Intraocular Pressure Trend Following Myopic Photorefractive Keratectomy

Ghasem Fakhraie  
Farabi Eye Hospital

Zakieh Vahedian  
Farabi Eye Hospital

Reza Zarei  
Farabi Eye Hospital

Yadollah Eslami  
Farabi Eye Hospital

seyed mehdi tabatabaei  
Farabi Eye Hospital  
meh.tabatabaei@gmail.com

Abdollah Hadi  
Farabi Eye Hospital

Sepideh Ghods  
Farabi Eye Hospital

Ali Fakhraie  
Farabi Eye Hospital

Research Article

Keywords: Photorefractive Keratectomy, Myopia, Steroid Response

Posted Date: September 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-891473/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Purpose

To evaluate the intraocular pressure (IOP) trend and risk factors for IOP rise after myopic photorefractive keratectomy (PRK).

Patients and Methods

One eye of each patient undergone PRK for myopia was randomly assigned to this study. All eyes underwent tonometry by CorVis Scheimpflug Technology (CST) tonometer (Oculus Optikgeräte GmbH, Wetzlar, Germany) 1 week, 2 weeks, 1 month, 2 months, 3 months and 4 months after surgery. The eyes with IOP rise more than 5 mmHg and the risk factors were evaluated by Kaplan-Meier graph and multiple Cox regression analysis.

Results

348 eyes of 348 patients were enrolled in this study. Forty-three eyes (12.35%) experienced an IOP rise of more than 5 mmHg. Eyes with IOP rise had higher baseline IOP (Median 19 mmHg (IQR 18 – 22) versus. Median 15 mmHg (IQR 14 – 16); \( p < 0.001 \)). Baseline central corneal thickness (CCT) was higher in eyes without IOP rise (Median 520 µm (IQR 509 – 541) versus. Median 535 µm (IQR 518 – 547); \( p = 0.009 \)). In multivariate Cox regression analysis higher baseline IOP was a risk factor for IOP rise (Hazard Ratio (HR) 1.59 (95% CI 1.43 – 1.77); \( p < 0.001 \)) while higher baseline CCT was protective (HR 0.97 (95% CI 0.95 – 0.98); \( p < 0.001 \)).

Conclusion

Eyes with higher baseline IOP and lower baseline CCT are at increased risk of IOP rise after PRK and should be monitored more frequently.

Introduction

Myopia is the most common form of refractive error (1) and its prevalence is increasing in our modern era (2). It is estimated that myopia and high myopia will affect 5 and 1 billion people by 2050, respectively (3). Parallel to the increasing prevalence of myopia the demand for refractive surgery has grown. Photorefractive keratectomy (PRK) is one of these procedures that has gained popularity for the correction of refractive error in myopia, particularly in thin corneas, because of its improved safety (4).

Topical steroids are routinely prescribed after myopic PRK for the reduction of corneal opacity and myopic regression (5). Intraocular pressure (IOP) elevation following steroid use is well-documented and long-term use of these agents can result in ocular hypertension (OHTN) and glaucoma. On the other hand, myopia itself is a risk factor for open-angle glaucoma (OAG) and steroid-induced OHTN (6).

So, understanding the incidence and magnitude of IOP elevation following PRK and also its associated risk factors may help clinicians detect, prevent, monitor, and treat any clinically significant IOP rise.

Given the inaccuracy of tonometry with Goldmann applanation tonometer in patients undergone PRK, we used CorVis Scheimpflug Technology (CST) tonometer (Oculus Optikgeräte GmbH, Wetzlar, Germany) for IOP...
measurement pre- and postoperatively. It has already been documented that biomechanical IOP (bIOP) provided by CST tonometer does not seem to be affected by corneal thickness and corneal biomechanics, and in the case of keratorefractive surgery, is similar to pre-surgery measurements (7,8).

This study aimed to evaluate IOP changes following PRK. To the best of our knowledge, the IOP trend after myopic refractive surgery has not been reported previously.

**Patients And Methods**

In this prospective study, patients that underwent PRK for correction of nearsightedness between July 2016 and April 2019 were recruited. All surgeries were done by the same attending ophthalmologists (G.F.). Ethics committee approval of Tehran University of Medical Sciences was granted and tenets of the declaration of Helsinki have adhered to.

