Corneal Transplantation Activity Over 7 Years: Changing Trends for Indications, Patient Demographics and Surgical Techniques From the Corneal Transplant Epidemiological Study (CORTES)

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ABSTRACT

This study aims to examine evolving indications and changing trends for corneal transplantation in Italy. Corneal transplantations performed with donor tissues distributed by the Veneto Eye Bank Foundation between 2002 and 2008 were prospectively evaluated. Of the 13,173 keratoplasties performed on 11,337 patients, 10,742 (81.5%) were penetrating (PK), 1644 (12.5%) were anterior lamellar (ALK), and 787 (6.0%) were endothelial (EK). Keratoconus (42.5%), regraft (18.9%), and pseudophakic bullous keratopathy (PBK, 11.9%) were the leading indications for PK, with keratoconus (69.6%) and regraft (6.5%) showing higher indications for ALK, whereas pseudophakic bullous keratopathy (50.1%) and regraft (18.7%) were the major indications for EK. There was an overall decrease observed in corneal grafting for keratoconus ($P = .0048$) and an increase for PBK ($P = .0653$) and regrafting ($P = .0137$). These indications differed by age and gender. The number of keratoplasties over 7 years was stable ($P = .2394$), although the annual number of PKs declined by 34.0% ($P = .0250$), ALKs began to rise from 2005 ($P = .0600$), whereas EKs showed a huge growth, with their number tripling in 2007 and further doubling in 2008 ($P = .0004$). Leading indications for keratoplasty showed similar data that have been reported elsewhere for Western countries over the past few decades, albeit with a higher percentage of keratoconus. However, the overall number of keratoplasties for keratoconus was in decline, whereas regraft keratopathy and PKs increased due to the application of the newer surgical techniques for corneal grafting. This highlights an important shift in managing corneal diseases toward the application of selective and more conservative surgeries and changes in indications in corneal transplantation.

DISEASES affecting the cornea are a major cause of blindness, second only to cataract in overall importance, and it is estimated that 23 million people worldwide have unilateral corneal blindness due to disease or injury [1].

The cornea is the transparent, dome-shaped surface of the eye that accounts for a large part of the eye's focusing power. At the microscopic level, the cornea comprises 5 morphologically distinct layers: (1) a stratified epithelium, which contributes to maintenance of optically smooth corneal surface, and provides a barrier to external biological and chemical insults; (2) the Bowman's layer (Bw), an acellular layer that does not regenerate after injury; (3) a highly organized collagenous stroma, whose anatomic and biochemical properties assure physical strength, stability of shape, and transparency of the cornea; (4) the Descemet membrane (DM), the basement membrane of a (5) single-cell layer endothelium, which maintains hydration of corneal stroma, functional

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corneal thickness and transparency. Alterations of corneal structure (stromal scars; blood vessel growth over the corneal surface; deposited materials in the stroma; keratoconus, where cornea loses its uniform oval shape and become conic) or function (endothelial cells deficiency) affect vision.

Therefore, corneal transplantation, also named corneal grafting or keratoplasty, remains the primary sight restoring method for corneal blindness. It consists of a surgical procedure to replace the diseased cornea with a healthy donor cornea. Depending on the corneal disorder, several surgical techniques to replace lamellar or full-thickness host corneal tissue have been developed. When a lamellar transplant is performed, only the anterior layers of the cornea (epithelium, Bw, and all or part of the stromal layers), or only the posterior layers of the cornea (posterior stroma, DM, and corneal endothelium), are substituted. In a full-thickness corneal transplant, all layers of the recipient cornea are replaced.

Historically, corneal transplant development began with the replacement of the anterior stromal layers, a prototype technique of the modern anterior lamellar keratoplasty (ALK), described by Mühlbauer in 1840 [2], more than a half century before the first successful full-thickness corneal transplantation (also known as penetrating keratoplasty [PK]), which was performed by Eduard Zirm in 1905 [3]. Indeed, despite the remarkable Zirm experience, the lamellar technique remained preferred among surgeons until Castroviejo improved the technique for PK and Filatov demonstrated the applicability of corneal tissues obtained after the donor's death [4,5].

The development of eye banks during the 1940s meant that corneal tissues became more readily available and the number of PKs steadily increased. The more comprehensive knowledge of the physiological role of corneal layers, the spreading use of antibiotics and corticosteroids, and the improvement of surgical techniques and instruments during 1960s and 1970s led to the PK becoming the gold standard for the treatment of corneal diseases and the most commonly performed procedure [6–8], whereas ALK remained devoted to recovering the structure of the cornea and not primarily for visual purposes [9].

Though PK has achieved great success, it presented several drawbacks, including post-keratoplasty astigmatism, corneal wound dehiscence, recurrent allograft rejection, and early and late endothelial failure.

