

Trends in Indications and Techniques of Corneal Transplantation in Iran from 2006 to 2013; an 8-year Review

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Abstract

Purpose: To report changing trends in indications and techniques of corneal transplantation in Iran.

Methods: We reviewed eye bank records of 47,129 patients who had undergone corneal transplantation between 2006 and 2013 at different eye centers throughout Iran.

Results: The most common indication for corneal transplantation was keratoconus (KCN, $n = 21,350$ eyes, 45.3%), followed by bullous keratopathy (BK, $n = 8,566$ eyes, 18.2%), corneal opacity and scar (COS, $n = 7,158$ eyes, 15.2%), graft failure ($n = 3,252$ eyes, 6.9%), corneal dystrophies ($n = 2,553$ eyes, 5.4%), and infectious keratitis ($n = 2,238$ eyes, 4.7%). Over the study period, there was a significant increase in the frequency of BK ($P = 0.001$) and graft failure ($P = 0.025$), and a significant decrease in the relative frequency of COS ($P = 0.012$). The prevalence of KCN ($P = 0.172$), infectious keratitis ($P = 0.107$), and corneal dystrophies ($P = 0.836$) remained unchanged. The most common technique of corneal transplantation was penetrating keratoplasty (PKP, $n = 33,476$ eyes, 71.0%), followed by deep anterior lamellar keratoplasty (DALK, $n = 8,363$ eyes, 17.7%), Descemet's stripping automated endothelial keratoplasty (DSAEK, $n = 3,516$ eyes, 7.5%), tectonic ($n = 1,752$, 3.7%), and keratolimbal allograft (KLAL, $n = 19$ eyes, 0.1%). Regarding the shift in surgical techniques, a significant increase was observed in DSAEK ($P < 0.001$), whereas PKP was significantly decreased ($P = 0.005$) over the 8-year period. No significant change was seen in the rates of DALK ($P = 0.354$), tectonic graft ($P > 0.999$) and KLAL ($P = 0.151$).

Conclusion: KCN was the most common indication and PKP was the most prevalent technique used for corneal transplantation. Significant changes in surgical techniques were observed over the past 8 years; DSAEK demonstrated an increasing trend while PKP showed a decrease.

Keywords: Corneal Transplantation; Keratoconus; Surgical Technique; Trends

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INTRODUCTION

Corneal disorders are the second leading cause of blindness in developing countries and it has been estimated that 23 million people suffer from unilateral corneal blindness worldwide.^[1] The epidemiology of

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corneal disorders leading to transplantation differs from one region to another. Keratoconus (KCN) has been the leading cause of corneal transplantation in some regions^[2-5] while in other countries bullous keratopathy (BK) is the most common indication.^[6-11] Phacoemulsification which has become the dominant technique for cataract surgery may inflict corneal endothelial cells more significantly as compared to the older extracapsular cataract extraction method.^[12,13] Therefore, indications for keratoplasty tend to change over time. A study by Zare et al^[14] revealed that BK and graft failure ranked as the second and third most common indications for corneal transplantation at a tertiary referral eye center in Tehran, Iran, over a 6-year period.

The introduction of new techniques of corneal transplantation has resulted in a shift in the technique of keratoplasty from full-thickness penetrating keratoplasty (PKP) to lamellar procedures which selectively replace affected layers. A nationwide report by Ple-Plakon and Shtein^[15] demonstrated a similar trend the United States over the past decade. We also have witnessed a significant change of surgical plans in Iran from full thickness corneal grafts to partial-thickness keratoplasty techniques over the past 8 years. For instance, deep anterior lamellar keratoplasty (DALK) and Descemet's stripping automated endothelial keratoplasty (DSAEK) have been implemented as alternatives to PKP for KCN and endothelial diseases, respectively. Herein, we report changing trends in indications and techniques of corneal transplantation over an 8-year period in Iran.

