular Length of Incision (Degrees)
2.50 to 3.75	6.75	75	60
4.00 to 5.00	6.50	75	60
5.00 to 6.25	6.50	75	70
6.50 to 7.50	6.25	75	70
7.75 to 8.75	6.25	75	80
9.00 to 15.00	6.00	75	80

*Older than or younger than age 30 years: increase or decrease efficacy by 0.05 diopters (D) per year

incisions for 6.0 diopters (D) of astigmatism, 70-degree paired incisions for 7.0 D, 80-degree paired incisions for 8.0 D, and 90-degree paired incisions for 9.0 D or more. At all sites, the depth of the AK incisions was based on a percentage of the corneal thickness in the area of the planned incisions as measured by preoperative ultrasound pachymetry.

At the Bascom Palmer Eye Institute, the postoperative regimen consisted of polymyxin B–trimethoprim eyedrops 4 times daily for 1 week and prednisolone acetate 1.0% eyedrops 4 times daily for 1 week, 3 times daily for 1 week, 2 times daily for 1 week, and then once daily for 1 week. At the University of Toronto, the postoperative regimen consisted of tobramycin 0.3%–dexamethasone 0.1% eyedrops 4 times daily for 1 week or moxifloxacin 0.5% and dexamethasone 0.1% eyedrops 4 times daily for 1 week. At the Jules Stein Eye Institute, the postoperative regimen consisted of gatifloxacin 0.5% and prednisolone acetate 1.0% eyedrops 4 times daily for 1 week.

Astigmatism Analysis

Vector analysis of astigmatism was performed as previously described.[23–26] The terminology used in the analyses was adapted from that used by Huang et al.[26] and Eydelman et al.[27]

Hypothetical Cases The following examples illustrate the analyses that were performed.

Cardinal and Oblique Components of Astigmatism The magnitude of preoperative keratometric astigmatism is 12.00 D with a steep axis of 148 degrees. Then, the cardinal component of preoperative keratometric astigmatism ($KA_{c\text{-}pre}$) is 12.00 D × cos(2 × 148 degrees) = 5.26 D. The oblique component of preoperative keratometric astigmatism ($KA_{o\text{-}pre}$) is 12.00 D × sin(2 × 148 degrees) = −10.79 D.

The magnitude of postoperative keratometric astigmatism is 4.70 D with a steep axis of 37 degrees. The cardinal component of postoperative keratometric astigmatism ($KA_{c\text{-}post}$) is 4.70 × cos(2 × 37 degrees) = 1.30 D. The oblique component of postoperative keratometric astigmatism ($KA_{o\text{-}post}$) is 4.70 × sin(2 × 37 degrees) = 4.52 D.

Intended Astigmatic Correction The intended astigmatic correction is the negative of the preoperative keratometric astigmatism. It represents the cylindrical lens that is needed to cancel preexisting keratometric astigmatism. For this hypothetical case, the intended astigmatic correction has a magnitude of 12.00 D and an axis of 58 degrees (90 degrees from the preoperative steep axis).

Surgically Induced Astigmatic Correction The surgically induced astigmatism (SIA) correction is the vector difference between the postoperative keratometric astigmatism and preoperative keratometric astigmatism. The cardinal component of SIA correction ($KA_{c\text{-}post} - KA_{c\text{-}pre}$) in this case is 1.30 −5.26 D = −3.96 D. The oblique component of SIA correction ($KA_{o\text{-}post} - KA_{o\text{-}pre}$) is 4.52 D − (−10.79 D) = 15.31 D. The magnitude of SIA correction is $|\text{SIA correction}| = \sqrt{(-3.96)^2 + (15.31)^2} = 15.81$ D and the axis of SIA correction is $0.5\,x\,\tan^{-1}\left(\frac{15.31\text{ D}}{-3.96\text{ D}}\right) + 90$ degrees = 52.3 degrees.

