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Early intraocular pressure changes following different keratoplasty techniques and association with cornea parameters and anterior chamber depth

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Abstract

Background: Corneal transplantation surgery is associated with an increased risk of intraocular pressure (IOP) elevation. Increased IOP may cause irreversible vision loss and graft failure.

Purpose: We aimed to evaluate early IOP changes following different keratoplasty techniques and to investigate the relationship between corneal thickness (CT), keratometry values, anterior chamber depth (ACD), and IOP changes.

Methods: We included patients who underwent penetrating keratoplasty (PK), deep anterior lamellar keratoplasty (DALK), and Descemet membrane endothelial keratoplasty (DMEK) in this observational study. ACD, CT, and keratometry measurements were repeated postoperatively at hour 24, week 1, and month 1. IOP measurements were repeated at postoperative hours 6 and 24, week 1, and month 1 by Tono-Pen XL.

Results: In total, 22 patients underwent PK, 12 patients underwent DALK, and 19 patients underwent DMEK. The difference between the IOP preoperatively and postoperatively hour 6, and between the IOP preoperatively and postoperatively hour 24 was statistically significant in the three types of surgery ($p < 0.05$ for each). The difference between preoperative and postoperative week 1 IOP was statistically significant only in the PK group ($p = 0.023$). When the IOP was compared between the three types of surgeries, the IOP at postoperative week 1 in the PK group was significantly higher than the DALK and DMEK groups ($p = 0.021$). There was no correlation between ACD, CT, K values, and IOP in any group.

Conclusion: IOP may increase in all types of keratoplasty during the first hours after surgery, but PK has a risk of high IOP longer in the early postoperative period. PK patients should be followed more carefully during postoperative week 1 to check for an increase in IOP.

Keywords: anterior chamber depth, corneal thickness, glaucoma, keratometry, keratoplasty

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Background

Penetrating keratoplasty (PK) has been a main surgical procedure for corneal transplantation since early 1990.[1] Improvements in graft preparation and developments in technology have increased the indications for selective lamellar techniques, which are less invasive. These include deep anterior lamellar keratoplasty (DALK) and Descemet membrane endothelial keratoplasty (DMEK).[2]

Intraocular pressure (IOP) measurement is an important part of ocular examination, especially after a surgical intervention in the anterior segment, which can affect aqueous humor flow dynamics.[3] Increased IOP and glaucoma are

known postoperative complications that occur in up to one-third of eyes after corneal transplantation surgery.[3] It is important to measure IOP accurately after keratoplasty because increased IOP can cause irreversible visual field loss, endothelial cell loss, decreased vision, and graft failure due to endothelial dysfunction.[2]

Both lamellar and PK procedures, which replace part of the recipient's corneal tissue with donor corneal tissue, may lead to significant anatomical changes to the cornea and anterior chamber structures.[4] Changes in the corneal thickness (CT) and curvature after corneal transplantation where corneal morphology is altered have an impact on IOP measurements. Lamellar techniques, such as DALK and DMEK, which have additional stromal tissue and an interface between host and graft tissue, may have a different significance on IOP measurements in terms of corneal parameters.[3]

In this study, we aimed to evaluate early IOP changes following keratoplasty that is performed using different techniques and to investigate the relationship between corneal and anterior chamber parameters and IOP changes.

Methods

In this prospective observational study, we included consecutive patients who underwent PK, DALK, or DMEK at the Cornea Department at our hospital between August 2020 and January 2021. Written informed consent to use their data was obtained from all patients in accordance with the Declaration of Helsinki. Approval was received from the University of Health Sciences Turkey Prof Dr Cemil Taşcıoğlu City Hospital Ethics Committee for the study (Decision No. 329) in August 2020.

Each patient's data included sex, age, eye laterality, indication for surgery, lens status, preoperative best corrected visual acuity (BCVA) *via* Snellen chart, IOP, presence of glaucoma, presence of anterior or posterior synechiae, anterior chamber depth (ACD), CT, and keratometry (K1, K2, and Kaverage) values that were recorded preoperatively. The type of surgical procedure and graft diameter were recorded as intraoperative data. Patients who had additional keratoplasty procedures, patients with incomplete study parameter data, and patients with intraoperative complications were excluded from the study. BCVA, ACD, CT, and keratometry measurements were repeated postoperatively at hour 24, week 1, and month 1. IOP measurements were repeated postoperatively at hours 6 and 24, week 1, and month 1. IOP was measured at each visit using a Tono-Pen XL (Reichert Technologies, Buffalo, NY, USA) tonometer. If a patient was prescribed antiglaucoma medication, it was recorded. The ACD was measured using anterior segment optical coherence tomography (Visante OCT; Carl Zeiss Meditec, Dublin, CA, USA). Keratometry (K1, K2, and Kaverage) and CT were measured using Sirius corneal topography and the abberometry system (Costruzioni Strumenti Oftalmici, Florence, Italy).

Surgical techniques

All surgeries were performed by experienced surgeons (Y.Y., N.K.B., S.G., A.K., and A.A.) in the Cornea Unit of our hospital, and the patients were under general anesthesia or retrobulbar anesthesia.

Penetrating keratoplasty

For all patients, the donor cornea was obtained within 6 h after death, and it was stored in Optisol solution at 4°C and used within 72 h. The donor cornea was prepared by cutting the endothelial side using a punch trephine (Barron Hessburg, Missouri, ABD) that was 0.25 mm larger than the recipient bed, and the recipient bed was cut using a vacuum trephine. Graft sizes were determined according to the size of the recipient corneal pathology. The donor cornea was sutured to the recipient bed using 16 single 10-0 nylon suture. The anterior chamber was created using a balanced salt solution after surgery, and subconjunctival gentamicin (20 mg) and dexamethasone (4 mg) were administered postoperatively.

