Trends in Keratoplasty procedures in the last 20 years at a tertiary referral center in Turkey: 2003 to 2023

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ABSTRACT

Purpose: The study aims to evaluate changing trends in corneal transplant indications and surgical techniques over the last 20 years in a tertiary clinic. Materials and Methods: Records of all corneal transplants performed between 2003 and 2023 were examined retrospectively. Those in the first 10 years were called group 1, and those in the last 10 years were called group 2. The patients demographic data, keratoplasty indications, and selected surgeries were compared between the two groups. Results: The grafts of 1300 eyes of 1149 patients were evaluated. The keratoplasty indications rates were similar in both groups, and the most common indication was keratoconus ($p>0.05$). The most frequently performed surgery in both groups was PKP. The difference between the two groups was significant in the surgeries selected according to indications. ($p<0.05$). In group 2, an increase in lamellar surgeries was observed. Conclusion: Although our surgical indications have not changed in the last 10 years, the surgical options chosen for these indications have changed. The rate of lamellar surgery has increased significantly, but penetrating keratoplasty is still the most preferred surgery.

Keywords: Keratoplasty indications, Penetrating keratoplasty, Lamellar keratoplasty.

INTRODUCTION

Keratoplasty is one of the oldest and most popular types of human tissue transplantation worldwide today. The first human corneal transplant was carried out by Austrian surgeon Eduard Zirm in 1905.[1] During penetrating keratoplasty (PKP), the full thickness of the cornea is removed and replaced with donor tissue. In recent years, lamellar surgeries, which involve replacing only the diseased layers of the cornea, have gained widespread use. Lamellar keratoplasty (LK) techniques have become increasingly popular, particularly because they reduce the disadvantages associated with full-thickness procedures, such as graft rejection, postoperative astigmatism, and prolonged recovery time. Additionally, lamellar surgery allows a single donor cornea to be used for more than one recipient. Anterior lamellar surgery offers advantages over PKP, including reduced risk of allograft rejection and less endothelial cell loss, as the recipient endothelium is preserved. However, it is technically more difficult, and the Descemet membrane may perforate.[2] Posterior lamellar surgery also has several advantages over PKP, including reduced postoperative astigmatism, preservation of corneal biomechanical stability, and faster visual rehabilitation. However, Descemet stripping automated endothelial keratoplasty (DSAEK) requires costly operating room equipment. Descemet membrane endothelial keratoplasty (DMEK) has a somewhat steep learning curve for the surgeon and affects intraoperative endothelial cell loss.[3]

In recent years, a number of comprehensive studies have reported varying keratoplasty indications across different geographic.[4-6] Indications in studies change over time due to factors such as demographic and socioeconomic differences between countries, technological advancements in keratoplasty techniques, and increased adoption of newer

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methods by surgeons. For example, in diseases affecting only the corneal endothelial layer, the use of DSAEK or DMEK surgery varies in different clinics depending on these variables.

We previously reported the changes in keratoplasty indications and techniques in our clinic between 1995 and 2014.[7] However, as the rate of lamellar keratoplasty procedures has increased in our clinic since that date, this study aimed to analyze the changes in surgical indications and techniques employed. The aim of this study is to evaluate the changes in keratoplasty techniques according to indications, re-keratoplasty rates, changes in lamellar surgery preferences, and graft transparency rates over the past decade.

MATERIALS AND METHODS

The records of patients who underwent corneal transplantation at the cornea unit of our tertiary referral center were retrospectively reviewed following approval by the institutional ethics committee (approval number: E-93471371-514.99). Before any procedures, informed consent was obtained from all patients, and all procedures adhered to the principles outlined in the Declaration of Helsinki.

The following variables were extracted from the patient files: The age at the time of surgery, gender, preoperative best-corrected visual acuity (BCVA), follow-up duration, number of keratoplasty procedures, year of surgery, indication for keratoplasty, type of keratoplasty technique, combined surgical procedures, and second and third keratoplasty interventions. Among patients who underwent re-keratoplasty, the reasons for surgery and preferred surgical techniques were evaluated.