Error of Angle The error of angle measures whether the treatment was applied at the correct axis. It is the angular difference between the axis of SIA correction and the axis of the intended astigmatic correction. In this hypothetical case, error of angle = 52.3 degrees to 58.0 degrees = −5.7 degrees.

Nomogram Development

To develop a nomogram for femtosecond laser AK, regression analysis was used to link incision parameters to surgical effect. Data regarding arc length, diameter, and depth of incision were used. The depth of incision in each surgical case included in the study was calculated by dividing the posterior depth of the incision by the lowest recorded corneal pachymetry. Because the effect of incision creation is related to depth, arc length, and the diameter of each incision, a composite measure of the incision magnitude was developed as follows:

$$\text{Incision magnitude} = (\text{arc length 1} + \text{arc length 2}) / (\text{residual \% stromal thickness} \times \text{incision diameter})$$

.

For the purpose of developing the nomogram, it was assumed that all femtosecond laser AK incisions would be paired and symmetrical. Astigmatic keratotomy incisions with an arc length of less than 60 degrees can split regular bowtie astigmatism into more complicated quadrafoil aberrations. Therefore, the minimum arc length of paired incisions in the nomogram was set at 60 degrees. In addition, to reduce the risk for corneal perforation, the maximum percentage depth of the incisions was set to 90%.

Statistical Analysis

Statistical analysis of visual acuities was performed in units of logMAR. The Student paired *t* test was used to assess the difference between preoperative and postoperative vision and refraction. Statistical analysis was performed using SAS software (version 9.3, SAS Institute, Inc.). A *P* value less than 0.05 was considered to be statistically significant.

RESULTS

Patient Characteristics

One hundred forty femtosecond laser AK procedures were performed for the management of residual astigmatism following penetrating keratoplasty (PKP) (n = 129) and deep anterior lamellar keratoplasty (DALK) (n = 11) from January 2007 to January 2015. In 1 case, the lowest recorded pachymetry was greater than 750 μm in the area of the incision; this case was excluded to avoid the expected altered response to the creation of AK incisions in the setting of moderate corneal edema. Fifty cases were excluded because of a missing key data value (preoperative and postoperative difference between the steep and flat keratometry values or axis, incision diameter, depth, and/or arc length). Eighty-nine procedures (PKP, n = 80; DALK, n = 9) were performed on 89 eyes of 82 patients who met the aforementioned criteria. The mean age of the 48 men and 34 women was 59 years ± 16 (SD) (range 18 to 91 years).

Operative and Clinical Findings

The mean incision diameter was 6.66 mm (range 5.5 mm to 7.8 mm). The mean AK incision depth (as a percentage of corneal thickness at the planned incision site) was 86% (range 62% to 94%), with all paired incisions performed at the same depth. The mean individual incision arc length was 64 degrees but ranged from 15 to 90 degrees. Each of the paired arcuate incisions was the same length in 79 (88.7%) of the 89 procedures; however, in 10 (11.0%) of the 89 procedures, the presence of asymmetric astigmatism prompted the creation of a longer incision on the steeper hemimeridian. The centers of the paired femtosecond laser AK incisions were 180 degrees apart in 5 (5.6%) of the 89 cases for which this information was available; however, in 71 (80.0%) of the 89 cases that showed skewing of the radial axes on corneal topography, the center of each femtosecond laser AK incision was located between 100 degrees and 178 degrees apart.

Postoperative Complications

No eye had dehiscence of the corneal transplant incision or infectious keratitis associated with the creation of the AK incisions. Graft rejection developed in 2 (2.2%) of the 89 eyes and was successfully reversed in both cases. Both patients with graft rejection had surgery at the University of Toronto. In addition, 1 patient at the University of Toronto developed elevated intraocular pressure, which was attributed to the topical steroids that the patient was treated with after the procedure.

Visual Acuity

The mean UDVA improved from 1.15 ± 0.45 logMAR (range 20/20 to counting fingers [CF]) preoperatively to 0.87 ± 0.44 logMAR (range 20/25 to CF) 1 to 3 months postoperatively ($P < .0001$) (n = 43).