Donor preparation for DMEK or DALK

The donor cornea's endothelium was partially detached from the stroma, and the donor cornea was cut using a donor corneal punch. The Descemet membrane side of the endothelial complex was marked with a capital letter. After a full-thickness cut, the previously detached end of the endothelium was held with tying forceps, and entire endothelium was peeled from the donor stroma. The endothelial graft was transferred to the Optisol corneal storage medium. The endothelial tissue was either transplanted into a

DMEK recipient on the same day or stored in an eye bank for a delayed endothelial transplant. The DALK surgery was performed using the remaining stroma.

DALK procedure

Under general or retrobulbar anesthesia, after marking the geometric center of cornea, the corneal stroma was incised using an adjustable trephine (Moria, Antony, France), and 80–90% of the thinnest measured CT that was obtained from corneal topographic imaging and the incised recipient bed was stained using trypan blue. A blunt probe was inserted at the base of the trephination and advanced centripetally while maintaining the depth that was achieved with trephination. Then, a 30G needle on a 5-cc injector with air inside was bent to 80° from its proximal 2/3 while the needle was in the bevel-down position. The needle was advanced through the stroma in close proximity to the Descemet membrane until the marked center of cornea. Air was injected carefully to separate the strands using the air bubbles in the stromal bed. A large bubble was formed. A corneal side port was created using a 20G MVR knife, and carbachol (Miostat, Alcon, Belgium) was injected intracamerally after removing a small amount of aqueous humor to provide miosis. The anterior stroma was dissected and removed in a lamellar manner, and a 20G MVR was used to open the bubble. Viscoelastic material was injected through a slit to carefully excise the remaining stroma. Blunt scissors were used to enlarge the slit, and corneal scissors were used to complete the excision of the deep corneal stroma. The recipient bed was then thoroughly irrigated to remove all viscoelastic and debris. The donor anterior lamellar graft was sutured onto the recipient bed with 16 interrupted 10-0 nylon sutures.

DMEK procedure

Under general or local anesthesia, four paracentesis sites at 2, 4, 6, and 10 o'clock limbus and a temporal corneal incision were created, and the anterior chamber was slowly filled with air using an anterior chamber maintainer. The disorganized central epithelium was stripped and removed. Descemetorhexis was performed by removing the central 8 mm of dysfunctional corneal endothelium using a reverse Sinskey hook. A peripheral iridotomy was created to prevent pupillary block using an anterior vitrectomy probe. The Descemet membrane endothelium complex scroll (DE) from the donor cornea was stained with trypan blue and placed into a custom-made injector. The DE complex was injected into the anterior chamber, and the main corneal incision was sealed using a 10-0 nylon suture. The DE complex was unfolded carefully after making a shallow anterior chamber. A sulfur hexafluoride (SF6) 20% bubble was injected to fill 80–90% of the anterior chamber to ensure adhesion of the DE complex to the recipient cornea. The corneal mark was checked for the correct position of the DE complex. Postoperatively, the patient was kept in the supine position for at least 30 min and was then transferred to his or her bed.

Postoperative follow-up

In the postoperative period, topical 1% prednisolone acetate (Pred Forte, Allergan, Dublin, Ireland) was applied eight times a day in PK patients and six times a day in DALK and DMEK patients. After 1 week, use of these drops was adjusted according to the ocular surface and the graft status using postoperative controls. Dosing of prednisolone was reduced for 6–12 months. Moxifloxacin ophthalmic drops (Vigamox 0.5%; Alcon) were applied five times a day during the first week for all patients. Preservative-free artificial tears were prescribed to be used for at least 1 month postoperatively. Loose and ruptured sutures were removed as soon as they were detected.

Statistical analysis

All statistical analyses were performed using SPSS 20.0® for Windows (IBM Corporation, Armonk, NY). Descriptive statistics included the mean ± standard deviation (SD), percentage, minimum (min), and maximum (max) for normally distributed variables. Distribution of variables was measured with Kolmogorov–Smirnov test. For quantitative analysis, the dependent-sample *t*-test was used for normally distributed variables, and the Wilcoxon signed-rank test was used when the measurements did not fit the normal distribution. To compare the measurements between groups, Kruskal–Wallis test was performed and *post hoc* test Tukey's B was used to compare the means between the groups. The Pearson correlation analysis was used for normally distributed variables, and the Spearman correlation analysis was used when the measurements did not fit the normal distribution. Multivariate linear regression analysis was

Table 1. The preoperative and postoperative sixth hour IOP and 24th hour, first week and first month BCVA, IOP, ACD, corneal thickness, K1, K2, and Kaverage values of all patients.