The rapid evolution of supportive surgical technologies during the 1980s, developed principally for refractive corneal surgery, renewed the interest in lamellar techniques, which were thought to overcome some of the weaknesses of PK. From the mid-1990s, innovative procedures were developed and adopted to remove diseased corneal anterior stroma up to the DM [10,11]. As a result, Deep Anterior Lamellar Keratoplasty (DALK) became the leading surgical approach for the treatment of corneal pathologies in which the recipient endothelium is unaffected by the disease [12,13].

The 1990s also saw the advent of endothelial keratoplasty (EK), developed by Melles et al, as the first posterior lamellar keratoplasty of its kind [14], exclusively designed for the treatment of endothelial pathologies, and later modified and renamed as deep lamellar endothelial keratoplasty (DLEK) by Terry and Ousley [15]. A further advancement was made by Melles himself, by the selective stripping of the DM (termed Descemet stripping endothelial keratoplasty [DSEK]) [16], followed by Gorovoy, who modified the technique by preparing the donor tissue with a microkeratome (Descemet stripping automated endothelial keratoplasty [DSAEK]) [17]. The last revolutionary technique originates once again with Melles et al, who describe the Descemet membrane endothelial keratoplasty (DMEK), the transplantation of an isolated donor DM carrying its endothelium [18]. EK procedures have rapidly gained popularity for transplantation in patients with corneal endothelial diseases [19].

At the same time, advances in the medical management of certain corneal diseases, changes in population demographics and in the incidence of primary and secondary corneal disorders, and the spreading of some eye surgical procedures, particularly cataract and intraocular lens (IOL) implantation, affected patterns in the clinical indications of corneal transplantation and numbers of grafts [20]. These changes have significant effects on the epidemiology of corneal transplantation among countries [21,22], and have important implications for ocular surgeons and eye banks to plan their activities.

To understand the epidemiology of corneal transplantation in Italy and to monitor long-term clinical results, the Veneto Eye Bank Foundation established the prospective CORneal Transplant Epidemiological Study (CORTES) [23,24]. The aims of this analytical report are to give an epidemiological overview of corneal transplantation in Italy over 7 years and to compare some results with data from the literature.

METHODS

The Veneto Eye Bank Foundation distributes >2000 corneal tissues every year in Italy, and this number represents ~40% of the corneal grafts performed in the country [25]. Corneas are allocated either as (a) corneoscleral rims stored in organ culture at 31°C; (b) corneal lenticules for ALK, either precut with a Hansatome microkeratome (Moria, Antony, France) or manually dissected and stored at 4°C in silica gel; or (c) precut corneas for EK prepared with a Hansatome microkeratome and stored in organ culture medium at 31°C.

The quality of each corneal tissue was assessed by light microscopy and slit lamp according to validated internal standard operating procedures prior to the delivery and/or processing of the tissues. Surgeons who received corneal tissues from January 1, 2002, to December 31, 2008, were requested to submit data on patient demographics, clinical history, and details on the type of intervention performed.

The study protocol was approved by the Ethics Committee for Human Experimentation of the University of Padua, in accordance with the Helsinki Declaration. Full details about the overall study protocol and the list of contributing surgeons were reported elsewhere [23].

Data were analyzed *per patient*, considering only the first graft received by each patient during the study, to describe the distribution

of corneal grafts with respect to recipient demographics. In addition, data were analyzed *per tissue*, including repeated grafting in the same eye or grafts also in the contralateral eye received by the same patient during the study, to examine indications for transplant and surgical procedures, to evaluate re-grafting, and to characterize patients with both eyes transplanted.

Results of descriptive analyses are expressed as mean and standard deviation (SD) for quantitative variables and as counts and percentages for categorical variables unless otherwise stated. Ages of males and females were compared for each type of surgery with the Mann-Whitney U (Wilcoxon) statistic. The χ^2 test was used to determine statistical significance of gender differences by indications. Linear regression on the number of tissues log transformed was used to analyze the time trend for type of surgery and results are reported as *P* values and estimates of the regression coefficient β. All *P* values were 2-tailed, and values of .05 or less were considered significant. Analyses were conducted with SAS statistical software version 9.2 (SAS Institute Inc, Cary, NC, United States).

RESULTS

From January 2002 to December 2008, 413 ophthalmic surgeons in 268 clinical centers performed 13,173 corneal transplantations, which included 10,742 (81.5%) PK, 1644 (12.5%) ALK, and 787 (6.0%) EK on 11,337 patients (58.8% males) with a mean age of 50.4 (±20.2) years, median 49 years, and 33–69 years interquartile range. Demographic data and clinical indications for the 11,337 patients are reported in Table 1.

The PK includes 126 (1.2%) tectonic grafts and 30 (0.3%) keratolimbal allografts. To perform ALK, surgeons cut donor corneas using a microkeratome (667; 40.6%), removed the DM to make the so-called *predescemetic* or *descemetic* DALK (485; 29.5%), and shaped corneal lenticules with a laser (93; 5.7%). Surgeons also used freeze-dried corneal lenticules, either precut by microkeratome (321; 19.5%) or manually dissected (78; 4.7%) in the eye bank.