METHODS

This retrospective study compiled and reviewed, eye bank records of patients who had undergone corneal grafting throughout the nation from March 2006 to March 2013. Approval from the Ethics Committee of the Ophthalmic Research Center, which is affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran was obtained prior to the study. Patient data including gender and age, surgical techniques and indications for keratoplasty were retrieved. The absolute and relative frequencies and percentages were provided for each indication and surgical technique.

SPSS software (version 22; SPSS, Inc., Chicago, IL, USA) was used for data analysis. We utilized 7 linear regression models to investigate any changing trend in the indications of corneal grafting over time. Five linear regression models were also used for each surgical technique. *P* values less than 0.05 were considered as statistically significant.

RESULTS

A total of 47,129 eye bank records of patients who had undergone corneal transplantation over the 8-year

period of the study were compiled. Patient age ranged from 6 months to 95 years and 61% of cases were male. The majority of patients were in the age range of 21-40 (38.7%), 61-80 (23.7%), and 41-60 (21.7%) years.

Main indications for corneal transplantation are summarized in Table 1. KCN was the most common indication ($n = 21,350$, 45.3%), followed by pseudophakic/aphakic BK ($n = 8,566$ [pseudophakic BK = 7,795, aphakic BK = 771], 18.2%), corneal opacities and scars (COS, $n = 7,158$, 15.2%), graft failure ($n = 3,252$, 6.9%), corneal dystrophies ($n = 2,553$, 5.4%), infectious keratitis ($n = 2,238$, 4.7%), and miscellaneous causes ($n = 2,012$, 4.3%). Macular corneal dystrophy was the most common corneal dystrophy leading to keratoplasty (52.0%) followed by Fuchs' endothelial dystrophy (23.4%), and congenital hereditary endothelial dystrophy (9.0%). An increasing trend was observed in the incidence of BK ($P = 0.001$) and graft failure ($P = 0.025$) over the study period; however, the rate of COS showed a decreasing trend ($P = 0.012$). There was no significant change in the incidence of KCN ($P = 0.172$), infectious keratitis ($P = 0.107$) and corneal dystrophies ($P = 0.836$).

PKP was the most common technique of corneal transplantation ($n = 33,476$, 71.0%), followed by DALK ($n = 8,363$, 17.7%), DSAEK ($n = 3,516$, 7.5%), tectonic graft ($n = 1,752$, 3.7%), and keratolimbal allograft (KLAL, $n = 19$, 0.1%) [Table 2]. Over the 8-year period, there was an increasing trend in the rate of DSAEK ($P < 0.001$), while PKP demonstrated a decreasing trend ($P = 0.005$). The rates of DALK, tectonic graft and KLAL revealed no significant change ($P = 0.354$, $P > 0.999$, and $P = 0.151$, respectively). Trends of the main indications for corneal transplantation and shifts of surgical technique are shown in Figures 1 and 2, respectively.

DISCUSSION

The present study evaluated 47,129 eye bank records of corneal transplantation procedures performed between 2006 and 2013. The trend of the indications for keratoplasty has changed significantly over the past 8 years in Iran. The top six indications in our study, in decreasing order, were KCN, BK, COS, graft failure, corneal dystrophies, and keratitis which is different from our previous nationwide report,^[2] where the top 5 diagnoses were KCN, COS, BK, corneal dystrophies, and graft failure. BK has now overtaken COS with an increasing trend during the past decade. This could be explained by the fact that phacoemulsification which has a higher risk of corneal endothelial damage has been performed more frequently over the past years.^[12,13] Another possible explanation is that DSAEK is performed earlier in such cases. The leading indications for corneal transplantation in the current study and in several studies conducted almost at the same time period are compared in Table 3.