	Preoperative	Postoperative			
		6th hour	24th hour	First week	First month
BCVA (decimal)	0.057 ± 0.079 (0.001–0.4)		0.071 ± 0.08 (0.001–0.4)	0.13 ± 0.15 (0.001–0.7)	0.22 ± 0.21 (0.001–0.8)
IOP (mmHg)	14.9 ± 2.6 (10–25)	27.8 ± 9.7 (12–54)	20.67 ± 6.43 (10–34)	17.35 ± 6.3 (10–38)	16.77 ± 6.52 (8–39)
ACD (mm)	3.86 ± 0.47 (2.67–4.55)		3.51 ± 0.86 (1.99–5.17)	3.53 ± 0.55 (2.43–4.56)	3.73 ± 0.51 (2.86–4.1)
Corneal thickness (μ)	424.74 ± 181.63 (207–906)		591.67 ± 133.77 (324–967)	533.71 ± 53.54 (447–643)	509.29 ± 49.03 (406–602)
K1	53.04 ± 9.28 (38.87–70.17)		44.18 ± 6.73 (20.97–46.29)	38.08 ± 8.23 (13.36–45.58)	39.14 ± 7.19 (16.71–45.53)
K2	57.80 ± 9.79 (44.18–72.25)		44.59 ± 5.25 (30.94–56.84)	44.65 ± 6.44 (29.7–56.8)	44.29 ± 5.86 (29.98–59.22)
Kaverage	55.13 ± 9.41 (41.36–70.49)		41.31 ± 5.89 (25.64–48.74)	40.59 ± 7.36 (21.09–48.74)	41.38 ± 6.36 (21.46–49.48)

ACD, anterior chamber depth; BCVA, best corrected visual acuity; IOP, intraocular pressure.

performed to evaluate the relationship between corneal parameters, ACD, and IOP. A *p*-value less than 0.05 was considered to be significant.

Results

The study included 53 eyes from 53 participants [26 females (49.1%), 27 males (50.9%)], and the patients' mean age was 50.4 ± 21.4 (11–83) years. In total, 24 patients (45.3%) had involvement of the right eye, while 29 patients (54.7%) showed involvement of the left eye. Moreover, 6 patients (11.3%) were aphakic, 25 patients (47.2%) were phakic, and 22 patients (41.5%) had a posterior chamber intraocular lens (IOL). All aphakic patients were in the PK group. One of the PK patients (4.5%) had anterior synechiae and one of the PK patients (4.5%) had posterior synechiae preoperatively. Two patients in the PK group and two patients in the DMEK group had glaucoma (four patients overall, 7.5%), which was controlled by medication, and two patients (3.8%) in the PK group had low-risk ocular hypertension (OHT) that did not require treatment preoperatively.

Overall, 22 (41.5%) patients underwent PK, 12 (22.6%) patients underwent DALK, and 19 (35.8%) patients underwent DMEK. Seven (31.8%) PK patients had a corneal scar, one (4.5%) patient had corneal dystrophy, five (22.7%) patients had corneal ectasia, five (22.7%) patients had bullous keratopathy, and four (18.2%) patients had graft rejection. All DALK procedures were performed due to keratoconus, and all DMEK surgeries were performed due to Fuchs' corneal dystrophy. The mean graft diameter was 7.79 ± 0.29 (7.25–8.50) mm. Two patients (10.5%) in DMEK group underwent rebubbling at postoperative Day 1, and measurements were started after rebubbling.

The preoperative values and postoperative hour 24, week 1, and month 1 values for BCVA, IOP, ACD, CT, K1, K2, and Kaverage, and IOP at hour 6 for all patients are presented in Table 1.

Overall, 40 (75.5%) patients at postoperative hour 6, 24 (45.3%) patients at postoperative hour 24, 13 (24.5%) patients at postoperative week 1, and eight (15.1%) patients at postoperative month 1 had an IOP that was greater than 21 mmHg. Antiglaucoma medications were initiated in six (27.3%) patients in the PK group, three (25%) patients in the DALK group, and four (21.1%) patients in DMEK group. The

mean time for initiating medication was 10.92 ± 9.83 (2–30) days, and the mean IOP was 29.38 ± 5.07 (22–39) mmHg when medications were initiated. The mean number of antiglaucoma medications that were used at honth 1 was 1.32 ± 0.6 (1–3). One antiglaucoma medication was added for one patient who had preoperative glaucoma and who had been using two antiglaucoma medications preoperatively when their IOP increased to 26 mmHg at postoperative week 1. There were no statistically significant differences in postoperative IOP changes at hours 6 and 24, week 1, and month 1 between patients with and without preoperative glaucoma or OHT ($p > 0.05$ for each). None of our patients needed glaucoma surgery, and postoperative pupil block did not occur in any patient during follow-up.

Postoperative IOP values were analyzed according to an increase above 5 mmHg, which was compared to the preoperative IOP. The results for patients with an increase above 5 mmHg were as follows: 20 (83.3%) patients in the PK groups, 8 (66.7%) patients in the DALK group, and 14 (73.7%) patients in the DMEK group at postoperative hour 6; 15 (62.5%) patients in the PK groups, 7(58.3%) patients in the DALK group, and 9 (47.4%) patients in the DMEK group at postoperative hour 24; 7 (29.2%) patients in the PK groups, 1 (8.3%) patients in the DALK group, and 4 (21.1%) patients in the DMEK group at postoperative week 1; and 7 (29.2%) patients in the PK groups, no patients in the DALK group, and 4 (21.1%) patients in the DMEK group at postoperative month 1. When the frequency difference between the groups was evaluated, there was no statistically significant difference ($p > 0.05$ for each).

When the IOP, corneal parameters, and ACD were compared between the three types of surgeries, the IOP at postoperative week 1 in the PK group was significantly higher than the DALK and DMEK groups ($p = 0.021$). However, there was no significant differences in IOP values at hours 6 and 24, and month 1 between the keratoplasty types ($p = 0.237$, $p = 0.165$, $p = 0.404$, respectively). When week 1 and month 1 corneal parameters were evaluated, K1 and Kaverage values were significantly lower in the PK group compared to the DMEK group ($p = 0.031$, $p = 0.041$). ACD values were significantly higher in the DALK group preoperatively and in the DMEK group at postoperative hour 24, week 1, and month 1 ($p = 0.027$, $p < 0.05$, $p = 0.044$, $p = 0.049$, respectively; Table 2). There was no significant difference in the time of antiglaucoma medication initiation and the number of medications between the three keratoplasty techniques ($p = 0.672$, $p = 0.639$; Table 2).