**Inclusion criteria**

One eye of each patient was randomly assigned for this study and Inclusion criteria were as follows: age older than 18 years old, spherical refraction between -1.00 and -10.00 diopters, stable refraction for at least 12 months, and cessation of wearing soft and rigid contact lenses for at least 2 and 3 weeks, respectively. All patients that were included in this study underwent PRK in both eyes and were followed for at least 4 months.

**Exclusion criteria**

Exclusion criteria included: a history of dry eye or any autoimmune disease that involves ocular surface, diabetes, previous ocular surgery, herpetic keratitis, OHTN, and glaucoma.

**Data collection**

All patients underwent thorough and comprehensive ophthalmic examination including measurement of corrected distance visual acuity (CDVA), slit-lamp biomicroscopy, tonometry by CST, gonioscopy, dilated funduscopy, measurement of the central corneal thickness (CCT) by pachymetry (Tomey Corporation, Nagoya, Japan) and corneal imaging by Pentacam (OCULUS Optikgerate GmbH, Wetzlar, Germany). Demographic data like age and gender were collected as well.

**Surgical technique**

All PRK procedures were done in the same manner and by the same surgeon (G. F.). Briefly, after instilling a drop of generic tetracaine in lower conjunctival fornices a lid speculum was inserted. Epithelial debridement was done after applying ethyl alcohol 20% on the cornea for 10-15 seconds. Next, a 500 Hz Wavelight Allegretto Laser excimer laser (Wavelight Laser Technologie AG) was used for laser delivery. After ablation, a piece of sponge soaked in mitomycin 0.02% was applied to the stroma accordingly. Then vigorous rinsing was done by balanced salt solution. At the end of the procedure a bandage contact lens (BCL) was placed on the cornea and a drop of levofloxacin 0.5% and diclofenac 0.1% was instilled on the ocular surface.

**Post-operative treatment**
Topical levofloxacin 0.5% and betamethasone 0.1% were prescribed for the patients during 1 and 2 weeks after the procedure, respectively. Both drops were ordered 4 times a day. BCL was removed after healing the epithelial defect, during the first week. After two weeks betamethasone 0.1% was replaced by fluorometholone 0.1% and the latter continued for 3 months in a tapered fashion. Meanwhile, the patient was advised to use preservative-free artificial tears regularly and “pro re nata”.

**Follow up**

Patients were examined 1 day, 1 week, 2 weeks, 1 month, 2 months, 3 months, and 4 months after surgery. Tonometry by CST was done in each visit except postoperative day 1. Post-operative CCT was measured at the 1-month visit.

**Statistical analysis**

To present data we used mean, standard deviation, median, and range. To assess the IOP changes we used a linear mixed model. Multiple comparisons were considered in this model by the Sidak method. The velocity of the patients to have an IOP rise more than 5 mmHg compared to the baseline IOP was evaluated by the Kaplan-Meier graph. Also, the comparison of the groups regarding the time to this IOP rise was evaluated by univariate and multiple Cox regression. In the last step to obtain the most important risk factors, we used the Backward Likelihood Ratio (LR) method in our multiple cox regression models. All the analyses were performed by SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). A P-value of less than 0.05 is considered statistically significant.

**Results**

173 eyes of 173 male patients and 175 eyes of 175 female patients who underwent uneventful PRK were enrolled in this study. The median value for age was 27 years (interquartile range (IQR): 23- 30). Pre-operative CCT, IOP and spherical equivalent (SE) were non-parametric and the median values were 534 µm (IQR 516- 546 µm), -4.50 D (IQR -5.50- -3.50 Diopter) and 16 mmHg (IQR 14- 18) respectively. The median for ablation depth was 64 µm (IQR 50.00 – 77.75 µm) (Table 1).

Linear mixed modeling was statistically significant (P < 0.001). Median IOP at first week after PRK was 15.5 mmHg (IQR 14 – 18 mmHg) and there wasn't statistically significant difference in comparison to baseline IOP (P= 0.592). But IOP at second week, first month, second month, third month and forth month were significantly higher than baseline IOP (median 16; IQR 14 – 19; P < 0.001, median 17; IQR 14 – 20; P= 0.001, median 16; IQR 16 – 20; P= 0.001, median 16; IQR 14 – 19.75; P < 0.001 and median 16; IQR 14 – 19; P < 0.001, respectively) (Table 2).