Indications were categorized into nine main groups: keratoconus, bullous keratopathy (BK), graft failure, corneal dystrophy, corneal scarring, perforation or melting, pellucid marginal degeneration (PMD), keratoglobus, and other indications. Corneal dystrophies were subcategorized as macular, granular, lattice, Fuchs endotelial dystrophy, congenital hereditary endothelial dystrophy (CHED), and others. Corneal scars were classified by etiology: infectious keratitis, trauma, chemical injury, congenital, other, and unknown cause. Bullous keratopathies were grouped as pseudophakic, aphakic, post-glaucoma surgery, traumatic, congenital glaucoma, Cogan syndrome, and unknown causes.

Keratoplasty techniques were classified as PKP, Deep anterior lamellar keratoplasty (DALK), DMEK, Anterior lamellar keratoplasty (ALK), patch graft, and DSAEK. Combined surgeries performed concurrently with keratoplasty were also recorded. Graft transparency was evaluated at the final follow-up examination. All data were reported as counts and percentages.

To enable comparative statistical analysis, patients were divided into two groups based on the year of surgery: Group 1 (2003–2012), when penetrating keratoplasty was predominant; and Group 2 (2013–2022), when lamellar techniques became more commonly used. Demographic characteristics, indications, surgical techniques, combined surgery rates, and rates of second and third keratoplasties were statistically compared between the two groups .

Statistical analysis

Data were analysed using IBM SPSS Statistics 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The Kolmogorov-Smirnov test was employed to asssess normality of distribution. Categorical variables were expressed as frequencies and percentages, while continuous variables were reported as mean ± standard deviation. Pearson's Chi-square test was used to compare categorical variables between two groups. A p-value of < 0.05 was considered statistically significant.

RESULTS

In the study, grafts of 1300 eyes (998 unilateral, 151 bilateral) from 1149 patients followed in the Cornea department between 2003 and 2023 were evaluated. There were more males than females, 632 (55.1%) and 517 (44.9%) respectively. Demographic data are presented in Table 1. While there was no significant difference in age at the time of operation, gender, preoperative BCVA, and mean number of keratoplasty between the two groups, follow-up times were different. Indications for keratoplasty were similar in both groups, and the most common indication was keratoconus (Table 2). The most frequently performed surgery in both groups was PKP. However, in the group 2, the PKP rate decreased significantly while the DALK, DMEK and ALK

Table 1. *The demographic data of the patients*

	GROUP 1 (n=387)	GROUP 2 (n=913)	p
Sex n (%) FEMALE MALE	 178 (46) 209 (54)	 417 (45.7) 496 (54.3)	 0.915*
AGE (year)	41.51 ± 0.9	43.68 ± 0.63	0.073[a]
PREOPERATIVE BCVA (LogMar)	1.45 ± 0.01 (0.5- 1.6)	1.44 ± 0.01	0.854[a]
FOLLOW-UP TIME (year)	6.99 ± 4.69 (1-20)	4.01 ± 2.76 (1-11)	<0.01[a]
NUMBER OF KERATOPLASTIES	1.1± 0.39 (1-4)	1.15 ± 0.44 (1-5)	0.296[a]

BCVA: best-corrected visual acuity
[a] Mann-Whitney U test
* Pearson Chi-Square test

Table 2. *Indications for keratoplasty*

	GROUP 1 n (%)	GROUP 2 n (%)	P*
KERATOCONUS	136 (35.1)	305 (33.4)	0.546
BULLOUS KERATOPATHY Pseudophakic Aphakic Glaucoma surgery Trauma Congenital glaucoma Cogan syndrome unknown	57 (14.7) 39 (10.1) 8 (2.1) 3 (0.8) 0 0 1 (0.3) 0	159 (17.4) 110 (12.1) 8 (0.9) 9 (1) 6 (0.7) 1(0.1) 0 2 (0.2)	0.164
GRAFT FAILURE	8 (2.1)	40 (4.4)	0.052
DISTROPHY MCD GCD LCD FUCHS CHED OTHER	67 (17.3) 34 (8.8) 7 (1.8) 5 (1.3) 5 (1.3) 9 (2.3) 4 (1)	155 (17) 76 (8.3) 18 (2) 22 (2.4) 23 (2.5) 10 (1.1) 7 (0.7)	0.312
KORNEAL SCAR Keratitis Trauma Chemical Congenital Other Unkown	94 (24.3) 33 (8.5) 18 (4.7) 2 (0.5) 1 (0.3) 4 (1.1) 37 (9.6)	203 (22.2) 84 (9.2) 40 (4.4) 11 (1.2) 6 (0.7) 6 (0.7) 55 (6)	0.318
MELT / PERFORATION	24 (6.2)	40 (4.4)	0.271
PMD	1 (0.3)	5 (0.5)	
KERATOGLOBUS	0	1 (0.1)	
OTHER	0	5 (0.5)	