The difference in IOP and ACD values between preoperative and postoperative follow-ups was evaluated separately in three types of surgery. The difference between the IOP preoperatively and 6 h postoperatively and between the IOP preoperatively and 24 h postoperatively were statistically significant in the three types of surgery ($p < 0.05$ for each). The difference between preoperative and postoperative week 1 IOP was statistically significant only in the PK group ($p = 0.023$), and the difference between IOP preoperatively and 1 month postoperatively was not significant in any group ($p > 0.05$ for each). There was a significant increase in ACD in the DMEK group and a significant decrease in the DALK and PK groups for all postoperative follow-ups compared with preoperative values ($p > 0.05$ for each; Table 3).

Multivariate linear regression analysis revealed that postoperative early IOP values were not correlated with ACD, CT, or K values in any group (Table 4).

Discussion

Increased IOP is an important clinical problem after corneal transplantation. Uncontrolled postoperative IOP is a major risk factor that causes graft failure after PK.[5] The rate of IOP increase after PK is higher than after lamellar keratoplasties.[3] Different studies have shown variable incidences of elevated IOP after different keratoplasty techniques as follows: 9–37% following PK;[5–8] 6.5–24% following DMEK;[9–11] and 1.3–36.1% following DALK.[12–14] This study aimed to provide new insight into the early changes in IOP in three different corneal transplantation surgeries (PK, DALK, and DMEK) and the effect of corneal parameters and ACD on IOP changes. To the best of our knowledge, this is the first study that compares early changes in IOP in three different keratoplasty techniques.

There are many possible causes of increased IOP after corneal transplantation surgery, but the causes may be different according to the type of surgery. Causes, such as structural changes in the angle anatomy after graft and suture placement,

Table 2. The preoperative and postoperative BCVA, IOP, ACD, corneal thickness, K1, K2, and Kaverage values differences between PK, DALK, and DMEK groups.

	PK	DALK	DMEK	*p*
Postoperative BCVA				
Preoperative	0.029 ± 0.042 (0.001–0.16)	0.065 ± 0.83 (0.01–0.3)	0.084 ± 0.101 (0.01–0.3)	0.075
First week	**0.067 ± 0.058 (0.001–0.2)**	0.136 ± 0.2 (0.08–0.7)	**0.2 ± 0.17 (0.001–0.5)**	**0.015**
First month	**0.143 ± 0.154 (0.001–0.7)**	0.217 ± 0.137 (0.05–0.4)	**0.361 ± 0.256 (0.016–0.8)**	**0.006**
IOP (mmHg)				
Preoperative	15.5 ± 3.46 (10–25)	14.17 ± 0.94 (12–16)	14.68 ± 2.00 (10–19)	0.327
6th hour	30.5 ± 9.16 (17–53)	25.18 ± 11.99 (12–54)	26.37 ± 8.63 (15–44)	0.237
24th hour	22.5 ± 6.62 (10–34)	20.40 ± 5.97 (11–27)	18.68 ± 6.14 (10–30)	0.165
First week	**20.65 ± 5.82 (12–35)**	15.70 ± 4.45 (12–27)	15.26 ± 6.54 (10–38)	**0.04**
First month	17.67 ± 5.53 (10–33)	14.11 ± 3.02 (10–19)	15.88 ± 5.76 (10–32)	0.404
ACD (mm)				
Preoperative	3.70 ± 0.54 (2.67–4.30)	**3.95 ± 0.34 (3.43–4.45)**	3.58 ± 0.45 (3.01–4.18)	**0.027**
24th hour	2.93 ± 0.67 (1.99–4.47)	3.12 ± 0.46 (2.53–4.03)	**4.12 ± 0.77 (2.40–5.17)**	**<0.05**
First week	3.16 ± 0.54 (2.43–3.94)	3.35 ± 0.33 (3.00–4.03)	**3.90 ± 0.50 (3.31–4.56)**	**0.044**
First month	3.19 ± 0.41 (2.69–3.76)	3.36 ± 0.22 (3.01–4.11)	**3.85 ± 0.56 (2.86–4.51)**	**0.049**
Corneal thickness (μ)				
24th hour	624.91 ± 135.4 (378–821)	535.16 ± 127.96 (324–689)	587.66 ± 135.34 (325–967)	0.42
First week	537.67 ± 45.03 (466–617)	553.00 ± 90.50 (462–643)	523.33 ± 53.02 (447–612)	0.7
First month	501.75 ± 37.17 (445–537)	551.50 ± 71.41 (501–602)	505.86 ± 57.14 (406–579)	0.454
K1				
First week	**33.14 ± 10.31 (13.36–45.51)**	43.01 ± 0.69 (42.57–43.80)	41.54 ± 3.28 (37.15–45.58)	**0.031**
First month	35.71 ± 8.68 (16.71–44.76)	38.90 ± 5.08 (35.31–42.49)	43.12 ± 3.35 (35.69–45.53)	0.135

(Continued)

Table 2. (Continued)

