

Changing Indications for Penetrating Keratoplasty in Greece, 1982–2006: A Multicenter Study

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Purpose: To evaluate the leading indications for penetrating keratoplasty (PKP) and their trends in Greece during the period 1982 to 2006.

Methods: Retrospective data review of 1,929 patients (2233 eyes) who underwent PKP in the period between 1982 and 2006 at three cornea transplantation units of three hospitals in Greece (Athens General Hospital, Heraklion University Hospital of Crete, and Thessaloniki University Hospital). Indications were classified into nine different groups: keratoconus, herpes simplex keratitis, microbial (nonviral) keratitis (fungal, bacterial, and acanthamoeba), aphakic/pseudophakic corneal edema, posttraumatic corneal scars, chemical/thermal injury, regrant, Fuchs' endothelial dystrophy, and other.

Results: The leading indications for PKP, in order of decreasing frequency, were aphakic/pseudophakic corneal edema (n = 649 [29.1%]), keratoconus (n = 580 [26%]), regrant (n = 265 [11.9%]), microbial (nonviral) keratitis (n = 188 [8.4%]), posttraumatic corneal scar (n = 171 [7.7%]), herpes simplex keratitis (n = 104 [4.6%]), Fuchs' endothelial dystrophy (n = 104 [4.6%]), chemical/thermal injury (n = 61 [2.7%]), and other (n = 111 [5%]). The prevalence of regrafts as an indication for PKP increased during the study period.

Conclusions: Aphakic/pseudophakic corneal edema was the most common indication for PKP in a multicenter series in Greece followed by keratoconus. The number of regrafts dramatically increased during the 25-year period.

Key Words: penetrating keratoplasty, indications, aphakic/pseudophakic corneal edema, keratoconus, regrant

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Penetrating keratoplasty (PKP) is one of the most widely practiced types of transplantation in humans.¹ In 1844, Richard Kissam² first transplanted a pig cornea into a human recipient eye and Zirm³ reported the first successful full-thickness human corneal graft in 1906. Since then, corneal transplantations significantly increased, especially after the establishment of the first eye bank in 1944.

During the last 50 years, the indications for PKP have changed.^{4–36} In most studies, bullous keratopathy^{6–11} seems to be the major indication for PKP in the developed countries, whereas infectious corneal diseases and corneal scars^{12–16} are more prevalent in the developing countries. The purpose of this multicenter study, to our knowledge the first from Greece, is to examine the leading indications for PKP and their trends during the period from 1982 through 2006.

METHODS

A retrospective data review was conducted on 1929 patients (2233 eyes) who underwent PKP at three cornea transplantation units of three hospitals in Greece (Athens General Hospital, Heraklion University Hospital of Crete, Thessaloniki University Hospital) during the period between January 1982 and December 2006. The study includes 951 women (42.6%) and 1282 men (57.4%), and the mean patient age was 50.8 ± 10.3 years (range, 18 months to 84 years).

Penetrating keratoplasty indications were divided into nine different groups: keratoconus, herpes simplex keratitis (HSK) (active and inactive cases), microbial (nonviral) keratitis (active and inactive cases), aphakic/pseudophakic corneal edema, posttraumatic corneal scars, chemical/thermal injury, regrant, Fuchs' endothelial dystrophy, and other.

Chi-square test was used for statistical analysis. A *P* value <0.05 was considered statistically significant.

RESULTS

The leading indication for PKP during the 25-year period was aphakic/pseudophakic corneal edema (n = 649 [29.1%]). The other causes of PKP in descending order were keratoconus (n = 580 [26%]), regrant (n = 265 [11.9%]), microbial (nonviral) keratitis (n = 188 [8.4%]), posttraumatic corneal scar (n = 171 [7.7%]), HSK (n = 104 [4.6%]), Fuchs' endothelial dystrophy (n = 104 [4.6%]), chemical/thermal injury (n = 61 [2.7%]), and other (n = 111 [5%]) (Table 1).

During the period from 1982 to 1986, aphakic/pseudophakic corneal edema was the most common indication (n = 22

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TABLE 1. Leading Indications for Penetrating Keratoplasty (PKP) in Greece Between 1982 and 2006

PKP Indication	1982–1986 n (%)	1987–1991 n (%)	1992–1996 n (%)	1997–2001 n (%)	2002–2006 n (%)	1982–2006 n (%)
Aphakic/pseudophakic corneal edema	22 (37.3)	62 (35)	115 (26.4)	231 (27)	219 (31)	649 (29.1)
Keratoconus	20 (33.9)	57 (32.2)	117 (26.8)	220 (25.7)	166 (23.5)	580 (26)
Regraft	0 (0)	7 (4)	27 (6.2)	105 (12.3)	126 (17.9)	265 (11.9)
Microbial (nonviral) keratitis	1 (1.7)	6 (3.4)	51 (11.7)	75 (8.8)	55 (7.8)	188 (8.4)
Posttraumatic corneal scars	0 (0)	8 (4.5)	36 (8.3)	82 (9.6)	45 (6.4)	171 (7.7)
Herpetic keratitis	6 (10.2)	9 (5.1)	27 (6.2)	40 (4.7)	22 (3.1)	104 (4.6)
Fuchs' endothelial dystrophy	0 (0)	7 (4)	28 (6.4)	35 (4.1)	34 (4.8)	104 (4.6)
Chemical/thermal injury	0 (0)	1 (0.6)	18 (4.1)	25 (2.9)	17 (2.4)	61 (2.7)
Other	10 (16.9)	20 (11.2)	17 (3.9)	42 (4.9)	22 (3.1)	111 (5)
Total	59	177	436	855	706	2233