MCD: macular corneal distrophy, GCD: granular corneal distrophy, LCD: lattice corneal distrophy, CHED: congenital hereditary endothelial dystrophy, PMD: pellucid marginal degeneration
*Pearson Chi-Square test

rates increased. In group 1 and group 2, the re-keratoplasty rate was 11.1% and 13.3%, respectively (Table 3). Among combined procedures, scleral fixation and intraocular lens (IOL) implantation were the most frequently performed (Table 3). Surgical procedures according to indications were compared between the two groups (Figure 1, Table 4). In keratoconus, BK, dystrophy and scar, the PKP rate decreased in the group 2 compared to the group 1, whereas the lamellar surgery rates increased significantly ($p<0.05$). No statistically significant difference was found between the groups regarding indications for re-keratoplasty, with graft failure being the most common cause. An increase in DMEK rates is observed in group 2 among re-keratoplasty cases. At the final follow-up, the overall graft transparency rate was 82.4%.

DISCUSSION

In recent years, the increasing adoption of lamellar keratoplasty has led to greater variation in surgical approaches based on clinical indications. Numerous studies from various countries and regions have explored this topic.[4,5,8,9] Similar studies have previously been published from institutions in our country.[6] The analysis of the changing indications and surgical techniques for corneal transplantation in our clinic between 1995 and 2014 was previously shared in a study.[7] At that time, however, lamellar surgery was infrequently performed in our clinic and PKP remained the predominant technique. Since lamellar surgery has become more popular since 2013, this study reevaluated the evolving indications and surgical options. Keratoplasty indications may differ between countries depending on many factors such as patient demographics, sociocultural factors, geographical location, access to medical services, and eye banking status.[10] Furthermore, surgical preferences have shifted over time, especially with advancements in lamellar techniques.[4,8,11] In a recent systematic analysis, the most common indications for PKP were keratoconus in Europe, Africa, the Middle East, Australia, New Zealand and Central and South America, bullous keratopathy in

Table 3. *Keratoplasty and combined surgery rates between groups*

	GROUP 1 n (%)	GROUP 2 n (%)	TOTAL n (%)	P*
PKP	372 (96.1)	626 (68.6)	998 (76.8)	<0.001
DALK	3 (0.8)	126 (13.8)	129 (9.9)	<0.001
DMEK	0	103 (11.3)	103 (7.9)	<0.001
ALK	5 (1.3)	47 (5.1)	52 (4)	0.001
PATCH GRAFT	6 (1.6)	11 (1.2)	17 (1.3)	0.616
DSAEK	1 (0.3)	0	1 (0.1)	
RE-GRAFT	43 (11.1)	122 (13.4)	165 (12.7)	0.265
COMBINED SURGERY Phacoemulsification Scleral fixation IOL Lens extraction IOL extraction Glaucoma surgery PPV	19 (4.7) 3 (0.8) 10 (2.6) 6 (1.6) 0 0 0	55 (6) 9 (1) 24 (2.6) 19 (2.1) 1 (0.1) 1 (0.1) 2 (0.2)	74 (5.6)	0.326
Second Keratoplasty PKP DALK DMEK DSAEK	 40 (93) 0 2 (4.7) 1 (2.3)	 84 (69.4) 3 (2.5) 34 (28.1) 0	 124 (75.6) 3 (1.8) 35 (22) 1 (0.6)	0.003
Third Keratoplasty PKP DALK DMEK	 7 (100) 0 0	 9 (64.3) 1 (7.1) 4 (28.6)	 16 (76.2) 1 (4.8) 4 (19)	0.194