Among 348 eyes, 43 eyes (12.35 %) experienced the rise of IOP more than 5 mmHg, eventually. The cumulative incidence of IOP rise derived from Kaplan-Meyer analysis was 0.9 %, 8.6 %, and 12.4% at the first week, second week, and the first month after PRK, respectively (Figure 1).

41.90% (18/43) of eyes that did and 50.80% (173/305) of eyes that didn't experience IOP rise belonged to the male patients (p= 0.329) (Table 3). The Hazard Ratio (HR) for IOP rise in male patients was 1.39 (95%
In eyes with IOP rise, the median age was 26 years (IQR 23 – 29). The median age in eyes without IOP rise was 28 years (IQR 23 – 30). There was no significant difference between these two groups ($p = 0.217$) (Table 3). Also, age wasn’t a significant risk factor for IOP rise in univariate analysis (HR 0.96 (95% CI 0.90 – 1.02); $p = 0.212$) (Table 4).

Baseline IOP was significantly higher in eyes that experienced IOP rise (Median 19 mmHg (IQR 18 – 22) versus. Median 15 mmHg (IQR 14 – 16); $p < 0.001$) (Table 3). In univariate analysis higher baseline IOP was a significant risk factor for IOP rise (HR 1.54 (95% CI 1.39 – 1.71); $p < 0.001$).

Median baseline CCT in eyes with and without IOP rise was 520 µm (IQR 509 – 541) and 535 µm (IQR 518 – 547), respectively, and was higher in the latter group ($p = 0.009$) (Table 3). In univariate analysis higher baseline CCT was a protective factor against IOP rise (HR 0.98 (95% CI 0.96 – 0.99); $p = 0.009$) (Table 4).

There was no significant difference in baseline refractive error (RE) between the eyes with and without IOP rise (Median -4.25 (IQR -5.75 - -3.25) versus Median -4.50 (IQR -5.50 - -3.50); $p = 0.732$). Also, proportion of eyes with high myopia (SE < -6.00 diopters) was not different between groups (18.6% versus 19.0%; $p > 0.9$) (Table 3). Baseline RE was not a risk factor for IOP rise in univariate analysis (HR 1.02 (95% CI 0.86 – 1.22); $p = 0.760$) (Table 4).

Ablation depth and post-operative CCT were not different between groups (Median 59 (IQR 47 - 75) versus Median 64 (IQR 51 - 78); $p = 0.279$ and Median 460 (IQR 436 - 478) versus Median 468 (IQR 448 - 483); $p = 0.108$, respectively) (Table 3). Neither of them was significant risk factors in univariate analysis (HR 0.99 (95% CI 0.98 – 1.00); $p = 0.433$ and HR 0.99 (95% CI 0.98 – 1.00); $p = 0.142$, respectively) (Table 4).

In the multivariate Cox regression analysis baseline IOP and CCT remained significant. Higher baseline IOP was a significant risk factor for rise of IOP more than 5 mmHg (HR 1.59 (95% CI 1.43 – 1.77); $p< 0.001$) while higher baseline CCT was protective (HR 0.97 (95% CI 0.95 – 0.98); $p< 0.001$) (Table 4).

**Discussion**

The present study was designed for the evaluation of the IOP trend after myopic PRK. Given the CCT and corneal biomechanics changes after myopic PRK, we used CST for the measurement of bIOP. Our study showed that higher baseline IOP and lower baseline CCT are significant risk factors for the IOP rise after myopic PRK. All IOP rises occurred during the first month (within the first 4 weeks) after the procedure.

In our study, there was no significant difference between the IOP at the first week and baseline IOP but mean IOP was higher in other follow-up visits. Previous studies considering this issue have mixed results. Lee et al. applied CST and a non-contact tonometer (NTC) for measurement of IOP in patients undergoing myopic transepithelial PRK. In their study, IOPs measured by NCT were lower in the 6-month visit in comparison to the baseline, while CST presented more similar IOPs to the baseline (7). In another study by Schallhorn et al, the IOP (measured by an NCT) one month after myopic PRK was $3.16 \pm 2.53$ mmHg lower than baseline (9). Also, Shousha et al showed that using Ocular Response Analyzer (ORA) for the
measurement of IOP two months after myopic epi-LASIK will lead to more similar values to the baseline (Baseline Median IOP 13.4 mmHg range 12 – 16 versus 2-month median IOP 13.45 mmHg range 10.1 – 15.4; \( p = 0.041 \)) (10). These studies show that the measurement of IOP by a tonometer that compensates CCT and corneal biomechanics is more reliable in patients that have undergone surface ablation.