In 397 (50.4%) cases, EK was performed with donor cornea endothelial lenticules precut with a microkeratome (DSAEK) in the eye bank or by surgeons in the operating room, in 383 (48.6%) cases, surgeons manually dissected the DM and endothelium of the donor corneas (DSEK), and in 7 (1%) cases, the lamellar dissection was femtosecond-laser assisted.

PK was the leading technique, with 82.0% of the patients receiving a full-thickness graft during the study; keratoconus was the leading indication, followed by regraft and pseudophakic bullous keratopathy (PBK). These 3 indications accounted for 71.1% of all PKs, whereas 74.9% of all ALKs were for keratoconus and regraft, and 68.7% of EKs were for PBK and regraft.

The association between the 3 most frequent indications and the sex of patients was statistically significant, with predominance of males among patients transplanted for keratoconus and females in those with PBK ($P < .0001$).

Males showed a median age of 44.0 years (range <1–97 years; mean 47.5, SD 19.6), in comparison with a median age of 55.0 years for females (range <1–101 years; mean 54.7, SD 20.2). Statistically significant differences were found for the median ages of males and females: 45 vs 56 years, 33 vs 38 years, and 72 vs 74 years in PK, ALK, and EK, respectively (Fig 1).

Table 1. Patient Demography and Clinical Indication for Type of Surgery (N = 11,337)

	PK n (%)	ALK n (%)	EK n (%)
Gender			
Male	5493 (59.1)	903 (63.0)	275 (45.4)
Female	3804 (40.9)	531 (37.0)	331 (54.6)
Indication for keratoplasty			
Keratoconus*	4084 (43.9)	1034 (72.1)	0 (0.0)
Regraft†	1291 (13.9)	40 (2.8)	43 (7.1)
PBK‡	1235 (13.3)	0 (0.0)	373 (61.6)
Primary endotheliopathies§	666 (7.2)	0 (0.0)	159 (26.2)
Mechanical trauma	418 (4.5)	26 (1.8)	3 (0.5)
Noninfectious ulcerative keratitis	333 (3.6)	46 (3.2)	0 (0.0)
Viral/post-viral keratitis	278 (3.0)	49 (3.4)	1 (0.2)
Microbial/post-microbial keratitis	206 (2.2)	25 (1.7)	0 (0.0)
Aphakic corneal edema	201 (2.2)	1 (0.1)	20 (3.3)
Stromal corneal dystrophy	119 (1.3)	45 (3.1)	0 (0.0)
Optical/refractive	98 (1.1)	45 (3.1)	5 (0.8)
Chemical injuries	56 (0.6)	10 (0.7)	0 (0.0)
Congenital opacities	22 (0.2)	1 (0.1)	0 (0.0)
Other causes	290 (3.1)	112 (7.8)	2 (0.3)
Total	9297 (100)	1434 (100)	606 (100)

*Includes 28 cases of pellucid marginal degeneration and 25 cases of keratoglobe.
†Includes primary and late endothelial failure (n = 861), failure due to other causes (n = 411), and failure related to graft rejection (n = 102).
‡PBK = pseudophakic bullous keratopathy, includes patients with posterior chamber IOL implantation, 87.6% in PK and 97.1% in EK.
§Includes Fuchs dystrophy.

Age distribution in PK appeared bimodal (Fig 2), with peaks in the age groups of 30 to 39 years and 70 to 79 years (17.5% and 16.2% of the total patients who underwent PK, respectively) whereas in ALK and in EK the distribution showed only 1 peak, in the 20 to 29 and 70 to 79 years age groups, respectively, which comprises for 28.8% and 37.8% of the transplanted patients in the 2 groups.

The number of transplanted corneal tissues exceeded those of patients by 1836. Of these tissues, 822 were grafted in patients who had previously received a corneal transplant during the study period (610 patients were regrafted once and 96 twice or more often), showing an incidence of regrafting of 6.2% during the 7 years of observation. The remaining 1014 corneas were transplanted in patients already grafted in 1 eye during the study period (8.9% of patients with bilateral graft). In particular, 55.7% of these corneas (N = 565) were transplanted in patients with keratoconus (5.0% of patients with bilateral disease).

The overall trend in terms of numbers of corneal transplantations performed over the 7-year period (Fig 3) was stable ($P = .2394$, $\beta = +0.00521$). However, the annual number of PKs declined by ~34% from 2002 to 2008, a statistically significant trend ($P = .0250$, $\beta = -0.06026$), whereas the number of ALKs performed each year

