TRENDS IN INDICATIONS OF PERFORATING KERATOPLASTY AT THE DEPARTMENT OF OPHTHALMOLOGY, FACULTY HOSPITAL, BRNO, CZECH REPUBLIC, EU, DURING THE PERIOD 2008-2012

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SUMMARY

Introduction: The aim of the study is retrospective analysis of perforating keratoplasty (PKP) indications at the Department of Ophthalmology, Faculty Hospital, Masaryk University, Brno, Czech Republic, E.U., during the period of 5 years, from January 1st, 2008 to December 31st, 2012.

Material and Methods: We performed the PKP indications' retrospective analysis at the Department of Ophthalmology, Faculty Hospital, Masaryk University, Brno, Czech Republic, E.U., during the period of 5 years, from January 1st, 2008 to December 31st, 2012, with complex evaluation of demographic and clinical data. The clinical diagnoses indicating the perforating keratoplasty were divided into 6 groups (keratoconus, bulous keratopathy, keratitis, corneal dystrophies, injuries, corneal transplant failure, and others) according to Cunningham et al. 2011 (2) and Boimer et al. 2012(1) methods.

Results: Our results correspond to data in the literature published abroad, where the majority of recently published papers refer significant increase of corneal transplant failure in the last years of follow-up.

Key words: perforating keratoplasty, indications

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INTRODUCTION

Perforating keratoplasty (PKP) ranks amongst the most common types of tissue transplantations performed worldwide. Since 1980, the most frequent indication for PKP in the USA and selected European countries has been pseudophakic and aphakic bullous keratopathy (4, 8, 11), whereas in developing countries keratitis has dominated amongst the indications (3, 18). Over the last decade, indications for PKP have changed rapidly, and the most recent studies from Central Europe indicate that the most common diagnoses are becoming bullous keratopathy, corneal transplant failure following previous PKP and keratoconus (9). The cause of these changes is the rapid development of new surgical techniques and advances in the development of instruments and pharmacological procedures.

During the course of the last 20 years, the introduction of viscoelastic substances, techniques of phacoemulsification and the constant increase in the knowledge of surgeons has fundamentally reduced the incidence of pseudophakic bullous keratopathy (5). For a long time, the standard technique for corneal transplantation was perforating keratoplasty alone, whilst at present ever increasing priority is being given to anterior and posterior lamellar transplantations.

The aim of this study is to analyse indications leading to PKP at the Department of Ophthalmology at the Faculty of Medicine of Masaryk University and the Faculty Hospital in Brno during the period 2008-2012 in relation to individual pathological conditions, to determine the developmental trend of these changes and to compare the observations gained with study samples from other workplaces.

STUDY SAMPLE AND METHOD

We conducted a retrospective analysis of indications for PKP at the Department of Ophthalmology at the Faculty of Medicine of Masaryk University and the Faculty Hospital in Brno over a time period of 5 years, from 1 January 2008 to 31 December 2012, with a complex evaluation of demographic and clinical parameters. The information was obtained from the medical records and surgical records of the Department of Ophthalmology at the Faculty of Medicine of Masaryk University and the Faculty Hospital in Brno. Transplantations were indicated for optic, tectonic and therapeutic causes (15). The patients were divided into 6 groups according to the clinical diagnoses, using the method of Cunningham et al. 2011 (2) and Bomier et al. 2012 (1), in which the following clinical groups were delineated: keratoconus, bullous keratopathy, keratitis, corneal dystrophies, injuries and corneal transplant failure. We classified other causes, with a frequency of incidence of 11%, under the item of Other in accordance with the above-stated methods (table 4).

RESULTS

In the period from 1 January 2008 to 31 December 2012, 236 PKP procedures were performed on 197 patients (206 eyes). Of the total number of 197 patients, 105 were men and 92 were women. The average age of the patients was 59 ± 18.62 years (median 36), amongst the men 54 years (median 56) and amongst the women 64 years (median 70), the difference was not statistically significant ($p = 0.20$). The largest

number of patients were in the age group of 70-79 years (n = 53) (graph 2). The age distribution of the group of men and women is illustrated by graph 3. Upon a comparison of the group of men and women, the differences in the age group of 20-29 years were demonstrated to be statistically significant in favour of men (p = 0.026) and in the age group of 80-89 years in favour of women (p = 0.04). This difference amongst young patients is probably caused by the more frequent incidence of keratoconus in men, which in our group, however, was not demonstrated to be statistically significant (p = 0.1375). In the age category of 80-89 years it is possible to explain the predominance of women with reference to the higher incidence of systemic pathologies and corneal dystrophies in women, as well as by the longer average length of

Tab. 1 Indications for PKP at the Dept. of Ophthalmology at the Faculty of Medicine of MU Brno during the period 2008-2012.