Table 1. Indications for corneal transplantation in Iran between 2006 and 2013

Indications	Number of corneal transplants (%)								Total (%)
	2006	2007	2008	2009	2010	2011	2012	2013	
KCN	2204 (47.7)	2278 (46.5)	2488 (45.9)	2552 (45.4)	2727 (44.6)	2703 (42.2)	3327 (47.7)	3071 (43.4)	21,350 (45.3)
PBK/ABK	642 (13.9)	701 (14.3)	922 (17.0)	933 (16.6)	1101 (18.0)	1261 (19.7)	1584 (22.7)	1422 (20.1)	8566 (18.2)
Opacity and scars	836 (18.1)	779 (15.9)	976 (18.0)	792 (14.1)	948 (15.5)	986 (15.4)	900 (12.9)	941 (13.3)	7158 (15.2)
Graft failure	277 (6.0)	284 (5.8)	357 (6.6)	427 (7.6)	428 (7.0)	461 (7.2)	509 (7.3)	509 (7.2)	3252 (6.9)
Corneal dystrophy	231 (5.0)	313 (6.4)	304 (5.6)	258 (4.6)	287 (4.7)	365 (5.7)	370 (5.3)	425 (6.0)	2553 (5.4)
Active keratitis	259 (5.6)	289 (5.9)	287 (5.3)	292 (5.2)	324 (5.3)	371 (5.3)	98 (1.4)	318 (4.5)	2238 (4.7)
Others	171 (3.7)	255 (5.2)	87 (1.6)	366 (6.5)	300 (4.9)	256 (4.0)	188 (2.7)	389 (5.5)	2012 (4.3)
Total	4620	4899	5421	5620	6115	6403	6976	7075	47,129

KCN, keratoconus; PBK, pseudophakic bullous keratopathy; ABK, aphakic bullous keratopathy

Table 2. Techniques of corneal transplantation in Iran between 2006 and 2013

	Number of corneal transplants (%)								Total (%)
	2006	2007	2008	2009	2010	2011	2012	2013	
PKP	3669 (79.4)	4037 (82.4)	4266 (78.7)	4207 (74.86)	3791 (62.0)	4399 (68.7)	4639 (66.5)	4468 (63.15)	33,476 (71.0)
DALK	813 (17.6)	754 (15.4)	711 (13.1)	827 (14.7)	1480 (24.2)	1204 (18.8)	1353 (19.4)	1224 (17.3)	8363 (17.7)
DSAEK	0 (0.0)	0 (0.0)	157 (2.9)	292 (5.2)	508 (8.3)	647 (10.1)	858 (12.3)	1054 (14.9)	3516 (7.5)
Tectonic	138 (3)	108 (2.2)	287 (5.3)	292 (5.2)	330 (5.4)	153 (2.4)	126 (1.8)	318 (4.5)	1752 (3.7)
KLAL	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.04)	6 (0.1)	0 (0.0)	0 (0.0)	11 (0.15)	19 (0.1)
Total	4620	4899	5421	5620	6115	6403	6976	7075	47,129

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

Despite its decreasing trend over the past decade, KCN remains the most common indication for keratoplasty in Iran. It has been the top indication for corneal transplantation in other countries such as Germany, New Zealand, Zimbabwe, and Italy^[3-5,16] [Table 3]. In a study by Ziaei et al, the annual incidence rate of KCN including suspected cases in an Iranian population was estimated as 25 per 100,000, Such a high incidence was comparable with rates in other studies in Asian ethnic populations and seems to be due to possible role of genetic and/or climatic factors, as well as the high prevalence of vernal keratoconjunctivitis.^[2,17] The decreasing trend of KCN as an indication for corneal transplantation over the past decade in Iran may be attributable to recent resurgence of interest in less invasive interventions including intracorneal ring implantation and collagen corneal cross-linking (CXL) in cases with moderate KCN. Furthermore, the rate of KCN could have been dwarfed by the increasing rates of BK and graft failure.