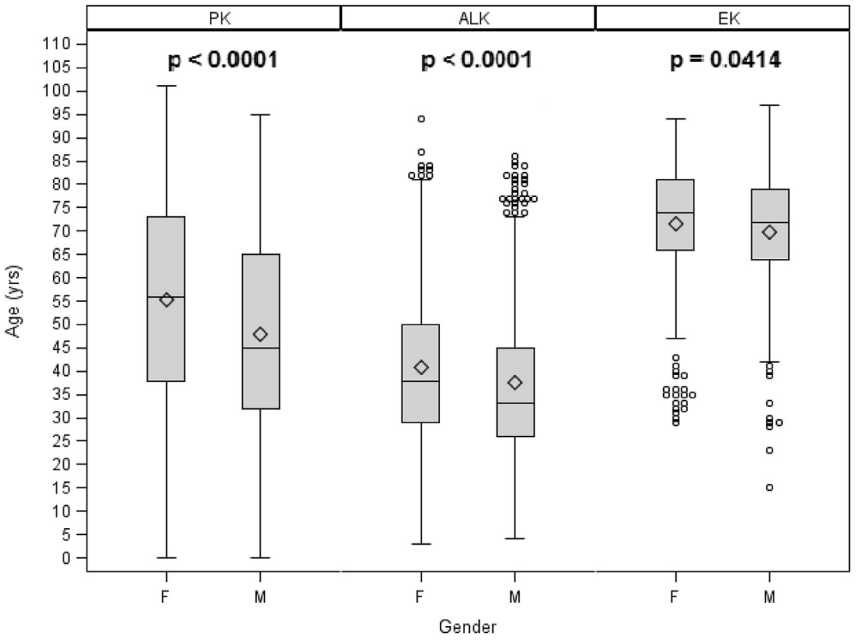

Fig 1. Patient demographics and type of keratoplasty (N = 11,337). Abbreviations: PK, penetrating keratoplasty; ALK, anterior lamellar keratoplasty; EK, endothelial keratoplasty; F, females; M, males.

remained fairly stable ($P = .0600$, $\beta = +0.10590$), although the annual number almost tripled from 2004 to 2008. EK showed a significant increased trend ($P = .0004$, $\beta = +1.08713$) and surprising growth in real numbers, which tripled in 2007 and further doubled in 2008 with respect to 2006.

Time trends for the 3 main indications (that explain 73.5% of all transplanted corneas) are illustrated in Fig 4. A statistically significant decreasing trend was found for keratoconus ($P = .0048$, $\beta = -0.04490$), for which the overall number of keratoplasties dropped by nearly 27.0% during the study period. On the contrary, interventions for PBK doubled ($P = .0653$, $\beta = +0.09429$) starting from 2006, due to the application of EK for certain corneal disorders, and regraft increased by one-third ($P = .0137$, $\beta = +0.04919$) between 2005 and 2008.

Variations in surgical techniques also has influenced the activity in the eye bank. New criteria to evaluate donor cornea suitability and new methods to process donor corneas were developed, enabling surgeons to receive the appropriate tissue for the intended graft. Such adjustments increased the number of corneas suitable for transplantation and the overall utilization of donor corneas by 15.0% and 18.0% between 2002 and 2008, respectively.

DISCUSSION

This study provides the first in-depth assessment of the epidemiology of corneal transplantation in Italy and is one of very few surveys centered around a single eye-bank database. The broad quantity of information gives the opportunity to compare our results with those published in the literature or provided by national and international institutions. The total number of corneal transplantations performed over the 7-year period proved to be stable, which is a rather common trend also shown during the first half of the past decade by countries with a long history of corneal transplantation [7,8,25,26], possibly related to the reduced incidence of specific corneal diseases, for example postinfective and postinjury corneal scars, that conversely characterize case series in countries with a more recent history of corneal transplantation [27]. However, in the 5 years following the end of the study, the mean annual number of corneas provided for keratoplasty increased of ~24.0%, from 1881 in 2002–2008 to 2341 in 2009–2013, a figure comparable to that in the United States, where the reported mean annual number of corneal transplants increased by 23.0%, from 35,000 in 2002–2008 to ~43,000 in 2009–2013 [7].

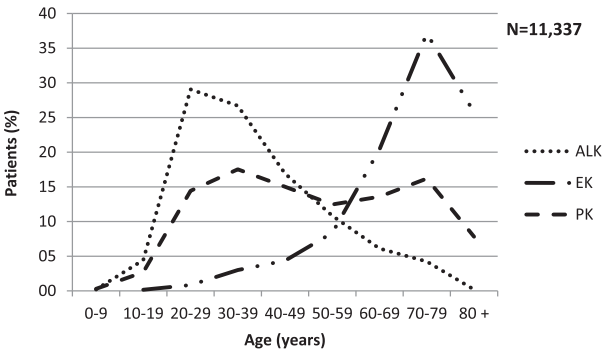

Fig 2. Distribution of patients by age (in decades), gender, and type of surgery over the period 2002–2008 (N = 11,337). Abbreviations: PK, penetrating keratoplasty; ALK, anterior lamellar keratoplasty; EK, endothelial keratoplasty.