PKP: penetrating keratoplasty, DALK: deep anterior lamellar keratoplasty, DMEK: Descemet's membrane endothelial keratoplasty, ALK: anterior lamellar keratoplasty, DSAEK: Descemet's stripping automated endothelial keratoplasty, PPV: pars plana vitrectomy
*Pearson Chi-Square test

Table 4. *Keratoplasty rates varying between groups depending on indications*

	GROUP 1 n (%)	GROUP 2 n (%)	*P**
Keratoconus *PKP* *DALK* *ALK*	 131 (96.3) 2 (1.5) 3 (2.2)	 214 (70.2) 55 (18) 36 (11.8)	<0.001
Bullous Keratopathy *PKP* *DMEK* *DSEAK*	 56 (98.2) 0 1 (1.8)	 82 (51.6) 77 (48.4) 0	<0.001
Graft Failure *PKP* *DMEK*	 8 (100) 0	 36 (90) 4 (10)	 0.470
Distrophy *PKP* *DALK* *DMEK* *ALK*	 65 (97) 0 0 2 (3)	 84 (54.2) 43 (27,7) 21 (13,5) 7 (4.5)	 <0.001
Corneal Scar *PKP* *DALK* *ALK* *PATCH*	 93 (98.9) 1 (1.1) 0 0	 175 (86.2) 23 (11.3) 4 (2) 1 (0.5)	 0.018

PKP: penetrating keratoplasty, DALK: deep anterior lamellar keratoplasty, DMEK: Descemet's membrane endothelial keratoplasty, ALK: anterior lamellar keratoplasty, DSAEK: Descemet's stripping automated endothelial keratoplasty.
*Pearson Chi-Square test