In the current study, bullous keratopathy (PBK/ABK) was the second most common indication for corneal transplantation. The number of keratoplasties due to BK has increased over the past 8-year period. In spite of improvements in the techniques of cataract surgery and intraocular lens (IOL) design, BK remains as one of the most common indications for keratoplasty in Italy,^[16] New Zealand,^[4] Colombia^[18] and Canada.^[19]

This fact may be explained by the high frequency of cataract surgery performed around the world. On the contrary, BK is not common in Far East regions such as China^[20] and Nepal.^[21] This may be due to the lower number of cataract surgery and Fuchs' endothelial dystrophy, which is an important cause of BK, in these two countries^[20] [Table 3]. The percentage of PBK cases in the current study was approximately twice higher than that of our previous report;^[2] which may be due to the shift in the technique of cataract surgery from extracapsular cataract extraction to the phacoemulsification.^[22]

Infectious keratitis comprised about 5% of all keratoplasties in the present study and the trend did not change significantly from 2008 to 2013. Frigo et al reported a similar rate in Italy (4.9%).^[16] In contrast, infectious keratitis has been reported as a prevalent indication for keratoplasty in China^[20] and Nepal^[21] [Table 3]. One explanation for the high rate of infectious keratitis may be limited medical resources and inadequate donor corneas for managing emergency cases in these countries.^[20]

Our study showed no significant change of trend in the rate of corneal dystrophies over the last decade. Similar to previous reports,^[2,23] more than half of the corneal dystrophies requiring corneal transplantation in the current study were macular corneal dystrophy. Fuchs' endothelial dystrophy which is the top indication