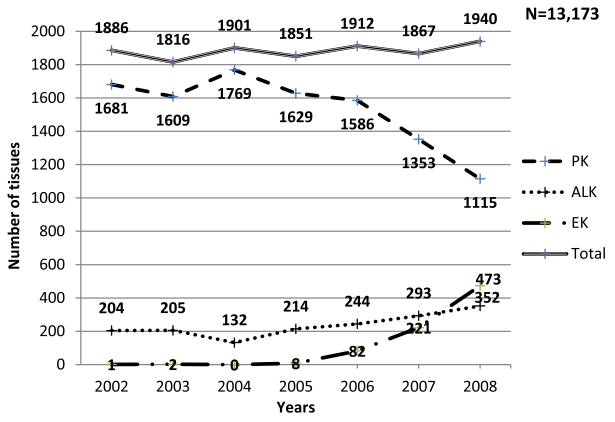

Fig 3. Distribution of corneal grafts by type of surgery during the years 2002–2008 (N = 13,173). Abbreviations: PK, penetrating keratoplasty; ALK, anterior lamellar keratoplasty; EK, endothelial keratoplasty.

The recent variation in the number of grafts performed in the United States is of the highest interest because it goes together with the increased popularity of EK, now spreading across Europe, and challenges possible sophisticated estimations on the potential decline in the number of corneal transplantations [28].

In fact, the annual number of EKs is increasing and that of PKs is declining, both in Europe and in the United States, where starting from 2011 EKs overtook PKs, demonstrating the current revolution in the surgical approach of corneal transplantation (Fig 5). Likewise, starting from 2005 we observed an increasing trend in the number of corneas provided for EK among Italian surgeons, which rapidly accounted for 24.4% of all corneas distributed in 2008, and reached 32.4% in 2013.

Our results also showed that the proportion of lamellar keratoplasty (either anterior or posterior) as a percentage of total grafts increased from 10% in 2002–2006 to 30% in the last 3 years of study (mean values). Although this growth is mainly due to the incidence of EKs, our findings are comparable to data reported by a number of other case series for lamellar keratoplasty [12,29].

Keratoconus, regraft, and PBK were the top 3 indications, in decreasing order, for keratoplasty in our study. Compared with 9 studies referring to nearly the same period (Table 2), we found these 3 indications to be the most frequent in Western and Middle Eastern countries [30–35], accounting for at least 50% to 70% or more of all indications. On the contrary, statistics from countries in the Far East showed that ~60% to 70% of keratoplasties are performed for corneal scarring and infectious keratitis, the most common indications for surgery in such countries [27,36,37].

Keratoconus alone accounted for more than one-third of all keratoplasties, an incidence comparable only to that reported by the New Zealand National Eye Bank Study [30] and by Zare et al [31], more than double that of North America countries, and much different to that of the remaining surveys. Whether this finding might depend on different prevalence of the disease or therapeutic approaches, in terms of priority or techniques, merits further investigation. Nevertheless, we found that the graft requirements for keratoconus decreased by 27.0% over 7 years (Fig 4A), despite the increased number of ALKs that partially balanced the reduction in the PKs. A possible

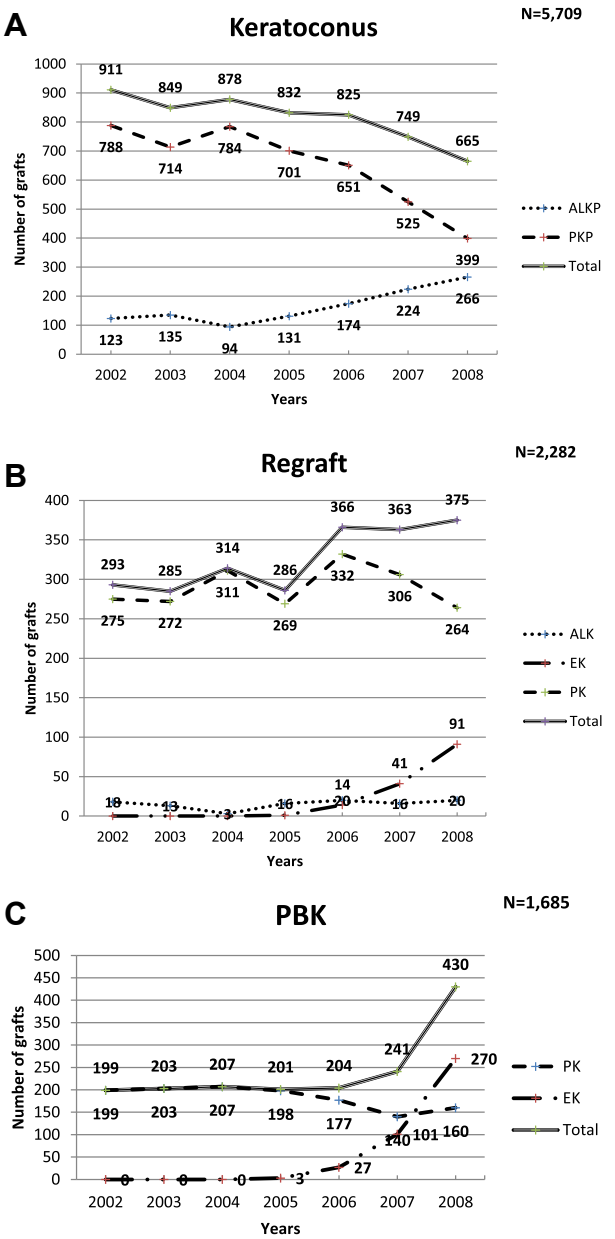

Fig 4. Distribution of corneal grafts by indications and type of surgery between 2002–2008 (N = 9676) for: (**A**) Keratoconus (N = 5709); (**B**) regraft (N, 2282); (**C**) PBK (N = 1685). Abbreviations: PBK, pseudophakic bullous keratopathy; PK, penetrating keratoplasty; ALK, anterior lamellar keratoplasty; EK, endothelial keratoplasty.