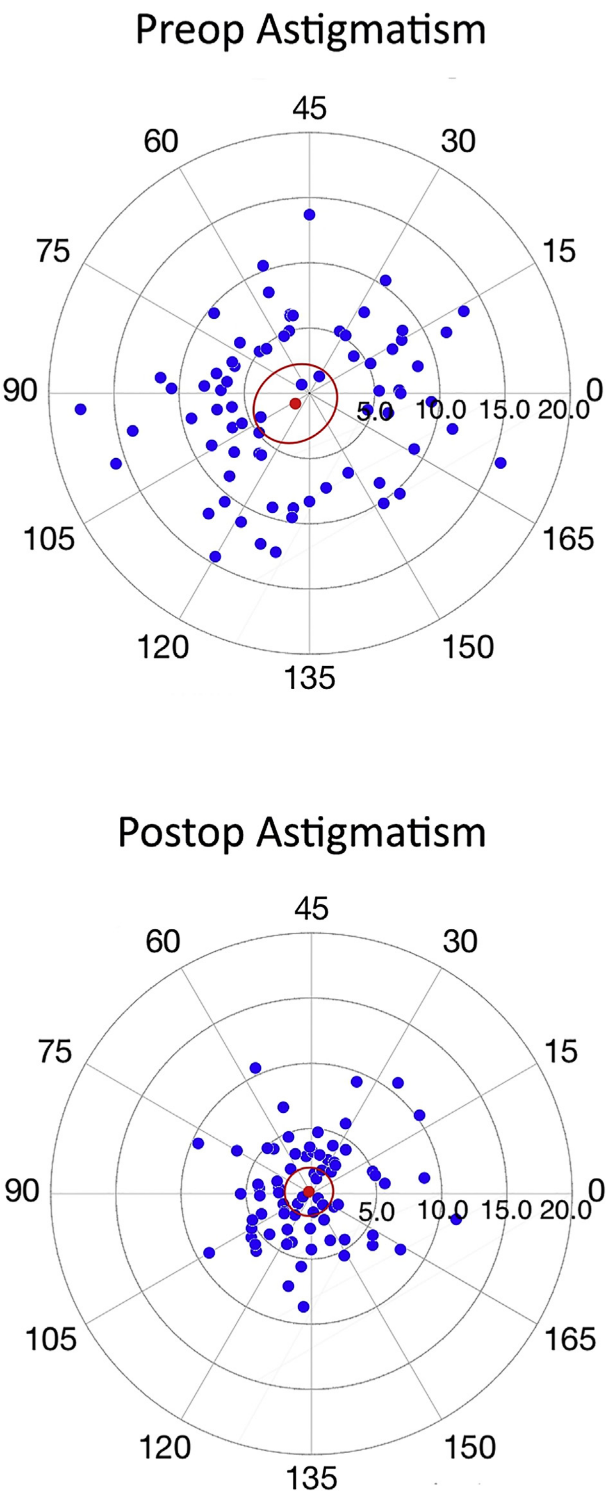

Figure 1. Double-angle polar plot of preoperative and postoperative keratometric astigmatism after femtosecond laser AK with preoperative and postoperative centroids. The red dots represent the mean vector astigmatism, and the red circles represent the vector centroid based on the standard deviation.

The mean CDVA improved from 0.47 ± 0.38 logMAR (range 20/20 to CF) preoperatively to 0.35 ± 0.31 logMAR (range 20/20 to CF) 1 to 3 months postoperatively (P = .013) (n = 46). Twenty-three (53.5%) of 43 eyes gained 2 or more lines of UDVA and 12 (27.9%) of 43 eyes gained 2 or more lines of CDVA postoperatively. In contrast, 3 (7.0%) of 43 eyes lost 2 or more lines of UDVA and 4 (9.3%) of 43 eyes lost 2 or more lines of CDVA postoperatively. The loss of CDVA was attributed to induced irregular astigmatism in 3 eyes and to overcorrection in 1 eye.