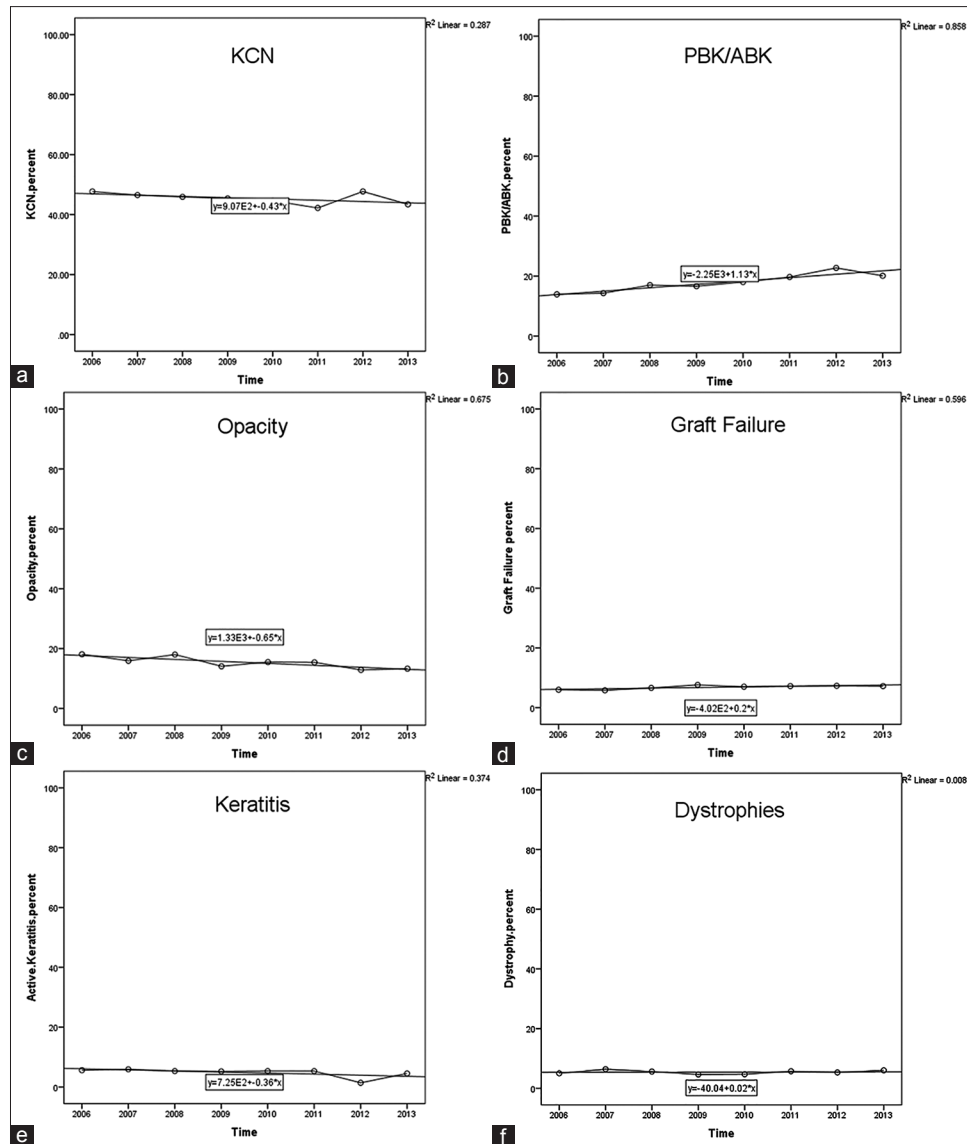


Figure 1. Trends of the leading indications for keratoplasty in Iran. (a) Keratoconus was the most common indication for keratoplasty, showing no statistically significant change of trend with regression analysis ($P = 0.172$). (b) An increasing trend was noted in BK ($P = 0.001$) and (d) graft failure ($P = 0.025$). (c) Corneal opacities and scar demonstrated a decreasing trend ($P = 0.012$). (e and f) Corneal dystrophies and keratitis fluctuated over this 8-year period and did not show any statistically significant change. The regression R2 measures the goodness of fit of the regression line.

Table 3. Indications for corneal transplantation in the current study versus studies performed during the same period

	Iran (current study) 2006-2013 Kanavi et al (n=47,129) (%)	New Zealand 2000-2009 Cunningham et al ^[4] (n=2205) (%)	Italy 2002-2008 Frigo et al ^[16] (n=13,173) (%)	Canada 2002-2011 Tan et al ^[19] (n=4843) (%)	Colombia 2004-2011 Galvis et al ^[18] (n=450) (%)	China 2005-2010 Wang et al ^[20] (n=875) (%)	Nepal 2005-2010 Bajracharya et al ^[21] (n=645) (%)
Keratoconus	45.3	41.1	41.3	15.5	12.7	11.2	7
PBK/ABK	18.2	13.9	23.5	17.4	34.6	8.5	9
Corneal opacity and scar	15.2	3.7	6	6.8	15.7	4.8	26.8
Re-graft	6.9	17	17.4	17.1	7.7	6.7	11.2
Active keratitis	4.7	7.9	4.9	9.3	14.4	56.2	40.9
FED	1.3	8.2	7.2	18.9	7.5	3.4	1.7

n, total number of corneal transplants; PBK/ABK, pseudophakic/aphakic bullous keratopathy; FED, Fuchs' endothelial dystrophy