Previous studies have shown that continuous administration of topical steroids in patients who are steroid responders will result in an IOP rise after 3 to 6 weeks (11). In a report by Javadi et al, the time needed for IOP rise in patients undergone PRK was the same. In their study betamethasone eye drop was prescribed for the patients after the procedure and the first steroid responders were diagnosed after 2 – 3 weeks (12). In our study 3 eyes showed the rise of IOP more than 5 mmHg, one week after the procedure. This short-term IOP elevation may be related to the high potency of betamethasone. The more potent steroids would lead to IOP elevation in a shorter period (13).

Generally, gender is not a risk factor for steroid response and IOP elevation, however, in the study run by Busool et al. the male gender was recognized as a risk factor for steroid response after PRK (14). In another study, Lau et al. evaluated IOP after intravitreal triamcinolone injection. Odds ratio for IOP elevation greater than 6 mmHg in male patients was 3.17 (\( p = 0.006 \)). They mentioned that there is no reasonable explanation for gender being a risk factor for steroid response (15). In our study gender was not a risk factor for IOP rise.

Age as a risk factor for steroid response has been explored in several studies. In a study by Lam et al. topical dexamethasone was prescribed for children after strabismus surgery. They found that children younger than 6 years old may be great steroid responders (16). Studies done in the adults have mentioned older age, age under fifty or thirty as risk factors for IOP elevation (17–19). In our study, the HR for age wasn't significant. This may be due to the relatively narrow age range (IQR 23 – 30) in our patients.

Association between myopia and glaucoma is well documented (20–23) and some studies have illustrated high myopia and longer axial length as predictors of steroid response. A study by Chang et al. showed that longer axial length, particularly longer than 29.0 mm will increase the risk of IOP elevation after uneventful cataract surgery (24). In a study by Busool et al. that was designed for evaluation of predictors of IOP response after PRK, there was a greater proportion of eyes with high myopia in steroid responders (14). In our study, the degree of myopia wasn't a risk factor for IOP elevation and there wasn't any difference between the proportion of eyes with high myopia among eyes with and without IOP elevation.

The thinner cornea has been known as a significant risk factor for the development and progression of glaucoma (25,26) however, the role of CCT in IOP elevation after steroid administration is not well established in the literature. Angelopoulos et al. compared the IOP of normal and keratoconic eyes after PRK. The latter group underwent combined partial PRK and Collagen cross-linking (CCL) and topical dexamethasone 0.1% was prescribed for both groups in the postoperative period. In their study, keratoconic eyes had lower CCT, and a greater proportion of keratoconic eyes were steroid responders (27). On the other hand, another study showed that thicker cornea is associated with increased steroid response (14). In the current study, the thicker cornea was shown to be protective against IOP elevation.

Baseline IOP was another predictor of IOP elevation in the current study. The higher the baseline IOP the higher risk for IOP elevation. In Rhee's study, which was designed for evaluation of IOP after intravitreal triamcinolone
acetonide injection (IVTA), higher baseline IOP (greater than 16 mmHg) was the only risk factor for IOP elevation (28). In another study by Smithen et al. nonglaucomatous eyes with baseline IOP greater than 15 mmHg were at higher risk for steroid response after IVTA injection (29). However, since the medication used and the route of administration was different in these studies, the comparison between the current study and the abovementioned reports has its own drawbacks.

Our study had several limitations. We only evaluated eyes that underwent myopic surface ablation. The intraocular pressure trend after lamellar and hyperopic refractive surgeries may be different. Also, the sample size of our study was limited. Future studies with larger sample size and with attention to the other forms of laser keratorefractive surgeries are recommended.

In conclusion, our study showed that IOP elevation may occur in the first week after surface ablation. Eyes with higher baseline IOP and lower CCT are at greater risk of steroid response and should be monitored more frequently.

Declarations

Acknowledgments: None.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Conflicts of interest/Competing interests: Ghasem Fakhraie declares that he has no conflict of interest. Zakieh Vahedian declares that she has no conflict of interest. Reza Zarei declares that he has no conflict of interest. Yadollah Eslami declares that he has no conflict of interest. Seyed Mehdi Tabatabaei declares that he has no conflict of interest. Abdollah Hadi declares that he has no conflict of interest. Sepideh Ghods declares that she has no conflict of interest. Ali Fakhraie declares that he has no conflict of interest.