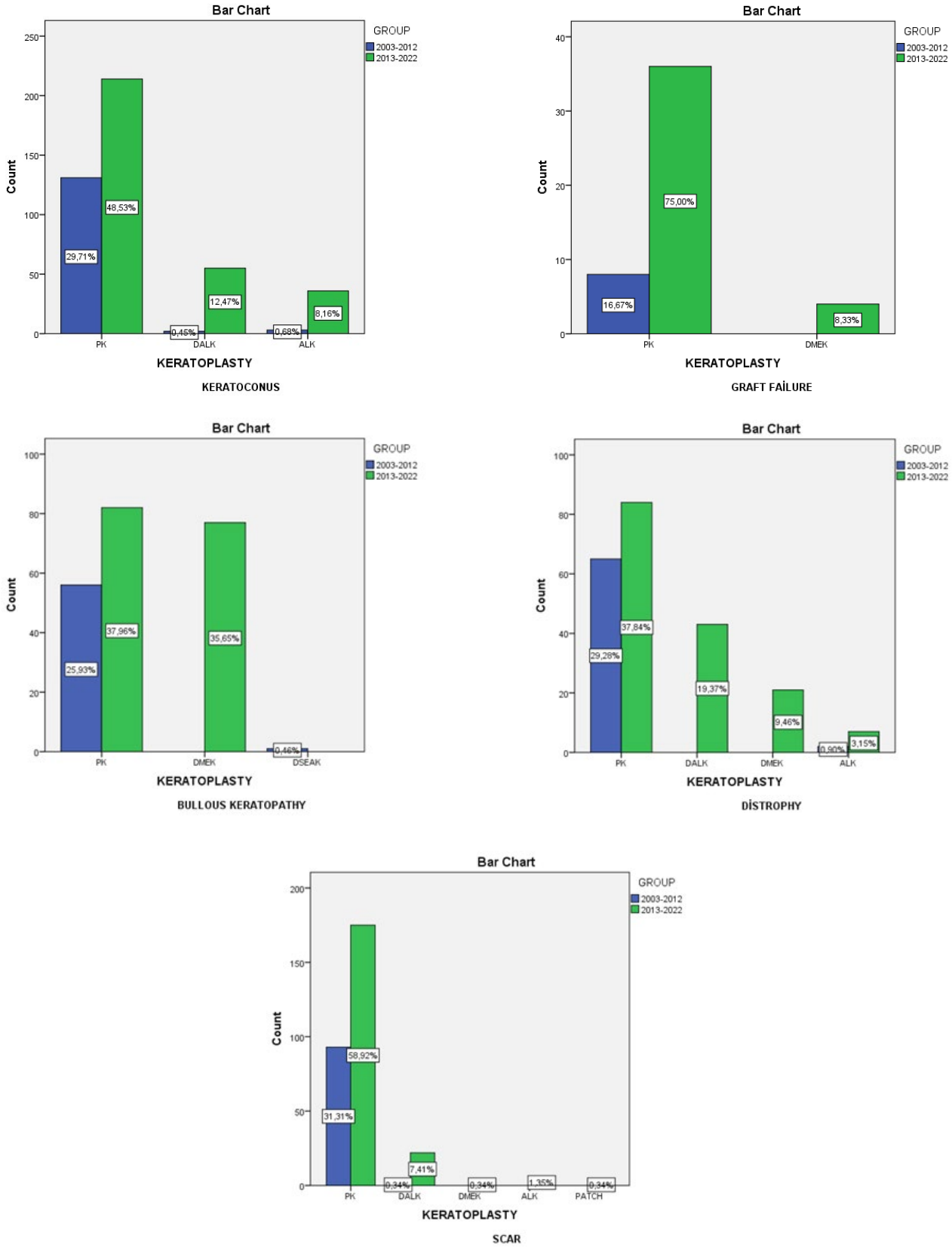

Figure 1. *Keratoplasty rates varying between groups depending on indications*

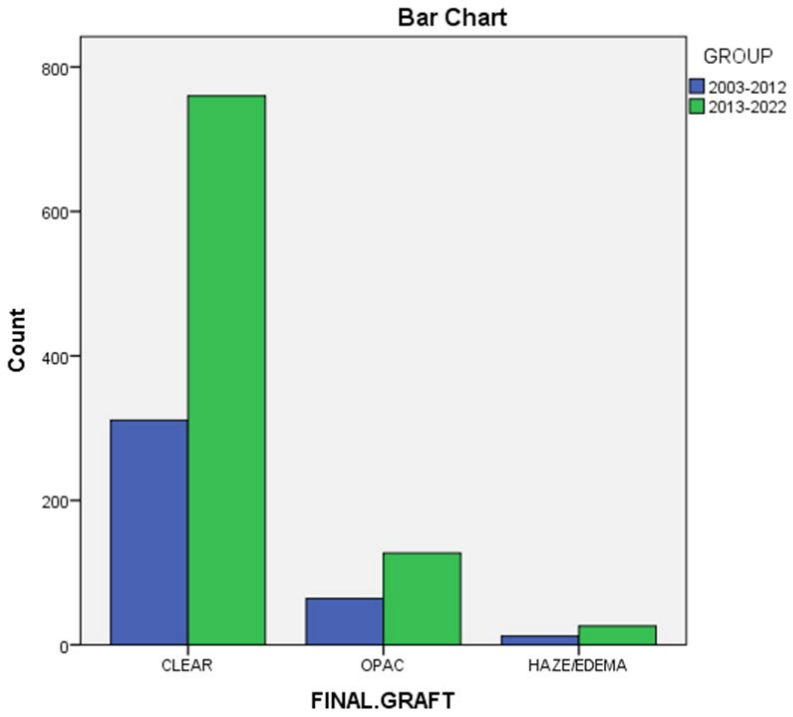

Figure 2. *Graft transparency rates at the last examination in both groups*

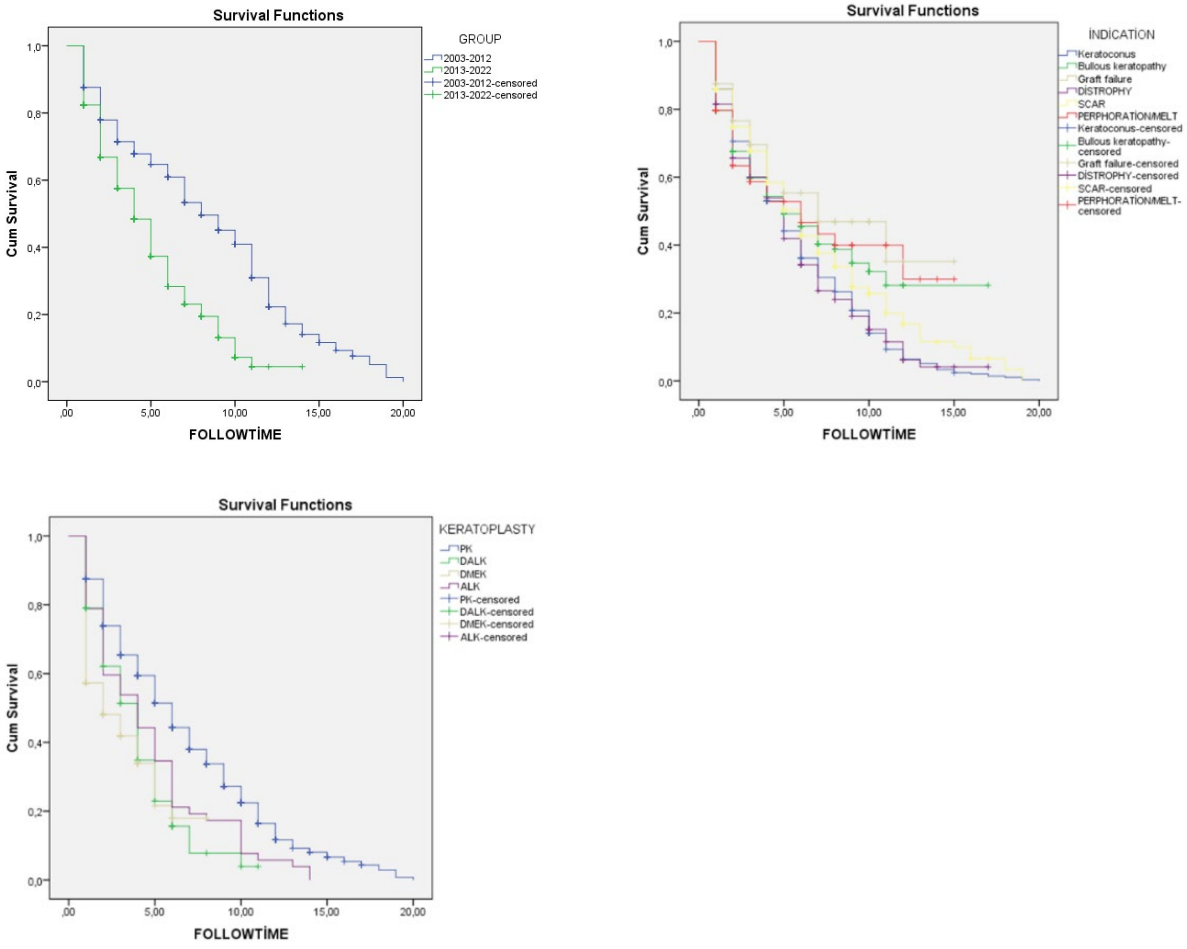

Figure 3. *Graft survival curves by Kaplan-Meier method.*

North America, and corneal scarring in Asia. [12] In the present study, keratoconus was identified as the most common indication for PKP, followed by bullous keratopathy and corneal scarring as the second and third most frequent indications, respectivelyAlthough similar to previous national data, international trends suggest evolving patterns: for instance, in France, secondary endothelial failure is now the most common indication for corneal transplantation followed by Fuchs endothelial dystrophy (FED), graft failure, and keratoconus.[5] In Germany, the predominant indications are FED and pseudophakic corneal decompensation, with DMEK becoming the most commonly performed procedure since 2016.[9] In the United States, between 2017 and 2020, the leading indications for PKP, EK, and ALK were repeat grafting, endothelial dystrophy, and ectasia/thinning, respectively. A decrease in PKP and a corresponding rise in DMEK have been documented over the past decade.[13] In Asia, common indications for optical grafts include pseudophakic BK, post-infectious corneal scarring and thinning, and keratoconus.[14] In this study, the leading keratoplasty indications in both groups were keratoconus, corneal scar, BK, and dystrophy. There were no significant differences between groups in terms of indications. Although the number of DALK procedures for keratoconus and corneal scars, and DMEK procedures for bullous keratopathy and endothelial dystrophies increased, the priorities in terms of indications remained unchanged. However, with the increasing incidence of graft failure over the years, along with the rising number of DMEK procedures performed for endothelial insufficiency and FED, the current order of surgical indications may shift.

