

Indications and Surgical Techniques for Corneal Transplantation at a Tertiary Referral Center

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Abstract

Purpose: The study aimed to review the indications and techniques for corneal transplantation at a tertiary referral center over a 5-year period.

Methods: Records of patients who underwent corneal transplantation at Khalili Medical Center, Shiraz, Iran from September, 2012 to September, 2017 were reviewed.

Results: A total of 1149 eyes of 956 patients underwent corneal transplantation. The most common indication was infectious corneal ulcers ($n = 296, 25.8\%$), followed by keratoconus ($n = 243, 21.1\%$), bullous keratopathy ($n = 219, 19.1\%$), failed grafts ($n = 117, 10.2\%$), non-herpetic corneal scars ($n = 113, 9.8\%$), corneal stromal dystrophies ($n = 33, 2.9\%$), pellucid marginal degeneration ($n = 31, 2.7\%$), and trauma ($n = 26, 2.3\%$); other indications included thin descemetocoele, post-herpetic corneal scar, endothelial corneal dystrophies, anterior segment dysgenesis, corneal ectasia after laser *in situ* keratomileusis, and corneal fibrosis. Corneal transplantation techniques included penetrating keratoplasty (PKP, $n = 789, 68.7\%$), deep anterior lamellar keratoplasty (DALK, $n = 187, 16.3\%$), Descemet's stripping automated endothelial keratoplasty ($n = 171, 14.9\%$), and keratolimbal allograft ($n = 2, 0.1\%$) in descending order. In children (aged ≤ 18 years), the most common indication was keratoconus ($n = 32, 41.6\%$), and the most common technique was PKP ($n = 50, 64.9\%$). In patients aged 19-27 years, the most common indication was keratoconus ($n = 89, 64.5\%$), and the most common technique was PKP ($n = 75, 54.4\%$).

Conclusion: Infectious corneal ulcer was the most common indication, and PKP was the most prevalent technique in patients undergoing corneal transplantation. DALK was an emerging alternative surgical treatment in patients with corneal disorders in which corneal endothelium is spared.

Keywords: Corneal Transplantation; Penetrating Keratoplasty; Deep Anterior Lamellar Keratoplasty; Descemet's Stripping Automated Endothelial Keratoplasty

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INTRODUCTION

Corneal blindness due to infection, ectasia, corneal dystrophy, or other pathology is a major health problem

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worldwide.^[1] Indications for corneal transplantation have changed overtime and differ based on location such as the city and country; moreover, allocation of resources is based on the epidemiology of corneal pathologies in each region. For example, bullous keratopathy is reported to be the most common indication for corneal transplantation in developed countries,^[2-7] and infectious corneal diseases and corneal scars are more prevalent in developing countries.^[8-10] Certain indications for penetrating keratoplasty have changed over time in Iran.^[11]

In this study, we reviewed the indications and techniques of corneal transplantation performed over a 5-year period at Khalili Medical Eye Center, a tertiary training and referral eye center in Shiraz, Iran.

METHODS

In this retrospective study, we reviewed the hospital records of patients who had undergone corneal transplantation at Khalili Medical Eye Center from September, 2012 to September, 2017 for demographic data, indications for keratoplasty, and surgical techniques.

Indications for keratoplasty consisted of the surgeons' clinical diagnoses at the time of surgery. In case of multiple transplantations, diagnosis of re-graft was considered regardless of the initial indication for transplantation and type of keratoplasty.

In this study, corneal opacification referred to non-herpetic corneal scar in the absence of active bacterial or viral infection; whereas, old corneal scars with confirmed diagnosis of herpes simplex keratitis based on the history and characteristic clinical features were reported separately. The causes of active infectious corneal ulcers were determined through clinical findings, confocal biomicroscopy, smears, cultures, and/or histopathologic examinations performed through corneal biopsy.

Thin descemetocoele referred to non-traumatic and non-surgical corneal thinning in the absence of active infection. Corneal fibrosis referred to old trachoma with corneal fibrosis. Endothelial corneal dystrophies comprised Fuchs endothelial dystrophy (FED) and congenital hereditary endothelial dystrophy.