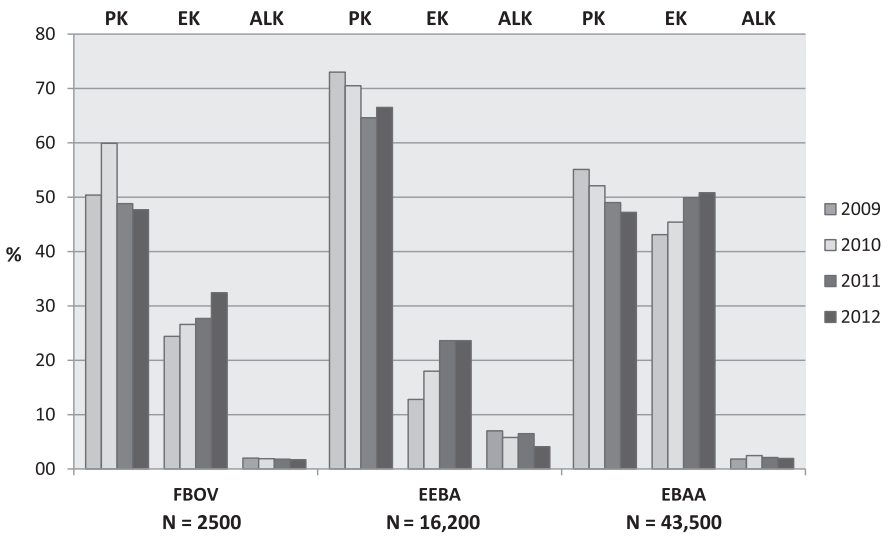

Fig 5. Comparison of corneal transplantation reported by the Veneto Eye Bank in 2009–2012 vs Europe (EEBA) and the United States (EBAA) in terms of different techniques (N = mean annual number). Abbreviations: PK, penetrating keratoplasty; ALK, anterior lamellar keratoplasty; EK, endothelial keratoplasty.

reason for the decline of PK in keratoconus could be the adoption of techniques shown to be effective in slowing or halting the progression of keratoconus, such as a greater use of contact lenses, intracorneal ring implantation or collagen cross-linking [38,39]. Considering intracorneal ring implantation, a study has been recently published by a single Italian center reporting 400 keratoconic eyes treated between April 2006 and April 2010, a very large number if we consider the number of patients with keratoconus treated in Italy each year by keratoplasty [40].

Regraft was the second most common indication in our study, and the mean number of grafts performed each year for replacing a failed graft paralleled that of other Western countries, whereas such numbers in the Middle East, Far East, and South America are 30% to 50% lower. Differences in the incidence of regraft among countries are difficult to interpret, mainly because each regraft is a consequence of a previous graft and the number of failed grafts is a proportion of the total grafts performed that accumulate in the short- and long-term follow-up. In our study, the increasing trend showed by regraft between 2002 and 2008 (3.8%) could be explained by the implementation of EK, largely adopted by ophthalmic surgeons to treat graft failure after PK but also applied to replace EK, due to the high incidence of failures during the learning curve [41].

The third indication in our study, PBK, deserves some particular consideration because corneal edema is the result of cataract and IOL surgery, the most frequent surgical intervention worldwide. Despite the increased understanding of the causes of PBK and the improvement in cataract and IOL techniques, PBK was the leading indication in the United States (28.4%) and Colombia (34.6%), the second leading indication in the United Kingdom (15.8%), and also the most frequent indication in India (13.5%) after keratitis and corneal scarring (Table 2). In our study, PBK was shown to increase rapidly after the introduction of EK and to overcome PK, especially in those patients, mostly aged (Fig 2), for whom a full-thickness graft has a lesser chance of being a safe, successful, and lasting therapeutic solution. In this regard, EK demonstrated faster visual recovery, better corneal biomechanical stability, and less chance of graft rejection [42].

Aside from the surgical interventions, patient demographics were also remarkable. Gender distribution showed a male predominance for PKs and ALKs, which could possibly be explained by the high prevalence of patients with keratoconus and the fact that this condition is more common in males than females, at least in our study. On the other hand, the higher number of females with PBK treated by EK is likely related to the higher prevalence of females in the elderly population.

In conclusion, trends in surgical techniques for keratoplasty have been driven primarily by clinical practice and our study demonstrates that ophthalmic surgeons are moving from the well-established and widely applied PK to customized techniques, such as EK and ALK, in relation to indications for transplants and demographics, with the aim of applying the most reliable intervention.