	PK	DALK	DMEK	*p*
K2				
First week	43.01 ± 8.52 (29.69–52.08)	51.18 ± 5.03 (47.21–56.84)	44.33 ± 2.39 (41.72–49.04)	0.153
First month	42.49 ± 5.89 (29.98–48.52)	52.55 ± 9.43 (45.88–59.22)	43.99 ± 3.01 (37.31–59.22)	0.085
Kaverage				
First week	**36.52 ± 9.39 (21.09–48.57)**	46.65 ± 1.81 (45.44–48.74)	42.85 ± 7.36 (39.55–46.42)	**0.041**
First month	38.64 ± 7.79 (21.46–46.56)	44.69 ± 6.77 (39.91–49.48)	43.56 ± 3.19 (36.48–45.97)	0.253
The time of antiglaucomatous medication initiation (days)	11.5 ± 11.11 (2–30)	4.67 ± 2.51 (2–7)	14.75 ± 10.01 (5–30)	0.672
The number of medication initiated	1.38 ± 0.52 (1–2)	1 ± 0 (1–1)	1.4 ± 0.89 (1–3)	0.639

ACD, anterior chamber depth; BCVA, best corrected visual acuity; DALK, deep anterior lamellar keratoplasty; DMEK, descemet membrane endothelial keratoplasty; IOP, intraocular pressure; PK, penetrating keratoplasty.

peripheral anterior synechiae, inflammation, pupillary block, iritis, hemorrhage, vitreous in the angle, malignant glaucoma, retained viscoelastic, and long-term use of topical corticosteroid drops may increase the IOP after corneal transplantation surgery.[1,3,14] Significant distortion of the angle, both anterior and posterior to the trabecular meshwork (TM), and the angle closure due to significant structural changes are the most frequent causes of increased IOP after PK.[1] Long and tight sutures that cause corneal edema and distortion of the TM anteriorly cause distortion anterior to the angle.[1,15] Losing the fixation afforded by the ciliary body-lens system after keratoplasty causes the collapse of the angle posteriorly.[1,15] Larger grafts may cause more angle distortion due to sutures.[16] Peripheral anterior synechiae secondary to PK, which occur at the time of surgery and slowly increase over time, lead to progressive angle closure glaucoma.[1] Although steroid use and angle closure may be the reasons for the increase in IOP after DMEK, complications due to air injection, such as TM damage, that is caused by an interoperative high-pressure air bubble, postoperative pupillary block that is caused by an air bubble, repeated air injection due to donor tissue dislocation, air migration posterior to the iris, and angle distortion by dislocated donor tissue may also contribute to the increase in IOP.[1,17] Causes of IOP elevation after DALK may include pupil

Table 3. The significance of the difference in IOP and ACD values in follow-ups in three types of surgery.

	PK	DALK	DMEK
IOP changes			
Preop–postop 6th hour	**<0.05**	**0.014**	**<0.05**
Preop–postop 24th hour	**<0.05**	**0.013**	**0.018**
Preop–postop first week	**0.023**	0.332	0.708
Preop–postop first month	0.157	0.685	0.422
ACD changes			
Preop–postop 24th hour	**0.015**	**<0.05**	**0.042**
Preop–postop first week	**0.016**	**0.045**	**0.048**
Preop–postop first month	**0.011**	**0.03**	**0.04**

ACD, anterior chamber depth; DALK, deep anterior lamellar keratoplasty; DMEK, Descemet membrane endothelial keratoplasty; IOP, intraocular pressure; PK, penetrating keratoplasty.

Table 4. Multivariate linear regression analysis of corneal parameters, ACD and IOP.

	24th hour IOP						First week IOP						First month IOP					
	PKP		DALK		DMEK		PKP		DALK		DMEK		PKP		DALK		DMEK	
	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*	β Coefficient	*p*
ACD	0.013	0.620	0.005	0.998	−1.964	0.504	0.172	0.986	−5.312	0.205	−1.481	0.368	−2.456	0.294	1.520	0.596	1.084	0.705
K1	2.321	0.276	0.386	0.780	1.118	0.629	1.473	0.788	0.766	0.708	0.572	0.881	−1.851	0.542	−1.990	0.324	−1.994	0.276
K2	0.776	0.304	0.491	0.593	1.646	0.787	0.672	0.656	0.264	0.715	0.508	0.867	−0.570	0.422	−2.254	0.421	2.608	0.300
Kaverage	−1.617	0.297	−0.407	0.403	−1.143	0.689	−1.862	0.781	−0.932	0.717	−1.324	0.872	1.471	0.515	0.705	0.385	1.234	0.497
CT	0.189	0.22	0.015	0.655	−0.004	0.863	0.029	0.765	0.012	0.768	0.044	0.694	0.096	0.263	0.009	0.752	0.001	0.974

ACD, anterior chamber depth; CT, corneal thickness; DALK, deep anterior lamellar keratoplasty; DMEK, descemet membrane endothelial keratoplasty; IOP, intraocular pressure; PK, penetrating keratoplasty.

block by air, a swollen graft, and corticosteroid response, but the angle distortion is minimal because there is no graft–host junction or shallowing of the anterior chamber.[14] A corticosteroid-associated increase in IOP is due to the inhibition of extracellular matrix degradation in the TM and the associated increase in outflow resistance.[18] Although the timing of the increase in IOP was reported to be mostly within 3–6 weeks after topical steroid use, an increase in IOP has also been reported as early as postoperative week 1.[19–21] An advantage of DALK over PK is earlier discontinuation of topical corticosteroids.[22]