Traumatic corneal opacity referred to any corneal opacities caused by mechanical trauma or chemical burns.

Aphakic or pseudophakic patients who underwent keratoplasty for corneal decompensation were considered as cases of aphakic bullous keratopathy (ABK) or pseudophakic bullous keratopathy (PBK), regardless of the underlying mechanism of corneal decompensation (e.g. complicated cataract surgery).

In case of tectonic or therapeutic corneal transplantation performed for ulceration or perforation, the primary pathology leading to an urgent keratoplasty was considered.

The indications for keratoplasty and surgical techniques performed in patients aged ≤ 18 years and those aged 19-27 years were separately investigated and reported.

RESULTS

Overall, the records of 1149 eyes of 956 patients including 588 male and 368 female subjects who underwent corneal transplantation during the 5-year period were compiled. Mean age was 51.47 ± 23.12 years (age range, 10 days to 99 years) with median of 49 years. Of 1149 eyes, 77 eyes were from 49 children (aged ≤ 18 years), and 138 eyes from 120 patients (aged 19-27 years). Patients with anterior segment dysgenesis (Peter's anomaly) were the youngest (mean age, 1 year) and subjects with bullous keratoplasty (BK) were the oldest (mean age, 68 years).

The most common indication for keratoplasty was infectious corneal ulcers ($n = 296, 25.8\%$)

The second most common indication for keratoplasty was keratoconus ($n = 243, 21.1\%$), followed by bullous keratopathy ($n = 219, 19.1\%$), failed graft ($n = 117, 10.2\%$), non-herpetic corneal scar ($n = 113, 9.8\%$), corneal stromal dystrophies ($n = 33, 2.9\%$), pellucid marginal degeneration (PMD) ($n = 31, 2.7\%$), traumatic corneal opacities ($n = 26, 2.3\%$), thin descemetocoele ($n = 22, 1.9\%$), and post-herpetic corneal scar ($n = 21, 1.8\%$); the remaining indications included endothelial corneal dystrophies, post-laser *in situ* keratomileusis (LASIK) keratectasia, corneal fibrosis, and anterior segment dysgenesis [Tables 1-8].

In children, the indications for corneal transplantation included keratoconus ($n = 32$), infectious corneal ulcer ($n = 12$), failed graft ($n = 9$), non-herpetic corneal scar ($n = 6$), post herpetic corneal scar ($n = 6$), anterior segment dysgenesis ($n = 6$), traumatic corneal opacities ($n = 4$), endothelial corneal dystrophies ($n = 1$), and stromal corneal dystrophies ($n = 1$) [Tables 9 and 10].

In the 19 to 27 years' age group, the indications for corneal transplantation included keratoconus ($n = 89$), infectious corneal ulcers ($n = 13$), stromal corneal dystrophies ($n = 12$), failed graft ($n = 7$), traumatic corneal opacities ($n = 5$), endothelial corneal dystrophies ($n = 3$),

Table 1. Types of corneal transplantation

	Frequency	Percentage
PKP	789	68.7
DALK	187	16.3
DSAEK	171	14.9
KLAL	2	0.2
Total	1149	100.0

DALK, deep anterior lamellar keratoplasty; DSAEK, Descemet's stripping automated endothelial keratoplasty; KLAL, keratolimbal allograft; PKP, penetrating keratoplasty

Table 2. Indications of corneal transplantation

	Frequency	Percentage
Infectious corneal ulcers	296	25.8
Keratoconus	243	21.1
Bullous keratopathy	219	19.1
Failed grafts	117	10.2
Non-herpetic corneal scar	113	9.8
Corneal stromal dystrophies	33	2.9
PMD	31	2.7
Trauma	26	2.3
Thin descemetocoele	22	1.9
Post-herpetic corneal scar	21	1.8
Endothelial corneal dystrophies	16	1.4
Anterior segment dysgenesis	6	0.5
Post-LASIK keratectasia	3	0.3
Corneal Fibrosis	3	0.3
Total	1149	100.0

LASIK, laser in-situ keratomileusis; PMD, pellucid marginal degeneration

PMD ($n = 2$), BK ($n = 2$), non-herpetic corneal scar ($n = 2$), post-herpetic corneal scar ($n = 1$), thin descemetocoele ($n = 1$), and post-LASIK keratectasia ($n = 1$) [Table 10].