Moreover, trends in corneal graft surgery for the 3 most frequent indications showed remarkable changes, possible due to ongoing treatment alternatives available to manage keratoconus, other than keratoplasty; the advantage of EK in PBK and other endothelial dysfunctions; the continuing presence of regraft, or its increasing as well, because older grafts are expected to fail.

Finally, changes in surgical techniques and in indications for graft affect the approach of eye banks in selecting and distributing donor corneas, as tissues with poor endothelial cell density should be delivered for ALK, whereas tissues with stromal defects but satisfactory endothelial cell density should be provided for EK. This certainly helps to enhance the number of donor corneas available for corneal grafting, as shown in this study, providing ocular surgeons with the

Table 2. Indications for Corneal Graft Surgery in the Present Study and in Several Studies Performed During Almost the Same Period (Mean Annual Number of Grafts %)

	Italy 2002–2008 n = 13,173 present study	New Zealand 2000–2009 n = 2205 Cunningham [30]	Iran 2004–2009 n = 1859 Zare [31]	U.K. 1999–2009 n = 22,779 Keenan [32]	U.S. 2001–2005 n = 1162 Ghosheh [33]
Keratoconus	41.3	41.1	38.4	24.0	16.0
Regraft	17.4	17.0	10.6	14.6	22.0
PBK	16.3	13.9	11.7	15.8	28.4
Primary endotheliopathies*	7.2	10.7	1.2	19.5	14.0
Infectious keratitis	4.9	7.9	10.1	7.6	6.7
Corneal scarring†	6.0	3.7	16.0	6.0	10.0
Others	6.9	5.7	12.0	12.5	2.9

	Canada 2002–2011 n = 4843 Tan [34]	Colombia 2004–2011 n = 450 Galvis [35]	China 2005–2010 n = 875 Wang [36]	Nepal 2005–2010 n = 645 Bajracharya [37]	India 1997–2003 n = 2022 Sony [27]
Keratoconus	15.5	12.7	11.2	7.0	2.4
Regraft	17.1	7.7	6.7	11.2	11.5
PBK	17.4	34.6‡	8.5	9.0	13.5‡
Primary endotheliopathies*	19.3	7.5	3.4	1.7	3.8
Infectious keratitis	9.3	14.4	56.2	40.9	28.4
Corneal scarring†	6.8	15.7	4.8	26.8	38.0
Others	14.6	7.5	9.2	3.4	2.4

Abbreviation: PBK, pseudophakic bullous keratopathy.
*Includes Fuchs dystrophy.
†Includes burn, trauma, stromal dystrophy.
‡Includes aphakic bullous keratopathy.

most suitable corneal tissue for the particular corneal disease of each patient.

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REFERENCES

[1] Oliva MS, Schottman T, Gulati M. Turning the tide of corneal blindness. Indian J Ophthalmol 2012;60:423–7.
[2] Geerling G, Duncker GI, Krumeich J, Melles GR. Lamellar keratoplasty. Back to the future? Ophthalmologe 2005;102:1140–8.
[3] Zirm E. Eine erfolgreiche totale keratoplastik. Graefes Arch Clin Exp Ophthalmol 1906;64:580–93.
[4] Filatov VP. Transplantation of the cornea. Arch Ophthalmol 1935;13:321–47.
[5] Laibson PR, Rapuano CJ. 100-year review of cornea. Ophthalmology 1996;103:S17–28.
[6] Moffatt SL, Cartwright VA, Stumpf TH. Centennial review of corneal transplantation. Clin Experiment Ophthalmol 2005;33:642–57.
[7] Eye Bank Association of America. 2013 Eye Banking Statistical Report. Washington, D.C., United States. April 2014.
[8] Hjortdal J, Armitage WJ, Jones GLA, Gareiss-Lok A. European Eye Bank Association Directory. 22nd ed. January 2014.
[9] Terry MA. The evolution of lamellar grafting techniques over twenty-five years. Cornea 2000;19:611–6.
[10] Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. J Cataract Refract Surg 2002;28:398–403.
[11] Marchini G, Mastropasqua L, Pedrotti E, et al. Deep lamellar keratoplasty by intracorneal dissection. Ophthalmology 2006;113:1289–300.
[12] Tan DTH, Mehta JS. Future directions in lamellar corneal transplantation. Cornea 2007;26(suppl1):S21–8.
[13] Sutphin JE, Goins KM, Wagoner MD. Deep anterior lamellar keratoplasty: when should it replace penetrating keratoplasty? Am J Ophthalmol 2009;148:629–31.
[14] Melles GRJ, Eggink FA, Lander F, et al. A surgical technique for posterior lamellar keratoplasty. Cornea 1998;17:618–26.
[15] Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty in the first United State patients: early clinical results. Cornea 2001;20:239–43.
[16] Melles GR. Posterior lamellar keratoplasty: DLEK to DSEK to DMEK. Cornea 2006;25:879–81.
[17] Gorovoy M. Descemet-stripping automated endothelial keratoplasty. Cornea 2006;25:886–9.
[18] Lie JT, Birbal R, Ham L, van der Wees J, Melles GRJ. Donor tissue preparation for Descemet membrane endothelial keratoplasty. J Cataract Refract Surg 2008;34:1578–83.
[19] Ple-Plakon PA, Shtein RM. Trends in corneal transplantation: indications and techniques. Curr Opin Ophthalmol 2014;25:300–5.
[20] Ghosheh FR, Cremona FA, Rapuano CJ, et al. Trends in penetrating keratoplasty in the United States 1980-2005. Int Ophthalmol 2008;28:147–53.
[21] Wong TY, Chan C, Lim L, et al. Changing indications for penetrating keratoplasty: a newly developed country's experience. Aust N Z J Ophthalmol 1997;25:145–50.
[22] Maeno A, Naor J, Lee HM, et al. Three decades of corneal transplantation: indications and patient characteristics. Cornea 2000;19:7–11.
[23] Fasolo A, Frigo AC, Bohm E, et al. The CORTES Study: Corneal transplant indications and graft survival in an Italian cohort of patients. Cornea 2006;25:507–15.
[24] Fasolo A, Capuzzo C, Fornea M, et al. Risk factors for graft failure after penetrating keratoplasty: 5-year follow-up from the