The increase in IOP is theoretically lower after lamellar procedures, such as DMEK and DALK, which affect the structure of the angle minimally, preserve the structural integrity of the cornea, and reduce corneal edema because there are fewer sutures compared to PK.[1,10] In contrast to PK, corneal anatomy may remain relatively the same after DMEK due to the absence of sutures and additional stroma in terms of corneal curvature (CC) and CT.[23] Sharma and Varajjant observed significantly higher IOP in the PK group compared with the Descemet striping endothelial keratoplasty (DSEK) group, which was technically similar to DMEK.[24,25] Sandhu *et al.*[26] observed the same rate of increase in IOP in the PK and DSEK groups, but 50% of the PK group and 25% of the DMEK group were patients with previous glaucoma, and most had undergone glaucoma surgery before keratoplasty. In our study, the rate of patients with previous glaucoma was 3.8% in the PK group and 3.8% in the DMEK group, and none of them had undergone glaucoma surgery before keratoplasty. Sharma *et al.*[25] evaluated the difference in the IOP increase after DSEK and after PK, and they observed a significantly higher increase in IOP in the PK group at postoperative week 1, 4, 8, and 12. Stanzel *et al.*[17] observed the increase in IOP in DMEK patients at postoperative hours 1, 2, 3, 5, 12, and 24 and week 1, and they reported that the increase in IOP was significantly higher than preoperative values at hours 1 and 2 and then decreased to preoperative values at other follow-up visits. Borderie *et al.*[27] compared the 5-year outcomes in DALK and PK patients who had increased IOP, and they reported 6% in DALK group and 26% in PK group, respectively. Zhang *et al.*[13] reported that the incidence of an increase in IOP was 1.3% and 46.2%, respectively, in DALK and PK patients who were followed for more than 5 years. Huang *et al.*[14] reported an increase in IOP at a rate of 36.1%,

which was seen at an average of 48.9 days after DALK, but they also reported that this increase was transient and there was a low incidence of glaucoma at 5 years. In this study, when preoperative and postoperative IOP changes were evaluated, IOP values measured at postoperative hours 6 and 24 were significantly higher than the preoperative IOP in three groups. The IOP values at postoperative hour 6 were approximately 15 mmHg higher than the preoperative IOP in the PK group, 11 mmHg in the DALK group, and 12 mmHg in the DMEK group; at postoperative hour 24, IOP values were approximately 7 mmHg higher than the preoperative IOP in the PK group, 6 mmHg higher in the DALK group, and 4 mmHg higher in the DMEK group; however, there was no statically significant difference between groups. The IOP changes between preoperative and postoperative month 1 were not statically significant in the three groups while the change between preoperative and postoperative week 1 was significant only in the PK group. In addition, we found a significantly higher increase in the IOP in the PK group compared to the DALK and DMEK groups at week 1, but there was no significant difference in the IOP increase between groups at hours 6 and 24, and month 1. This result may indicate that the increase in IOP remains at week 1 after PK, and that it may decrease to preoperative values at month 1 after PK and week 1 after DALK and DMEK. Although DMEK has a potential risk of an early increase in IOP because of an air bubble in the anterior chamber, our study showed that PK has more risk in the early period.

Sandhu *et al.* observed a 30% increase in IOP above baseline and a rate of 39% in both PK and DSEK groups in their 1-year follow-up study. A higher percentage of patients with preoperative glaucoma were included in their study compared to our study.[26] Stanzel *et al.*[17] observed an IOP above 30 mmHg postoperatively at a rate of 13% in the first 2 h and no increase at hours 3, 5, 12, and 24 and week 1 in DMEK patients. We evaluated the frequency of postoperative IOP increase that was more than 5 mmHg compared to the preoperative IOP. We found that the frequency of this increase was higher in PK groups in all postoperative follow-ups but the frequency difference between the groups was not statically significant.

A higher incidence of postoperatively increased IOP was also reported in eyes with preexisting glaucoma that underwent corneal transplantation surgery.[1] Although the number of patients with previous glaucoma/OHT was low, we did not find any difference in the increase in IOP between patients who did and did not have preexisting glaucoma or OHT in the early period after three types of surgery.

Astigmatism, CC, corneal hysteresis, and the presence of sutures may affect IOP measurement after keratoplasty.[3] Although Goldmann applanation tonometry (GAT) is the gold standard in IOP measurement, its use is limited, especially in the early period after keratoplasty.[28] The Tono-Pen has advantages, such as the possibility for its use on abnormal corneas due to its small applanation area (1.00 mm), disposable covers that prevent contamination, a digital readout that makes user bias minimal, good repeatability, and it is portable and easy to use.[29]

Tono-Pen showed that IOP may be higher in thicker and lower in thinner healthy corneas.[30] Salvetat *et al.*[31] compared iCare and GAT measurements in both healthy and post-keratoplasty eyes, and they found that CT significantly affected both GAT and iCare IOP measurements in healthy corneas, but not in post-keratoplasty eyes, which they evaluated in PK, DSEK, and DALK patients. In addition, the increased CT did not falsely elevate the IOP, which was measured using GAT both post-DSEK[24,32,33] and post-DALK.[31,34] Maier *et al.*[9] reported a significant correlation between non-contact tonometer (NCT), iCare, and CT at months 1 and 3 postoperatively in DMEK patients, but there was no correlation between CT, GAT, and Dynamic Contour Tonometry (DCT). These results may indicate that the correlation depends on the type of IOP measurement device. Hugo *et al.*[2] claimed that the CT measurements were less reliable after lamellar keratoplasty due to interfaces and changes in the corneal shape. We evaluated the correlation between IOP that was measured using a Tono-Pen and CT, and there was no correlation between them in the three types of surgery.