Of 296 eyes that received a corneal graft for the management of infectious corneal ulcers, 49 eyes were culture positive; of these, 44 eyes had bacterial infection, and 5 eyes had fungal infection. The remaining cultures were negative for growth based on the laboratory report.

Macular corneal dystrophy was the most common stromal dystrophy as indication for corneal transplantation, followed by granular and lattice corneal dystrophies.

In this study, corneal transplantation techniques included penetrating keratoplasty (PKP) ($n = 789, 68.7\%$), deep anterior lamellar keratoplasty (DALK) ($n = 187, 16.3\%$), Descemet stripping automated endothelial keratoplasty (DSAEK) ($n = 171, 14.9\%$), and keratolimbal allograft (KLAL) ($n = 2, 0.2\%$) [Table 1].

The most common techniques in children was PKP ($n = 50$), followed by DALK ($n = 24$), and DSAEK ($n = 3$); in the 19-27 years' age group, PKP ($n = 75$), followed by DALK ($n = 63$).

With regard to surgical techniques for management of keratoconus during the 5-year period, there was relative reduction in the frequency of patients undergoing PKP, whereas increase in the frequency of those undergoing DALK. PKP was the dominant technique for surgical management of infectious corneal ulcer, failed graft and corneal scars.

DISCUSSION

The current study was conducted in one of the hospitals affiliated to Shiraz University of Medical Sciences, which attends patients from around the country, especially southern Iran. The study results reflected recent changes

Table 3. Types of corneal transplantation under different indications

Type	Frequency	Percentage
PKP		
Infectious corneal ulcers	296	37.5
Non-herpetic corneal scar	106	13.4
Failed graft	94	11.9
Keratoconus	85	10.8
Bullous keratopathy	77	9.8
Corneal stromal dystrophies	27	3.4
Trauma	25	3.2
Thin descemetocoele	22	2.8
PMD	19	2.4
Post-herpetic corneal scar	17	2.2
Endothelial corneal dystrophies	10	1.3
Anterior segment dysgenesis	6	0.8
Corneal Fibrosis	3	0.4
Post-LASIK keratectasia	2	0.3
Total	789	100.0
DALK		
Keratoconus	158	84.5
PMD	12	6.4
Corneal stromal dystrophies	6	3.2
Post-herpetic corneal scar	4	2.1
Non-herpetic corneal scar	4	2.1
Failed graft	2	1.1
Post-LASIK keratectasia	1	0.5
Total	187	100.0
DSAEK		
Bullous keratopathy	142	83.0
Failed graft	20	11.7
Endothelial corneal dystrophies	6	3.5
Non-herpetic corneal scar	3	1.8
Total	171	100.0
KLAL		
Failed graft	1	50.0
Trauma	1	50.0
Total	2	100.0

DALK, deep anterior lamellar keratoplasty; DSAEK, Descemet's stripping automated endothelial keratoplasty; KLAL, keratolimbal allograft; LASIK; laser in-situ keratomileusis; PMD, pellucid marginal degeneration; PKP, penetrating keratoplasty

in indications for corneal transplantation and surgical techniques in Iran; however, patient selection may have bias due to presentation of challenging and complicated cases that are not routinely managed in private and less specialized centers.

In our study, infectious corneal ulcer was the most common indication over the 5-year study period. Similarly, in some countries, such as India and China, corneal infections were the leading cause of keratoplasty.^[8,10,12]

The reason for this finding is that our center is a primary center, and secondary and tertiary referral center in southern Iran for patients with corneal ulcers.