Availability of data and material: The data that support the findings of this study are available from the corresponding author, [SMT], upon reasonable request.

Code availability: Not Applicable.

Ethics approval: All procedures performed in this study which involve human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate: Informed consent was obtained from all individual participants included in the study.

Consent for publication: There is no identifying information about participants available in the article, so this issue is not applicable.

References
1. Morgan IG, Ohno-Matsui K, Saw S-M. Myopia. The Lancet. 2012;379(9827):1739–48.

2. Vitale S, Sperduto RD, Ferris FL. Increased prevalence of myopia in the United States between 1971-1972 and 1999-2004. Arch Ophthalmol. 2009;127(12):1632–9.

3. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016 May;123(5):1036–42.

4. Vestergaard AH. Past and present of corneal refractive surgery: a retrospective study of long-term results after photorefractive keratectomy and a prospective study of refractive lenticule extraction. Acta Ophthalmol (Copenh). 2014 Mar;92 Thesis 2:1–21.

5. Marques EF, Leite EB, Cunha-Vaz JG. Corticosteroids for reversal of myopic regression after photorefractive keratectomy. J Refract Surg Thorofare NJ 1995. 1995 Jun;11(3 Suppl):S302-308.

6. Marcus MW, de Vries MM, Junoy Montolio FG, Jansonius NM. Myopia as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. Ophthalmology. 2011 Oct;118(10):1989-1994.e2.

7. Lee H, Roberts CJ, Kim T-I, Ambrósio R, Elsheikh A, Yong Kang DS. Changes in biomechanically corrected intraocular pressure and dynamic corneal response parameters before and after transepithelial photorefractive keratectomy and femtosecond laser-assisted laser in situ keratomileusis. J Cataract Refract Surg. 2017;43(12):1495–503.

8. Hugo J, Granget E, Ho Wang Yin G, Sampo M, Hoffart L. Intraocular pressure measurements and corneal biomechanical properties using a dynamic Scheimpflug analyzer, after several keratoplasty techniques, versus normal eyes. J Fr Ophtalmol. 2018 Jan;41(1):30–8.

9. Schallhorn JM, Schallhorn SC, Ou Y. Factors that influence intraocular pressure changes after myopic and hyperopic LASIK and photorefractive keratectomy: a large population study. Ophthalmology. 2015 Mar;122(3):471–9.

10. Shousha SM, Steit MAA, Hosny MH, Ewais WA, Shalaby AM. Comparison of different intraocular pressure measurement techniques in normal eyes, post surface and post lamellar refractive surgery. Clin Ophthalmol Auckl NZ. 2013;7:71.

11. Armaly MF. Effect of corticosteroids on intraocular pressure and fluid dynamics. II. The effect of dexamethasone in the glaucomatous eye. Arch Ophthalmol Chic Ill 1960. 1963 Oct;70:492–9.

12. Javadi M-A, Mirbabaei-Ghafghazi F, Mirzade M, Yazdani S, Yaseri M. Steroid induced ocular hypertension following myopic photorefractive keratectomy. J Ophthalmic Vis Res. 2008;3(1):42.

13. Yamamoto Y, Komatsu T, Koura Y, Nishino K, Fukushima A, Ueno H. Intraocular pressure elevation after intravitreal or posterior sub-Tenon triamcinolone acetonide injection. Can J Ophthalmol. 2008;43(1):42–7.
14. Busool Y, Mimouni M, Vainer I, Levartovsky S, Sela T, Munzer G, et al. Risk factors predicting steroid-induced ocular hypertension after photorefractive keratectomy. J Cataract Refract Surg. 2017;43(3):389–93.

15. Lau L-I, Chen K-C, Lee F-L, Chen S-J, Ko Y-C, Liu CJ-L, et al. Intraocular pressure elevation after intravitreal triamcinolone acetonide injection in a Chinese population. Am J Ophthalmol. 2008;146(4):573–8.

16. Lam DSC, Fan DSP, Ng JSK, Yu CBO, Wong CY, Cheung AYK. Ocular hypertensive and anti-inflammatory responses to different dosages of topical dexamethasone in children: a randomized trial. Clin Experiment Ophthalmol. 2005 Jun;33(3):252–8.

17. Garbe E, LeLorier J, Boivin JF, Suissa S. Risk of ocular hypertension or open-angle glaucoma in elderly patients on oral glucocorticoids. Lancet Lond Engl. 1997 Oct 4;350(9083):979–82.