Refraction

The mean magnitude of preoperative keratometric astigmatism was 8.29 ± 2.90 D (range 1.50 to 17.6 D), which decreased to 4.62 ± 2.42 D (range 0.62 to 11.28 D) 1 to 3 months postoperatively (P < .0001) (n = 88) (Figure 1). The mean manifest refractive cylinder and defocus equivalent decreased from 6.85 ± 2.71 D (range 0.75 to 14.25 D) and 7.41 ± 3.96 D (range 1.50 to 17.75 D), respectively, preoperatively to 4.08 ± 2.25 D (range 0.50 to 11.75 D) and 6.36 ± 4.34 D (range 1.25 to 17.00 D), respectively, postoperatively (P < .0001 and P = .001, respectively) (n = 68 for both parameters). The mean spherical equivalent did not change significantly after femtosecond laser AK. It was −2.98 ± 4.19 D (range −14.00 to 6.50 D) preoperatively and −3.58 ± 4.43 D (range −15.13 to 5.38 D) postoperatively (P = .51) (n = 68).

The mean cardinal component of the keratometric astigmatism ($KA_{c\text{-}pre}$) was −1.18 ± 6.61 D, and the mean oblique component ($KA_{o\text{-}pre}$) was −0.70 ± 5.69 D. Postoperatively, the mean cardinal component of the keratometric astigmatism ($KA_{c\text{-}post}$) was −0.38 ± 3.77 D (P = .15), and the mean oblique component of the keratometric astigmatism ($KA_{o\text{-}post}$) was 0.09 ± 3.62 D (P = .27).

The mean SIA correction was 4.62 ± 2.42 D, and the mean axis of the SIA correction was 87.3 ± 56.5 degrees. The mean surgically induced change in the cardinal and oblique components of astigmatism was 0.87 ± 5.57 D and 0.70 ± 5.97 D, respectively. Overcorrection of the preoperative keratometric astigmatism (change in keratometric astigmatism >0 postoperatively) occurred in 6 (6.7%) of the 89 eyes.

Nomogram Development

Linear regression analysis with the simplest model that showed that the magnitude of SIA correction was significantly correlated with the incision magnitude (P < .0001).

The regression equation for model 1 was

$$\text{SIA correction magnitude} = 2.571 \times \text{incision magnitude}$$

This simple model yielded $R^2 = 0.67$ and a root-mean-square (RMS) residual error of 2.99 D. However, previous studies show that the degree of achieved astigmatic correction is highly correlated with the magnitude of preoperative astigmatism, even when the incision parameters are held constant. Therefore, to develop an accurate nomogram, both the incision magnitude and preoperative astigmatism should be considered.

The regression equation for model 2 was

$$\text{SIA correction magnitude} = 1.260 \times \text{incision magnitude} + 0.152 \times \text{incision magnitude} \times \text{preoperative keratometric astigmatism}$$

The more complex model yielded $R^2 = 0.69$ and an RMS residual error of 2.92 D. A provisional nomogram was developed using model 2 and a 10% undercorrection factor. The nomogram-generating equation is as follows:

$$\text{Incision magnitude} = (0.90) \times \text{preoperative keratometric astigmatism} / (1.260 + 0.156 \times \text{preoperative keratometric astigmatism})$$

For the nomogram, progressive increases in incision arc lengths and depths for increasing magnitudes of astigmatism correction were used. The percentage incision depths were selected to stay within the range that was used in this case series. Then, a comprehensive nomogram (Table 2) with varying arc lengths and depths to incorporate different surgical preferences and clinical settings was generated.

DISCUSSION

Astigmatic keratotomy attempts to reduce corneal astigmatism by placing 1 or 2 deep curved corneal incisions concentric to the limbus and perpendicular to the steep axis of astigmatism. Studies[26,28] show that the efficacy of AK incisions is dependent on the length and depth of incisions, the diameter of the optical zone, and the age and sex of the patient. In addition, the magnitude of SIA correction associated with femtosecond laser AKs in post-PKP eyes has been shown to be correlated with the degree of preoperative astigmatism.[5]

By relating the preoperative astigmatism, arc length, depth, and diameter of the corneal incisions created in 89 eyes that had femtosecond laser AK for the

Table 2. Nomogram for femtosecond laser AK after keratoplasty.