Table 4. Indications of corneal transplantation

	Frequency	Percentage
Keratoconus		
PKP	85	35.0
DALK	158	65.0
Total	243	100.0
Infectious corneal ulcers		
PKP	296	100.0
Bullous keratopathy		
PKP	77	35.2
DSAEK	142	64.8
Total	219	100.0
Non-herpetic corneal scar		
PKP	106	93.8
DALK	4	3.5
DSAEK	3	2.7
Total	113	100.0
PMD		
PKP	19	61.3
DALK	12	38.7
Total	31	100.0
Failed graft		
PKP	94	80.3
DALK	2	1.7
DSAEK	20	17.1
KLAL	1	0.9
Total	117	100.0
Corneal stromal dystrophies		
PKP	27	81.8
DALK	6	18.2
Total	33	100.0
Endothelial corneal dystrophies		
PKP	10	62.5
DSAEK	6	37.5
Total	16	100.0
Post-herpetic corneal scar		
PKP	17	81.0
DALK	4	19.0
Total	21	100.0
Trauma		
PKP	25	96.2
KLAL	1	3.8
Total	26	100.0
Thin descemetocele		
PKP	22	100.0
Corneal Fibrosis		
PKP	3	100.0
Post-LASIK keratectasia		
PKP	2	66.7
DALK	1	33.3
Total	3	100.0
Anterior segment dysgenesis		
PKP	6	100.0

DALK, deep anterior lamellar keratoplasty; DSAEK, Descemet's stripping automated endothelial keratoplasty; KLAL, keratolimbal allograft; LASIK; laser in-situ keratomileusis; PMD, pellucid marginal degeneration; PKP, penetrating keratoplasty

Table 5. Types of penetrating keratoplasty

Type	Frequency	Percentage
Optical PKP	599	76
Tectonic PKP	92	11.6
Re PKP	98	12.4
Total	789	100

PKP, penetrating keratoplasty

Table 6. Endothelial corneal dystrophies

Type	PKP	DSAEK	Total
FED	6	6	12
CHED	4	0	4
Total	10	6	16

CHED, congenital hereditary endothelial dystrophy; DSAEK, Descemet's stripping automated endothelial keratoplasty; FED, Fuchs endothelial dystrophy; PKP, penetrating keratoplasty

Table 7. Trauma

Type	Tectonic PKP	Optical PKP	KLAL	Total
Burn	0	1	1	2
Laceration	2	22	0	24
Total	2	23	1	26

PKP, penetrating keratoplasty

Table 8. Bullous keratopathy

Type	PKP	DSEAK	Total
PBK	70	142	212
ABK	7	0	7
Total	77	142	219

ABK, aphakic bullous keratopathy; DSAEK, Descemet's stripping automated endothelial keratoplasty; PBK, pseudophakic bullous keratopathy; PKP, penetrating keratoplasty

Table 9. Types of corneal transplantation by age group

	Frequency	Percentage
≤18 years		
PKP	50	64.9
DALK	24	31.2
DSAEK	3	3.9
Total	77	100.0
19-27 years		
PKP	75	54.3
DALK	63	45.6
Total	138	100
>27 years		
PKP	739	68.9
DALK	163	15.2
DSAEK	168	15.7
KLAL	2	0.2
Total	1072	100.0

DALK, deep anterior lamellar keratoplasty; DSAEK, Descemet's stripping automated endothelial keratoplasty; KLAL, keratolimbal allograft; PKP, penetrating keratoplasty.

Table 10. Indications of corneal transplantation by age group

	Frequency	Percentage
≤18 years		
Keratoconus	32	41.6
Infectious corneal ulcers	12	15.6
Non-herpetic corneal scar	6	7.8
Failed graft	9	11.7
Corneal stromal dystrophies	1	1.3
Endothelial corneal dystrophies	1	1.3
Post-herpetic corneal scar	6	7.8
Trauma	4	5.2
Anterior segment dysgenesis	6	7.8
Total	77	100.0
19-27 years		
Keratoconus	89	64.5
Infectious corneal ulcers	13	9.4
Bullous keratopathy	2	1.4
PMD	2	1.4
Failed graft	7	5.1
Endothelial corneal dystrophies	3	2.1
Stromal corneal dystrophies	12	8.8
Non-herpetic corneal scar	2	1.4
Trauma	5	3.6
Post-herpetic corneal scar	1	0.7
Thin descemetocoele	1	0.7
Post-LASIK keratectasia	1	0.7
Total	138	100
>27 years		
Keratoconus	211	19.7
Infection corneal ulcers	284	26.5
Bullous keratopathy	219	20.4
Non-herpetic corneal scar	107	10.0
PMD	31	2.9
Fail graft	108	10.1
Corneal stromal dystrophies	32	3.0
Endothelial corneal dystrophies	15	1.4
Post-herpetic corneal scar	15	1.4
Trauma	22	2.1
Thin descemetocoele	22	2.1
Corneal Fibrosis	3	0.3
Post-LASIK keratectasia	3	0.3
Total	1072	100.0