[37.3%]). Aphakic/pseudophakic corneal edema, keratoconus, and herpes simplex virus account for 81.4% (161 eyes) of all surgeries. The following 5 years (1987–1991), the main PKP diagnosis was aphakic/pseudophakic corneal edema (n = 62 [35%]), keratoconus (n = 57 [32.2%]), and others (n = 19 [10.7%]). Keratoconus was the predominant indication in the period between 1992 and 1996 (n = 117 [26.8%]) followed by aphakic/pseudophakic corneal edema (n = 115 [26.4%]) and microbial (nonviral) keratitis (n = 51 [11.7%]). During the last decade (1996–2006), aphakic/pseudophakic corneal edema was the first and keratoconus the second indication for PKP. Regrafting became the third most common reason for PKP with constantly increasing tendency from 1982 to 2006.

During the interval studied (1982–1986 versus 2002–2006), a significant increase in the prevalence of regrafts ($P < 0.001$), microbial (nonviral) keratitis ($P = 0.005$), and post-traumatic corneal scar ($P = 0.008$) was observed, whereas the prevalence of HSK significantly decreased over time ($P = 0.037$).

DISCUSSION

In the current study, we report the clinical indications for PKP in 2233 cases from three university hospitals in Greece between the years 1982 and 2006. To the best of our knowledge, this is the first study of this type in this location. The major indications for PKP in this report were aphakic/pseudophakic corneal edema (29.1%), keratoconus (26%), regraft (11.9%), microbial (nonviral) keratitis (8.4%), post-traumatic corneal scar (7.7%), HSK (4.6%), Fuchs' endothelial dystrophy (4.6%), chemical/thermal injury (2.7%), and others (5%).

Aphakic/pseudophakic corneal edema was the leading indication for PKP in our report, which is in accordance with many studies from all over the world.^{6–11,17–26} Some of them conclude that the prevalence of bullous keratopathy has decreased^{6,10,27–30} over the past decade. There was also a decrease tendency in the relative frequency in our study, from 37.2% (1982–1986) to 31% (2002–2006), but this difference was not statistically significant ($P = 0.065$).

Keratoconus was the second most common reason for PKP in our study and it was the predominant indication during the period 1992 to 1996. This is in accordance with previous

reports that describe keratoconus as one of the major^{6–8,10,11,13–29} or the leading indication for PKP.^{9,30–36} At the same time, in reports from the United States, China, India, and Taiwan,^{12–16} the proportion of keratoconus as an indication for PKP is low. This discrepancy may be the result of genetic demographics and/or climatic factors that may contribute to a higher prevalence of keratoconus in certain geographic areas. Indeed, keratoconus was the leading indication for PKP in a study by Frucht-Pery and associates in the neighboring Israel.³⁴

Regraft was the third most common indication for PKP in our study with a statistically significant constantly increasing prevalence ($P < 0.001$) from 0% (1982–1986) to 17.9% (2002–2006). This trend is similar in many reports^{8,10,14,27,30,36} and probably reflects the increasing number of PKP recipients in the population. In Dorrepaal et al's retrospective study, regraft was the leading indication for PKP²⁸ and many studies agree that graft replacement is one of the predominant reasons for surgery.^{4–11,17–36}

Microbial (nonviral) keratitis (8.4%), corneal scar (7.7%), HSK (4.6%), Fuchs' endothelial dystrophy (4.6%), and chemical/thermal injury (2.7%) are the next most common causes for PKP in our study. The majority of the herpes simplex virus keratitis and microbial (nonviral) keratitis cases were postinfectious scarring. We further noted a significant increase in the prevalence of microbial (nonviral) keratitis ($P = 0.005$) and posttraumatic corneal scars ($P = 0.008$) over time, which is in agreement with Dobbins et al's study.¹⁰ This tendency is probably the result of the expansion of the indications for PKP to other pathologies. Infectious keratitis and corneal scars seem to be major indications in China,^{13,14} India,^{10,11} and Taiwan.¹²

On the other hand, we found a statistically significant decrease in the prevalence of HSK ($P = 0.037$). This finding could be explained by the improvement in medical management of herpetic corneal infections and the use of oral acyclovir. Similar findings were reported in a number of other studies.^{6,29,30,36} Fuchs' endothelial dystrophy (4.6%) was the next more common indication in our report. The prevalence of Fuchs' endothelial dystrophy in other studies varies from 2.6%³⁶ to 23.2%^{10,14} but in most studies is one of the top six indications worldwide.^{4–36} Fuchs' dystrophy is relatively rare in the Middle East and Mediterranean basin but quite common in Scandinavia, northern Europe, and the American Midwest.

Many parameters may influence the indications for PKP in the future. Today, new grafting methods like Descemet's stripping endothelial keratoplasty are also performed for Fuchs' endothelial dystrophy or bullous keratopathy; post-cataract patients have a longer life expectancy; there is also higher availability of donor tissue that may further extend indications for PKP. Therefore, more studies from different regions are necessary to detect the changes to predict future directions in the field.

In conclusion, the data examined from three cornea transplantation units in Greece showed that the total number of keratoplasties increased dramatically from 1982 to 2006, probably as a result of more trained cornea surgeons as well as the expansion and improvement in the eye bank network system in the United States and Europe that increases the availability of donor corneas. Aphakic/pseudophakic corneal edema was the leading indication for PKP. The relative frequency of regrafts, non-HSK, and traumatic corneal scars significantly increased, whereas the prevalence of HSK decreased during the 25-year period.

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