Preop DK	Incision Magnitude	Correction (%)	Incision Depth (% Corneal Thickness)	Arc Length (Degrees)	Optical Zone Diameter (mm)
2	1.311	0.87	85	60	7.0
3	1.784	0.82	85	75	6.8
4	2.176	0.78	85	85	6.7
5	2.508	0.72	85	90	6.6
6	2.791	0.98	90	90	6.6
7	3.036	0.91	90	90	6.5
8	3.249	0.87	90	90	6.4
9	3.438	0.83	90	90	6.3
10	3.605	0.81	90	90	6.2

DK = delta K (difference between the steepest and flattest keratometry values)

correction of post-keratoplasty astigmatism to SIA correction, we generated a nomogram for planning of femtosecond laser AK after PKP and DALK. The coefficient of determination of our nomogram-generating equation was 0.67; thus, 67% of the variation in SIA correction magnitude can be explained by the preoperative astigmatism, arc length, depth, and diameter of the incisions. Thus, 33% of the variation in SIA correction magnitude can be attributed to unknown variables or to inherent variability.

The efficacy of femtosecond laser AK for the management of high post-keratoplasty astigmatism is shown by the significant increase in the mean UDVA and CDVA and the significant reduction in the mean keratometric astigmatism 1 month postoperatively. The decrease in the magnitude of the mean keratometric astigmatism and the improvement in UDVA and CDVA that we found are similar to the mean decrease in keratometric astigmatism and the improvement in visual acuity observed in previously published smaller series of femtosecond laser AK for post-keratoplasty astigmatism.[15,25] We noted a trend toward undercorrection in our series, with a 3.62 D difference between the mean magnitude of intended astigmatic correction and the mean SIA correction. This resulted in a relatively low incidence of overcorrection (6.7%) in our series, which is comparable to the 8% to 10% of eyes overcorrected in previously published series.[15,25] The safety of the procedure is shown by the low incidence of other associated postoperative complications, such as wound dehiscence, infection, and graft rejection, and that only 7.0% of eyes lost 2 or more lines of UDVA, whereas 53% of eyes gained 2 or more lines of UDVA postoperatively.

Variable effects have been observed in a series of standard arc length AKs in post-PKP eyes,[5] leading the authors to conclude that nomograms have no useful role in the planning of AKs for post-PKP astigmatism. We respectfully disagree. We acknowledge that the effect on corneas of AKs for post-PKP astigmatism is different than that on native corneas, most likely because of the oblique and irregular tension in the corneal graft resulting from less than perfect tissue distribution during the PKP surgery. However, the coefficient of determination of our nomogram-generating equation shows that a majority of the effect of femtosecond laser AK incisions on post-PKP eyes can be explained by preoperative astigmatism and incision variables such as arc length, depth, and diameter. Thus, we believe that we have developed an effective nomogram for femtosecond laser AK in the management of high post-keratoplasty astigmatism that will likely increase the utility of this already established procedure. The accuracy and predictive value of this nomogram can be improved by regression analyses of the outcomes of femtosecond laser AK using this nomogram by surgeons at the 3 centers involved in this study.

WHAT WAS KNOWN

- Femtosecond laser AK is an effective method for treating astigmatism in post-keratoplasty eyes.
- In post-keratoplasty eyes, the effect of AK is proportional to the magnitude of preoperative astigmatism.

WHAT THIS PAPER ADDS

- Femtosecond laser AK was safe and effective in the management of post-keratoplasty astigmatism.
- A nomogram for surgical planning of femtosecond laser AK for post-keratoplasty astigmatism was created using regression analysis of outcomes of the procedure in a series of eyes treated at 3 centers.

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