18. Friedman DS, Holbrook JT, Ansari H, Alexander J, Burke A, Reed SB, et al. Risk of elevated intraocular pressure and glaucoma in patients with uveitis: results of the multicenter uveitis steroid treatment trial. Ophthalmology. 2013 Aug;120(8):1571–9.

19. Parekh A, Srivastava S, Bena J, Albini T, Nguyen QD, Goldstein DA. Risk factors associated with intraocular pressure increase in patients with uveitis treated with the fluocinolone acetonide implant. JAMA Ophthalmol. 2015 May;133(5):568–73.

20. Leske MC, Connell AM, Wu SY, Hyman LG, Schachat AP. Risk factors for open-angle glaucoma. The Barbados Eye Study. Arch Ophthalmol Chic Ill 1960. 1995 Jul;113(7):918–24.

21. Chihara E, Liu X, Dong J, Takashima Y, Akimoto M, Hangai M, et al. Severe myopia as a risk factor for progressive visual field loss in primary open-angle glaucoma. Ophthalmol J Int Ophtalmol Int J Ophthalmol Z Augenheilkd. 1997;211(2):66–71.

22. Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. Ophthalmology. 1999 Oct;106(10):2010–5.

23. Xu L, Wang Y, Wang S, Wang Y, Jonas JB. High myopia and glaucoma susceptibility the Beijing Eye Study. Ophthalmology. 2007 Feb;114(2):216–20.

24. Chang DF, Tan JJ, Tripodis Y. Risk factors for steroid response among cataract patients. J Cataract Refract Surg. 2011;37(4):675–81.

25. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002;120(6):714–20.

26. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol. 2003;121(1):48–56.

27. Kanellopoulos AJ, Cruz EM, Ang RET, Asimellis G. Higher incidence of steroid-induced ocular hypertension in keratoconus. Eye Vis. 2016;3(1):4.
28. Rhee DJ, Peck RE, Belmont J, Martidis A, Liu M, Chang J, et al. Intraocular pressure alterations following intravitreal triamcinolone acetonide. Br J Ophthalmol. 2006;90(8):999–1003.

29. Smithen LM, Ober MD, Maranan L, Spaide RF. Intravitreal triamcinolone acetonide and intraocular pressure. Am J Ophthalmol. 2004;138(5):740–3.

Tables

Table 1. Baseline demographic and clinical data.

|                          | Mean ± SD | Median | IQR     |
|--------------------------|-----------|--------|---------|
| Gender                   |           |        |         |
| Male                     | 173       | 49.7%  |         |
| Female                   | 175       | 50.3%  |         |
| Age (Years)              | 27.4 ± 5.49 | 27     | 23 - 30 |
| Baseline CCT (µm)        | 532.84 ± 23.05 | 534    | 516 - 546 |
| Ablation Depth (µm)      | 65.47 ± 21.91 | 64     | 50 - 77  |
| Baseline RE (Spherical equivalent (Diopters)) | -4.73 ± 1.75 | -4.50 | -3.50 - -5.50 |

IOP= Intraocular pressure; CCT= Central Corneal Thickness; RE= Refractive Error; IQR= Interquartile Range
Table 2. Pairwise comparison between IOP at follow-up visits and baseline IOP by Sidak method.

| Time   | Status | IOP     | Median (range) | IOP Rise | \( p \) |
|--------|--------|---------|----------------|----------|---------|
|        |        | Mean ± SD |                | > 5 mmHg |         |
| Baseline | Value  | 16 ± 3  | 16 (10 to 24) |          |         |
| 1 Week  | Value  | 16 ± 4  | 16 (9 to 29)  |          | 0.592   |
|         | Change | 0.19 ± 1.95 | 0 (-4 to 13) | 3 (0.9%) |         |
| 2 Week  | Value  | 17 ± 5  | 16 (9 to 37)  |          | 0.000   |
|         | Change | 1.35 ± 2.6 | 1 (-3 to 13) | 29 (8.3%) |         |
| 1 Month | Value  | 18 ± 5  | 17 (1 to 38)  |          | 0.001   |
|         | Change | 1.99 ± 2.9 | 2 (-12 to 16) | 37 (10.6%) |         |
| 2 Months| Value  | 17 ± 4  | 16 (10 to 34) |          | 0.001   |
|         | Change | 1.31 ± 1.97 | 1 (-3 to 10) | 7 (2.0%) |         |
| 3 Months| Value  | 17 ± 4  | 16 (8 to 30)  |          | 0.000   |
|         | Change | 0.91 ± 1.76 | 1 (-7 to 6) | 1 (0.3%) |         |
| 4 Months| Value  | 17 ± 4  | 16 (9 to 33)  |          | 0.000   |
|         | Change | 0.74 ± 1.69 | 1 (-3 to 9) | 1 (0.3%) |         |

