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

Hossein Jamali, MD; Ahmad Reza Gholampour, MD

Poostchi Ophthalmology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

ORCID:
Hossein Jamali: https://orcid.org/0000-0001-6633-2268
Ahmad Reza Gholampour: https://orcid.org/0000-0002-0511-108X

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 descemetocele, 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 = 50, 64.9%).

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

INTRODUCTION

Corneal blindness due to infection, ectasia, corneal dystrophy, or other pathology is a major health problem...
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, and infectious corneal diseases and corneal scars are more prevalent in developing countries. Certain indications for penetrating keratoplasty have changed over time in Iran.

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 graft regraft 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 descemetocele 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 descemetocele (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
Indications for corneal transplantation: Jamali and Gholampour

Table 2. Indications of corneal transplantation

| Indication                                      | 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 descemetocele                             | 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**  |

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

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 3].

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 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

| Condition                        | 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   | DSAEK | 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

| Age Group       | PKP | DALK | DSAEK | KLAL | Total |
|-----------------|-----|------|-------|------|-------|
| ≤18 years       | 50  | 24   | 3     |      | 77    |
|                  |     |      |       |      | 100.0 |
| 19-27 years     | 75  | 63   | 3     |      | 138   |
|                  |     |      | 45.6  |      | 100.0 |
| >27 years       | 739 | 163  | 168   | 2    | 1072  |
|                  |     |      | 68.9  | 0.2  | 100.0 |

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

Kanavi et al 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 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 and Zare et al.

As compared to previous reports from Iran, 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].

---

Table 10. Indications of corneal transplantation by age group

| 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 descemetocele | 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 descemetocele | 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
Indications for Corneal Transplantation; Jamali and Gholampour

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, 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.

Acknowledgment
The present article was extracted from the thesis written by Ahmad Reza Gholampour under the supervision of Dr. Hossein Jamali and was financially supported by Shiraz University of Medical Sciences grants No. 16732.

The authors wish to thank Mr. H. Argasi at the Research Consultation Center (RCC) of Shiraz University of Medical Sciences for his invaluable assistance in editing this manuscript.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

REFERENCES
1. Maurin JF, Cornand G. Corneal blindnesses in tropical environment. Rev Int Trach Pathol Ocul Trop Subtrop Sante Publique 1990;67:23-138.
2. Cosar CB, Sridhar MS, Cohen EJ, Held EL, Alvim Pde T, Rapuano CJ, et al. Indications for penetrating keratoplasty and associated procedures, 1996-2000. Cornea 2002;21:148-151.
3. Liu E, Slomovic AR. Indications for penetrating keratoplasty in Canada, 1986-1995. Cornea 1997;16:414-419.
4. Maeno A, Naor J, Lee HM, Hunter WS, Rootman DS. Three decades of corneal transplantation: Indications and patient characteristics. Cornea 2000;19:7-11.
5. Legeais JM, Parc C, Hermies F, Pouliquen Y, Renard G. Nineteen years of penetrating keratoplasty in the Hotel-Dieu hospital in Paris. Cornea 2001;20:603-606.
6. Dobbins KR, Price FW Jr, Whitson WE. Trends in the indications for penetrating keratoplasty in the midwestern United States. Cornea 2000;19:813-816.
7. Inoue K, Amano S, Oshika T, Sawa M, Tsuru T. A 10-year review of penetrating keratoplasty. Jpn J Ophthalmol 2000;44:139-145.
8. Sony P, Sharma N, Sen S, Vaipayee R. Indications of penetrating keratoplasty in northern India. Cornea 2005;24:989-991.
9. Chen WL, Hu FR, Wang JJ. Changing indications for penetrating keratoplasty in Taiwan from 1987 to 1999. Cornea 2001;20:141-144.
10. Dandona L, Raghu K, Janarthanan M, Naduvilath TJ, Shenoy R, Rao GN. Indications for penetrating keratoplasty in India. Indian J Ophthalmol 1997;45:163-168.
11. Zare M, Javadi MA, Einollahi B, Karimian F, Rafie AR, Feizi S, et al. Changing indications and surgical techniques for corneal transplantation between 2004 and 2009 at a tertiary referral center. Middle East Afr J Ophthalmol 2012;19:323-329.
12. Zhang C, Xu J. Indications for penetrating keratoplasty in East China, 1994-2003. Graefes Arch Clin Exp Ophthalmol 2005;243:1005-1009.
13. Al-Towerki AE, Gonnah ES, Al-Rajhi A, Wagoner MD. Changing indications for corneal transplantation at the King Khaled eye specialist hospital (1983–2002). Cornea 2004;23:584-588.
14. Altay Y, Burcu A, Aksoy G, Ozdemir ES, Ornek F. Changing indications and techniques for corneal transplantations at a tertiary referral center in Turkey, from 1995 to 2014. Clin Ophthalmol 2016;10:1007-1013.
15. Kanavi MR, Javadi MA, Sanagoo M. Indications for penetrating keratoplasty in Iran. Cornea 2007;26:561-563.