In a previous study conducted in our clinic comparing keratoplasty indications and surgeries between 1995-2004 and 2005-2014, the leading indications in the first group were keratoconus (34.1%), bullous keratopathy (17%) and non-herpetic corneal scar (13.3%), while in the second group, keratoconus (33.8%), corneal stromal dystrophy (14.2%) and bullous keratopathy (12.7%).[7] In the same study, all keratoplasties performed in the 1995-2004 period were PKP, while in the 2005-2014 period, PKP constituted 93% of all keratoplasties, DSEAK 5.8% and DALK 1.2%.[7] Although there was no significant difference in the indications in the current study, significant increases were observed in DALK and DMEK rates in the surgeries selected for these indications.

Although the overall distribution of indications has remained relatively constant, surgical approaches have changed markedly in the last decade (Group 2), with a notable decline in PKP and a significant rise in lamellar procedures since 2013. In recent years, studies from Europe and the United States have reported that DALK is the most commonly performed procedure for keratoconus, while DMEK is the preferred technique for endothelial dystrophies and endothelial insufficiencies.[5,9,13] In the present study, despite the observed rise in lamellar keratoplasty procedures, their usage remains relatively low compared to reported rates in Europe and the United States. The rate of PKP for keratoconus decreased from 96.3% in Group 1 to 70.2% in Group 2. The rate of DALK increased to 18% and ALK to 11.8% in Group 2. Since DMEK was not performed for bullous keratopathy prior to 2013, the PKP rate in Group 1 was 98.2%, and DSAEK was performed in only one case. After 2013, DMEK became the preferred procedure at a rate of 48.4%, while the rate of PKP declined to 51.6%. For stromal dystrophies, the combined rate of DALK and ALK increased to 32.2%, while the DMEK rate for endothelial dystrophies rose to 13.5%. In cases of corneal scarring, the rate of PKP was 98.9% in Group 1 and 86.2% in Group 2, with the rates of DALK and ALK increasing to 13.3%.

In a similar study conducted by Bozkurt et al., the leading indications for keratoplasty between 2004 and 2014 were reported as keratoconus, BK, post-infectious corneal scars, regrafts, corneal dystrophies, and non-infectious corneal scars.[6] In lamellar surgeries, a significant increase was observed particularly in DALK and DSAEK rates and a decrease in PKP rates.[6] That study also found a notable increase in DALK and DSAEK and a decline in PKP rates. While our results showed similar trends (except for regrafts), we observed a greater preference for DMEK over DSAEK.

In both groups, the rates of keratoplasty combined surgery were comparable, and scleral fixation and IOL implantation were the leading combined surgery. Graft failure was the leading cause of re-keratoplasty, following both PKP and DMEK. In both groups, PKP was the most frequently performed re-keratoplasty method. However, with growing experience in DMEK, its use in cases of graft failure has increased. In Group 2, DMEK accounted for 28.1% of

Table 5. *Comparison of complication rates between groups*

	GROUP 1 n (%)	GROUP 2 n (%)	TOTAL n (%)	P*
Graft Rejection	34 (8.8)	74 (8.1)	108 (8.3)	
Graft Failure	44 (11.4)	104 (11.4)	148 (11.4)	
Microbial Keratitis	17 (4.4)	44 (4.8)	61 (4.7)	0.571
Cataract	63 (16.3)	109 (11.9)	172 (13.2)	
Glaucoma **Medical** **Trabeculectomy** **AGV implantation** **Siclophotocoagulation** **Laser**	45 (11.6) 24 (6.2) 11 (2.8) 7 (1.8) 1 (0.3) 1 (0.3)	135 (14.8) 84 (9.2) 19 (2.1) 24 (2.6) 8 (0.9) 0	175 (13.5)	
Persistent Epithelial Defect	2 (0.5)	4 (0.4)	6 (0.5)	
Dehiscence/ Perforation	2 (0.5)	11 (1.2)	(0.9)	
Fitizis	0	2 (0.2)	2 (0.2)	
Choroidal detachment	1 (0.3)	3 (0.3)	4 (0.3)	
Retinal detachment	1 (0.3)	2 (0.2)	3 (0.4)	
Melting	3 (0.8)	1 (0.1)	4 (0.3)	
Ektazi	3 (0.8)	8 (0.9)	11 (0.8)	
Optic Atrophy	0	1 (0.1)	1 (0.1)	
Endophthalmitis	0	2 (0.2)	2 (0.2)	
Disease relapse (distrophy)	0	4 (0.4)	(0.3)	