\( p \) the P-value for the comparison of the values at different times compared to the baseline value, based on the Linear mixed model, multiple comparisons considered by Sidak Method.

IOP, Intraocular Pressure
Table 3. Clinical and ophthalmological characteristics of the included eyes with or without IOP Rise.

| p value | No IOP Rise, n= 305 (87.64%) | IOP Rise, n= 43 (12.35%) | Variable |
|---------|-----------------------------|--------------------------|----------|
| 0.329<sup>a</sup> | 50.80%                  | 41.00%                  | Gender (Male) |
| 0.217<sup>b</sup> | 28 (23 - 30)             | 26 (23 - 29)             | Age (Median and IQR) |
| <0.001<sup>b</sup> | 15 (14 - 16)             | 19 (18 - 22)             | Baseline IOP (Median and IQR) |
| 0.009<sup>b</sup> | 535 (518 - 547)          | 520 (509 - 541)          | Baseline CCT (Median and IQR) |
| 0.732<sup>b</sup> | -4.50 (-5.50 - -3.50)   | -4.25 (-5.75 - -3.25)   | Baseline RE (Median and IQR) |
| >0.9<sup>a</sup>  | 19.00%                  | 18.60%                  | Myopia (High Myopia, SE < -6.00) |
| 0.279<sup>b</sup> | 64 (51 - 78)            | 59 (47 - 75)            | Ablation Depth (Median and IQR) |
| 0.108<sup>b</sup> | 468 (448 - 483)         | 460 (436 - 478)         | Post-op CCT (Median and IQR) |

<sup>a</sup>Fisher’s Exact Test  
<sup>b</sup>Mann-Whitney U Test

IQR= Interquartile Range; IOP= Intraocular Pressure; CCT= Central Corneal Thickness; RE= Refractive Error
Table 4. Results of univariate and multivariate analysis (Cox regression) of the association between IOP rise and other variables.

| Parameter     | Level | Univariate         |                     |          |          |          |          |          |          |          |          |          |
|---------------|-------|---------------------|---------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|               |       | HR  | 95% CI  | P    | HR  | 95% CI  | P    |
|               |       |     | Lower   | Upper |       | Lower   | Upper |
| Gender        | Male  | 1  | 1.394   | 0.760 | 2.555 | 0.283   |       | 0.975   | 0.514   | 1.851   | 0.975   | 0.760   | 2.555   | 0.283   | 0.975   | 0.514   | 1.851   | 0.975   |
|               | Female |   | 1.394   | 0.760 | 2.555 | 0.283   |       | 0.975   | 0.514   | 1.851   | 0.975   | 0.760   | 2.555   | 0.283   | 0.975   | 0.514   | 1.851   | 0.975   |
| Age           |       | 0.963 | 0.908 | 1.022 | 0.212 | 0.969 | 0.91 | 1.031 | 0.315 |
| Baseline IOP  |       | 1.548 | 1.393 | 1.719 | <0.001 | 1.599 | 1.438 | 1.779 | <0.001 |
| Baseline CCT  |       | 0.982 | 0.969 | 0.995 | 0.009 | 0.973 | 0.958 | 0.988 | <0.001 |
| Baseline RE   |       | 1.028 | 0.863 | 1.223 | 0.760 | 1.128 | 0.805 | 1.582 | 0.484 |
| Ablation Depth|       | 0.994 | 0.98  | 1.009 | 0.433 |       |       |       |       |
| Post-op CCT   |       | 0.992 | 0.981 | 1.003 | 0.142 | 0.994 | 0.981 | 1.007 | 0.353 |

IOP= Intraocular Pressure; CCT= Central Corneal Thickness; RE= Refractive Error (Spherical Equivalent); HR= Hazard Ratio

Figures
Figure 1

Kaplan-Meyer survival curve of the eyes with intraocular pressure rise more than 5 mmHg.