PMD, pellucid marginal degeneration; LASIK, laser in-situ keratomileusis

The prevalence of infectious corneal ulcers in Iran has not been reported previously. However, we observed relatively high prevalence rates possibly due to the association between infectious corneal ulcers and the climatic condition in southern Iran, patients' socioeconomic level, education level, safety at work place, prevalence of ocular surface diseases in this region, and ophthalmic medication abuse; moreover, the time interval between screening, diagnosis, and

management can affect the prevalence of corneal transplantation in patients with infectious corneal ulcers in Iran.

Reduced prevalence of corneal transplantation in patients with keratoconus may be due to the increased rate of CXL procedure in patients with early diagnosis of keratoconus. In our center, the frequency of CXL gradually increased from 29 patients in 2010 to 412 patients in 2017, which may be the reason for reduced frequency of corneal transplantation under indication of keratoconus, the second most common indication for corneal transplantation in our study.

Another reason for this decline may be that private centers which manage patients with keratoconus have access to donated corneas in the Eye Banks, leading to early operation, especially DALK which has recently gained resurgence; whereas, patients with infectious corneal ulcers are referred to our center.

Studies conducted in western countries reported that FED was as an important indication, with a rate of 9.3% to 23.2%.^[6] However, the present study revealed that FED was a rare condition, with a prevalence rate of 1.1%, similar to reports from studies conducted in the Middle East and Mediterranean region.^[13,14]

Kanavi et al^[15] reported the indications of PKP nationwide in Iran from 1997 to 2003; their results revealed that keratoconus was the most common indication, followed by corneal opacities and scars, PBK, corneal dystrophies, ABK, and re-graft in descending order. Zare et al,^[11] reported that the leading indication for corneal transplantation in a tertiary referral center from 2004 to 2007 was keratoconus, but bullous keratopathy was the second most common indication, followed by non-herpetic corneal scar and infectious corneal ulcers.

In the current study, macular corneal dystrophy was the most common dystrophy with indication for corneal transplantation, which is in agreement with the report of Kanavi et al^[15] and Zare et al.^[11]

As compared to previous reports from Iran,^[11] we observed that infectious corneal ulcers showed increased incidence attaining the rank of most common indication from that of fourth most common, followed by keratoconus and bullous keratopathy.

In our study, PKP was the most common technique of corneal transplantation (68.7%), followed by DALK (16.3%) and DSAEK (14.9%). However, there was an alteration in the relative frequency of surgical technique in patients with keratoconus over the 5-year period, reflecting the introduction of new corneal transplantation techniques that address the underlying pathology. In our center, DALK using either the Anwar big-bubble or Melles technique is used exclusively. Other techniques included tectonic graft [Table 4].

DSAEK was the preferred transplantation technique in patients with bullous keratopathy [Table 7].

Mean age of patients included in this study was 52 years, due to the large number of elderly patients with ulcer and bullous keratopathy, and young patients with keratoconus. Subjects with anterior segment dysgenesis (Peter's anomaly) were the youngest and patients with BK were the oldest.

In conclusion, in contrast to previous reports in Iran,^[11] our study reported the novel finding that infectious corneal ulcers were the leading indication for keratoplasty followed by keratoconus and Bullous keratopathy. Similarly, there was a significant shift in corneal transplantation technique from the more invasive PKP to the less invasive DALK in patients with keratoconus.

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Conflicts of Interest

There are no conflicts of interest.

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