Corneal Transplant Epidemiological Study. Cornea 2011;30:1328–35.

[25] National Italian Transplant Centre (CNT). Official statistics on tissue transplantation activity. http://www.trapianti.ministerosalute.it/cnt/; accessed on January 2014.

[26] Johnson ES. Transplant activity in the UK. Activity Report 2009-2010. http://www.organdonation.nhs.uk/statistics/transplant_activity_report/current_activity_reports/ukt/cornea.pdf; accessed on January 2014.

[27] Sony P, Sharma N, Sen S, Vajpayee RB. Indications of penetrating keratoplasty in Northern India. Cornea 2005;24:989–91.

[28] Darlington JK, Adrean SD, Schwab IR. Trends of penetrating keratoplasty in the United States from 1980 to 2004. Ophthalmology 2006;113:2171–5.

[29] Ting DS, Sau CY, Srinivasan S, et al. Changing trends in keratoplasty in the West Scotland: a 10-year review. Br J Ophthalmol 2012;96:405–8.

[30] Cunningham WJ, Brookes NH, Twohill HC, et al. Trends in the distribution of donor corneal tissue and indications for corneal transplantation: the New Zealand National Eye Bank Study 2000-2009. Clin Experiment Ophthalmol 2012;40:141–7.

[31] Zare M, Javadi MA, Einollahi B, 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;19:323–9.

[32] Keenan TD, Jones MN, Rushton S, et al. Trends in the indications for corneal graft surgery in the United Kingdom: 1999 through 2009. Arch Ophthalmol 2012;130:621–8.

[33] Ghosheh FR, Cremona F, Ayres BD, et al. Indications for penetrating keratoplasty and associated procedures, 2001-2005. Eye Contact Lens 2008;34:211–4.

[34] Tan JCH, Holland SP, Dubord PJ, et al. Evolving indications for and trends in keratoplasty in British Columbia, Canada, from 2002 to 2011: a 10-year review. Cornea 2014;33:252–6.

[35] Galvis V, Tello A, Gomez AJ, et al. Corneal transplantation at an ophthalmological referral center in Colombia: indications and techniques (2004-2011). Open Ophthalmol J 2013;7:30–3.

[36] Wang JY, Xie LX, Song XS, Zhao J. Trends in the indications for penetrating keratoplasty in Shandong, 2005-2010. Int J Ophthalmol 2011;4:492–7.

[37] Bajracharya L, Gurung R, Demarchis EH, et al. Indications for keratoplasty in Nepal: 2005-2010. Nepal J Ophthalmol 2013;5:207–14.

[38] Hellstedt T, Mäkelä J, Uusitalo R, et al. Treating keratoconus with intacs corneal ring segments. J Refract Surg 2005;21:236–46.

[39] Wollensak G. Crosslinking treatment of progressive keratoconus: new hope. Curr Opin Ophthalmol 2006;17:356–60.

[40] Vinciguerra R, Romano MR, Camesasca FI, et al. Corneal cross-linking as a treatment for keratoconus: four-year morphologic and clinical outcomes with respect to patient age. Ophthalmology 2013;120:908–16.

[41] Monnereau C, Quilendrino R, Dapena I, et al. Multicenter study of Descemet membrane endothelial keratoplasty: first case series of 18 surgeons. JAMA Ophthalmol 2014;132:1192–8.

[42] Hjortdal J, Pedersen IB, Bak-Nielsen S, Ivarsen A. Graft rejection and graft failure after penetrating keratoplasty or posterior lamellar keratoplasty for Fuchs endothelial dystrophy. Cornea 2013;32:60–3.