Salvetat *et al.*[31] showed that the CC was inversely related to IOP, which were measured using iCare in only post-PK eyes but not in post-DSEK and DALK, and it was not related to the CC when it was measured using GAT in any group. Jóhanessen *et al.*[35] found a positive correlation between IOP that was measured using GAT, DCT, and CC. It was also reported that the mean keratometry results were not correlated with IOP measurements after DALK.[1,34] Several studies have reported no statistically significant

relationship between CC and IOP in normal eyes.[35–37] We found that week 1 IOP values were higher and week 1 K1 and Kaverage values were lower in the PK group. However, there were no significant correlations between IOP and K values. We think that corneal parameters may be unreliable due to reflex tear secretion that was caused by corneal irritation, graft edema, surface irregularity due to disruption of the mechanical integrity, remodeling of corneal tissue, variable graft-host interface mechanics, and suture placement, especially in the early postoperative period.

ACD and keratometry values were reported to decrease significantly after PK due to tightened sutures, which straightened the cornea, and this effect increases with increased suture tension.[4] Onuchi *et al.*[38] reported a significant increase in ACD and a posterior iris shift in patients at months 1, 3, 6, and 12 after DMEK surgery, which explained the ACD increase using the iris shift due to gas tamponade. ACD is known to increase depending on coning of the cornea in patients with keratoconus.[39] In our study, the preoperative diagnosis of all DALK patients and five (22.7%) PK patients were keratoconus. We also found a significant decrease in postoperative week 1 and month 1 after ACD values in DALK and PK patients and a significant increase in DMEK cases. However, there were no correlations between ACD and IOP in any group.

The limitations of our study are the lack of long-term results, lack of corneal biomechanics evaluation, and small number of patients in the DALK and DMEK groups. More frequent use of postoperative steroid in the PK group may have affected IOP. Postoperative IOP in the early stage may be dependent on the degrees of intraocular inflammation; prospective studies with flaremeter can be useful to clarify this issue. One of the other limitations of our study is that the operations were performed by five different experienced surgeons. They performed the surgeries using the same techniques, but there may be minor differences between each surgeon. All aphakic eyes and one patient with preoperative anterior synechiae and one patient with preoperative posterior synechiae were in the PK group and these conditions are known to predispose to glaucoma.

Conclusion

In conclusion, IOP may increase in all types of keratoplasty during the first hours after surgery, but the possibility of IOP increasing is higher with PK than with DALK and DMEK, and PK has a risk of high IOP values longer in the early postoperative period. There was no difference between the three types of keratoplasty in terms of an IOP increase in postoperative month 1. PK patients should be followed more carefully during postoperative week 1 to check for an increase in IOP. Although limited patient numbers, according to our results, there was no correlation between ACD, CT, K values, and IOP in any group. Prospective, comparative studies with longer follow-up periods and with more patients are needed.

Author contributions

Gulsah Gumus: Data curation; Formal analysis; Writing – original draft.

Cigdem Altan: Project administration; Supervision; Writing – review & editing.

Yusuf Yildirim: Supervision; Writing – review & editing.

Nilay Kandemir Beşek: Data curation; Visualization.

Selim Genç: Data curation; Formal analysis; Validation.

Ahmet Kirgiz: Data curation; Formal analysis; Validation; Visualization.

Gonul Karatas Durusoy: Data curation; Software; Writing – original draft.

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Conflict of interest statement

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Ethics statement

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References

1. Banitt M and Lee RK. Management of patients with combined glaucoma and corneal transplant surgery. *Eye* 2009; 23: 1972–1979.
2. Hugo J, Granget E, Ho Wang Yin G, *et al*. Intraocular pressure measurements and corneal biomechanical properties using a dynamic Scheimpflug analyzer, after several keratoplasty techniques, versus normal eyes. *J Fr Ophtalmol* 2018; 41: 30–38.
3. de Padua Soares Bezerra B, Chan E, Chakrabarti R, *et al*. Intraocular pressure measurement after corneal transplantation. *Surv Ophthalmol* 2019; 64: 639–646.
4. Ort A, Gunes A, Kandemir B, *et al*. Evaluation of the cornea and anterior chamber morphologic changes after penetrating keratoplasty in patients with keratoconus. *Eye Contact Lens* 2017; 43: 236–239.
5. Huber KK, Maier AK, Klamann MK, *et al*. Glaucoma in penetrating keratoplasty: risk factors, management and outcome. *Graefes Arch Clin Exp Ophthalmol* 2013; 251: 105–116.
6. Franea ET, Araeri ES and Roche FJ. A study of glaucoma after penetrating keratoplasty. *Cornea* 2002; 21: 284–288.
7. Hemanth Raj MN, Bhanushree G, Hlinaykor RM, *et al*. Preoperative risk factors and incidence of glaucoma after penetrating keratoplasty. *Int J Clin Trials* 2014; 1: 55–61.
8. Irvine AR and Kaufman HE. Intraolar pressure following penetrating keratoplasty. *Am J Ophthalmol* 1969; 68: 835–844.
9. Maier AK, Gundlach E, Pahlitzsch M, *et al*. Intraocular pressure measurements after descemet membrane endothelial keratoplasty. *J Glaucoma* 2017; 26: 258–265.
10. Naveiras M, Dirisamer M, Parker J, *et al*. Causes of glaucoma after descemet membrane endothelial keratoplasty. *Am J Ophthalmol* 2012; 153: 958–966.
11. Deng SX, Lee WB, Hammersmith KM, *et al*. Descemet membrane endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. *Ophthalmology* 2018; 125: 295–310.
12. Han DC, Mehta JS, Por YM, *et al*. Comparison of outcomes of lamellar keratoplasty and penetrating keratoplasty in keratoconus. *Am J Ophthalmol* 2009; 148: 744e741–751.
13. Zhang YM, Wu SQ and Yao YF. Long-term comparison of full-bed deep anterior lamellar keratoplasty and penetrating keratoplasty in treating keratoconus. *J Zhejiang Univ Sci B* 2013; 14: 438–450.
14. Huang OS, Mehta JS, Htoon HM, *et al*. Incidence and risk factors of elevated intraocular pressure following deep anterior lamellar keratoplasty. *Am J Ophthalmol* 2016; 170: 153–160.
15. Zimmerman T, Olson Waltman S and Kaufman H. Transplant size and elevated intraocular pressure. *Arch Ophthalmol* 1978; 96: 2231–2233.
16. Sharma N, Jain M, Sehra SV, *et al*. Outcomes of therapeutic penetrating keratoplasty from a tertiary eye care centre in northern India. *Cornea* 2014; 33: 114–118.
17. Stanzel TP, Ersoy L, Sansanayudh W, *et al*. Immediate postoperative intraocular pressure changes after anterior chamber air fill in descemet membrane endothelial keratoplasty. *Cornea* 2016; 35: 14–19.
18. Kersey JP and Broadway DC. Corticosteroid-induced glaucoma: a review of the literature. *Eye (Lond)* 2006; 20: 407–416.
19. Armaly MF. Effect of corticosteroids on intraocular pressure and fluid dynamics. I. The effect of dexamethasone in the normal eye. *Arch Ophthalmol* 1963; 70: 482–491.
20. Armaly MF. Effect of corticosteroids on intraocular pressure and fluid dynamics. II. The effect of dexamethasone in the glaucomatous eye. *Arch Ophthalmol* 1963; 70: 492–49930.
21. Becker B and Mills DW. Corticosteroids and intraocular pressure. *Arch Ophthalmol* 1963; 70: 50031–50507.
22. Reinhart WJ, Musch DC, Jacobs DS, *et al*. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty a report by the american academy of ophthalmology. *Ophthalmology* 2011; 118: 209–218.
23. Rudolph M, Laaser K, Bachmann BO, *et al*. Corneal higher-order aberrations after Descemet's membrane endothelial keratoplasty. *Ophthalmology* 2012; 119: 528–535.
24. Vajaranant TS, Price MO, Price FW, *et al*. Intraocular pressure measurements following Descemet stripping endothelial keratoplasty. *Am J Ophthalmol* 2008; 145: 780–786.
25. Sharma RA, Bursztyn LL, Golesic E, *et al*. Comparison of intraocular pressure post