AGV: Ahmed glaucoma valve
*Pearson Chi-Square test

Table 6. *Comparison of graft transparency rates at last examination*

	Group 1 n (%)	Group 2 n (%)	Total n (%)	*p**
Clear	311 (80.4)	760 (83.2)	1071 (82.4)	
Opac	64 (16.5)	127 (13.9)	191 (14.7)	
Haze/ Semi-opaque	12 (3.1)	26 (2.8)	38 (2.9)	0.447

*Pearson Chi-Square test

Table 7. *1-year and 5-year graft survival rates by groups, keratoplasty and indications*

	1-year (%)	5-year (%)	P*
Group 1	87.6	64.7	<0.001
Group 2	82.4	37.3	
KERATOPLASTY			
PKP	87.5	51.4	<0.001
DALK	79.1	22.9	
DMEK	57.3	21.6	
ALK	78.8	34.6	
INDICATION			
Keratoconus	85.9	44.2	0.001
Bullous keratopathy	79.6	49.2	
Graft failure	87.5	55.4	
Distrophy	81.5	41.9	
Scar	85.9	50.3	
Perphoration	79.7	46.6	

PKP: penetrating keratoplasty, DALK: deep anterior lamellar keratoplasty, DMEK: Descemet's membrane endothelial keratoplasty, ALK: anterior lamellar keratoplasty.
*Log Rank (Mantel-Cox)

Table 8. *Univariate analysis of risk factors associated with graft failure*

	Graft Survival		*P**
	Succes	Failure	
SEX			
Female	459 (77.1)	136 (22.9)	0.176
Male	521 (73.9)	184 (26.1)	
Ocular Comorbidite	268 (60)	179 (40)	**<0.001**
Glaucoma	70 (38.9)	110 (61.1)	**<0.001**
Corneal vascularization			
<2 quadrant	67 (63.8)	38 (36.2)	**0.004**
>2 quadrant	24 (64.9)	13 (35.1)	
Limbus failure	15 (65.2)	8 (34.8)	0.253
Indication			
Keratoconus	410 (93)	31 (7)	**<0.001**
Bullous Keratopathy	108 (50)	108 (50)	
Graft failure	22 (45.8)	26 (54.2)	
Dystrophy	192 (86.5)	30 (13.5)	
Scar	208 (70)	89 (30)	
Perphoration	31 (48.4)	33 (51.6)	
Keratoplasthy			
PKP	749 (75.1)	249 (24.9)	**<0.001**
DALK	107 (82.9)	22 (17.1)	
DMEK	65 (63.1)	38 (36.9)	
ALK	52 (100)	0	
Combined Surgery	43 (58.9)	30 (41.1)	**0.001**

PKP: penetrating keratoplasty, DALK: deep anterior lamellar keratoplasty, DMEK: Descemet's membrane endothelial keratoplasty, ALK: anterior lamellar keratoplasty..
*Pearson Chi-Square test

re-keratoplasty procedures. Nonetheless, this remains low compared to the rates reported in developed countries. [5,9,13]

One limitation of this study is that tectonic keratoplasty procedures were not analyzed separately from optical keratoplasties.

CONCLUSION

As a result, the rates of DMEK and DALK at our clinic significantly increased after 2013. Still, PKP is the most common type of keratoplasty. The surgical options used for these indications have transformed over the past ten years, even though our surgical indications have not changed significantly. We anticipate that usage of lamellar keratoplasty techniques will increase as our familiarity with lamellar keratoplasty grows in the upcoming years.

Conflict of Interest: The authors report no conflicts of interest.

Ethical approval: All procedures performed in study comply with the ethical standards of the Institutional research committee of the University of Health Sciences Ankara Training and Research Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Data availability statement: The data that support the findings of this study are available from the corresponding author [ATB], upon reasonable request.

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