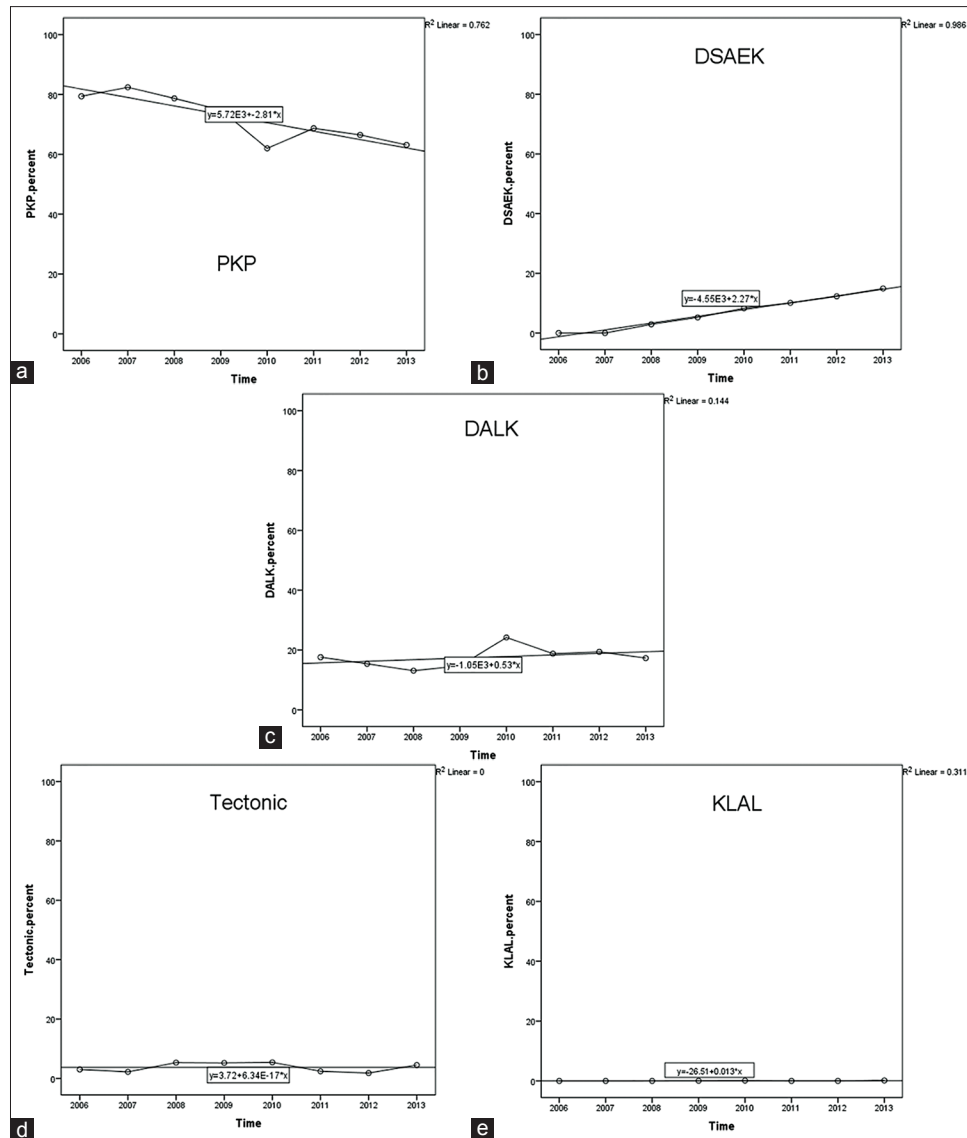


Figure 2. Trends of surgical techniques for keratoplasty from 2006 to 2013 in Iran. (a) PKP was the top technique of corneal transplantation, showing a statistically significant decreasing trend with regression analysis ($P = 0.005$). (b) An increasing trend was noted for DSAEK ($P < 0.001$). (c-e) DALK, tectonic, and KLAL fluctuated over this 8-year period but did not show a significant change of trend. The regression R2 measures the goodness of fit of the regression line.

for keratoplasty in Western countries^[4,8,10,19] ranked second in our study. This finding is in line with the results of previous reports.^[2,14] This difference may be explained by the aging population in the western countries.^[19] Furthermore, earlier surgical intervention employing DSAEK or Descemet’s membrane endothelial keratoplasty (DMEK) in cases with Fuchs’ endothelial dystrophy in western countries^[19] may be another reason for such a difference.

Other minor eye banks in Iran were established after 2015. The period of our study was between 2006 and 2013. The Central Eye Bank of Iran, located in the capital of Iran, Tehran, has been the only eye bank during the study period which supplied tissue requirements for corneal and scleral grafts throughout the country.

^[2,23] The number of transplants performed in Iran has increased steadily, from 19,668 PKPs between 1994 and 2004 (average, 1,788 PKPs per year),^[2] to 33,476 PKPs between 2006 and 2013 (average, 4,184 PKPs per year). An increase in the number of available donor tissues, as well as improved surgical techniques are possible explanations for the increasing number of corneal transplantations performed in Iran. Other studies from Canada,^[19] USA^[24] and Italy^[16] have shown comparable results [Table 4].