penetrating keratoplasty vs Descemet's stripping endothelial keratoplasty. *Can J Ophthalmol* 2016; 51: 19–24.

26. Sandhu S, Petsoglou C, Grigg J, *et al*. Elevated intraocular pressure in patients undergoing penetrating keratoplasty and descemet stripping endothelial keratoplasty. *J Glaucoma* 2016; 25: 390–396.
27. Borderie VM, Sandali O, Bullet J, *et al*. Long-term results of deep anterior lamellar versus penetrating keratoplasty. *Ophthalmology* 2012; 119: 249–255.
28. Dielemans I, Vingerling JR, Hofman A, *et al*. Reliability of intraocular pressure measurement with the Goldmann applanation tonometer in epidemiological studies. *Graefes Arch Clin Exp Ophthalmol* 1994; 232: 141–144.
29. Bhartiya S, Bali SJ, James M, *et al*. Test retest variability of TonoPen AVIA. *Indian J Ophthalmol* 2013; 61: 129–131.
30. Bhartiya S, Bali SJ, Sharma R, *et al*. Comparative evaluation of TonoPen AVIA, Goldmann applanation tonometry and non-contact tonometry. *Int Ophthalmol* 2011; 31: 297–302.
31. Salvetat ML, Zeppieri M, Miani F, *et al*. Comparison of iCare tonometer and Goldmann applanation tonometry in normal corneas and in eyes with automated lamellar and penetrating keratoplasty. *Eye (Lond)* 2011; 25: 642–650.
32. Yi K, Bae G, Kong M, *et al*. Intraocular pressure measured with Goldmann, noncontact, Schiøtz, and dynamic contour tonometry after DSEK. *Cornea* 2013; 32: 1089–1093.
33. Clemmensen K and Hjortdal J. Intraocular pressure and corneal biomechanics in Fuchs' endothelial dystrophy and after posterior lamellar keratoplasty. *Acta Ophthalmol* 2014; 92: 350–354.
34. Ceruti P, Morbio R, Marraffa M, *et al*. Comparison of dynamic contour tonometry and Goldmann applanation tonometry in deep lamellar and penetrating keratoplasty. *Am J Ophthalmol* 2008; 145: 215–221.
35. Jóhannesson G, Hallberg P, Eklund A, *et al*. Pascal, ICare and Goldmann applanation tonometry–a comparative study. *Acta Ophthalmol* 2008; 86: 614–621.
36. Eysteinsson T, Jonasson F, Sasaki H, *et al*. Central corneal thickness, radius of the corneal curvature and intraocular pressure in normal subjects using non-contact techniques: Reykjavik Eye Study. *Acta Ophthalmol Scand* 2002; 80: 11–15.
37. Paranhos A Jr, Paranhos FR, Prata JA Jr, *et al*. Influence of keratometric readings on comparative intraocular pressure measurements with Goldmann, Tono-Pen, and noncontact tonometers. *J Glaucoma* 2000; 9: 219–223.
38. Onouchi H, Hayashi T, Shimizu T, *et al*. Anatomical changes in the anterior chamber volume after descemet membrane endothelial keratoplasty. *Cornea* 2020; 40: 690–695.
39. Rabinowitz YS. Keratoconus. *Surv Ophthalmol* 1998; 42: 297–319.