In addition to changes in the relative frequency of indications, our study demonstrated a significant change of trend in surgical techniques of corneal grafting over the past 8 years in Iran. PKP was the most prevalent technique for corneal transplantation in Iran. In contrast

Table 4. Techniques of corneal transplantation in the current study versus studies performed during the same period

	Iran (current study) 2006-2013 Kanavi et al (n=47,129) (%)	New Zealand 2000-2009 Cunningham et al ^[4] (n=2205) (%)	Canada 2002-2011 Tan et al ^[19] (n=4843) (%)	Italy 2002-2008 Frigo et al ^[16] (n=13,173) (%)	Colombia 2004-2011 Galvis et al ^[18] (n=450) (%)	USA 2009-2013 EBAA ^[24] (%)
PKP	71	90	86.5	81.5	89.6	49.3
AK	17.7	6.2	0.6	12.5	-	2
EK	7.5	2.8	12.9	6	10.5	40.5
Tectonic	3.7	0.3	-	-	-	-

n, total number of corneal transplants; EBAA, Eye Bank Association of America; PKP, penetrating keratoplasty; AK, anterior keratoplasty; EK, endothelial keratoplasty

to the increasing trend of DSAEK, the rate of PKP demonstrated a decrease over the 8-year period. The shift in the technique of corneal transplantation from full-thickness PKP to anterior and posterior lamellar keratoplasty in Iran during this period parallels the report by the Eye Bank Association of America in 2013, demonstrating that lamellar techniques particularly endothelial keratoplasty have supplanted PKP in the USA over the past decade.^[24]

Although the rate of DALK has increased from 813 cases in 2006 to 1,224 cases in 2013, the relative ratio remained stable over this period. Other studies have shown different results.^[19,25,26] Reporting on the trends of techniques for corneal transplantation in Ontario, Canada from 2002 to 2012, Zhang et al^[25] observed a continual increase in the number of DALK cases performed for KCN, specifically from 2011 to 2012, constituting approximately 30% of all corneal grafts for KCN.^[25] Other published data from British Columbia, Canada during a similar time period also indicated a growing trend of DALK after the Anwar and Teichman big bubble technique was implemented in 2009. However, DALK accounted for only 0.6% of all corneal grafts.^[19] In the UK, big-bubble DALK constituted 8.8% and 40.1% of all transplantations for KCN in 1999-2000 and in 2008-2009, respectively.^[26] In the USA, although there was a 34.5% increase of using corneal tissue for anterior lamellar keratoplasty (ALK) in 2010, it markedly decreased in the subsequent years; so that the DALK accounted for 2% of all keratoplasties performed in 2013 in the USA.^[15,24] DALK, in comparison with PKP entails longer surgical time and has a steep learning curve,^[19] which may be the main reasons for the lack of increase in the trend of DALK in our study.

The present study exhibited an increasing trend in endothelial keratoplasty (DSAEK) from 2.90% in 2008 to 14.9% in 2013. Such an increasing trend is comparable to reports from the USA,^[24] Canada,^[19] Italy,^[16] New Zealand^[4] and Colombia.^[18] This technique has now become the most common corneal graft procedure in the USA^[24] [Table 4]. This ascending trend may be due to the advantages of endothelial keratoplasty in comparison to PKP such as fewer ocular surface complications, reduced

risk of wound dehiscence,^[15] decreased rejection rate^[19] and faster visual recovery^[15] in addition to improved surgeons' experience.

Keratolimbic allograft (KLAL) was introduced in a few tertiary eye centers in Iran in 2009 for patients with bilateral total limbal stem cell deficiency. The number of KLAL surgeries was small and had no significant change in trend, which might be due to the small number of patients scheduled for this type of surgery.

In summary, KCN was the top indication for corneal transplantation in Iran, followed by BK over the 8-year period. There was a shift from PKP to DSAEK for corneal decompensation, and from PKP to DALK for KCN.

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Conflicts of Interest

There are no conflicts of interest.

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