Indication	n=	% of total
Keratoconus	34	14.41%
Bullous keratopathy	50	21.19%
Pseudophakic	35	14.83%
Aphakic	1	0.42%
In Fuchs's endothelial dystrophy	10	4.24%
Other	4	1.69%
Corneal transplant failure	78	33.05%
With rejection	51	21.61%
Other	27	11.44%
Corneal dystrophies	11	4.66%
Fuchs's endothelial dystrophy	7	2.97%
Stromal dystrophy	3	1.27%
Unspecified	1	0.42%
Keratitis	34	14.41%
Viral	8	3.39%
Bacterial	7	2.97%
Fungal	1	0.42%
Unspecified	6	2.54%
Non-infectious	3	1.27%
Exposure	4	1.69%
Neurotrophic	5	2.12%
Injury	2	0.85%
Chemical	1	0.42%
Mechanical	1	0.42%
Other	27	11.44%

Developmental trends in indications for PKP at the Department of Ophthalmology at the Faculty of Medicine of Masaryk University and the Faculty Hospital in Brno during the period 2008-2012.

	Keratoconus	Bullous keratopathy	Keratitis	Corneal transplant failure	Corneal dystrophy	Other
2008 (n = 56)	9 (16.07%)	18 (32.14%)	6 (10.71%)	14 (25%)	5 (8.93%)	3 (5.36%)
2009 (n = 58)	8 (13.79%)	14 (24.14%)	11 (18.97%)	12 (20.69%)	5 (8.62%)	8 (13.79%)
2010 (n = 54)	7 (12.96%)	12 (22.22%)	8 (14.81%)	20 (37.03%)	0 (0%)	7 (12.96%)
2011 (n = 37)	7 (18.92%)	2 (5.41%)	6 (16.22%)	16 (43.24%)	1 (2.7%)	5 (13.51%)
2012 (n = 31)	3 (9.68%)	4 (12.9%)	3 (9.68%)	16 (51.61%)	0 (0%)	4 (12.9%)

Tab. 3 Main indications for perforating keratoplasty abroad.

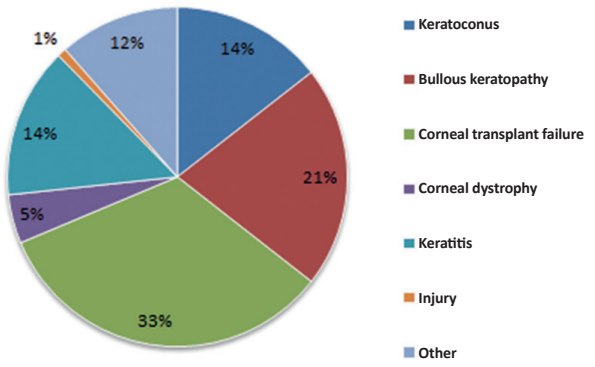
	Author	Country	Centre	Years of observation	Year of publication	n=	1st place	2nd place	3rd place	Note
Europe	Módis	Hungary	University of Debrecen	2006-2009	2011	402	Corneal edema (28.9%)	Corneal transplant failure (18.4%)	Corneal ectasia (14.9%)	Only PKP
	Rahman	Great Britain	Manchester Royal Eye Hospital	2000-2003	2009	203	Corneal ectasia (24%)	Bullous keratopathy (22%)	Corneal transplant failure (20%)	Only PKP
	Wang	Germany	Saarland University Medical Centre	2001-2010	2012	1200	Keratoconus (25.5%)	Fuchs's dystrophy (21.2%)	Bullous keratopathy (14.6%)	Only PKP
	Siagnos	Greece	Athens General Hospital, Heraklion University, Hospital of Crete, Thessaloniki University Hospital	2002-2006	2010	706	Corneal edema (31%)	Keratoconus (23.5)	Corneal transplant failure (17.9%)	Only PKP
	Ting	Great Britain	Ocular Pathology Laboratory Glasgow	2001-2010	2011	921	Keratoconus (28.7%)	Corneal transplant failure (19.2%)	Fuchs's endothelial dystrophy (13.5%)	
	Jirásková	Czech Republic	Department of Ophthalmology, FH Hradec Králové	1997	1999	100	Keratoconus (24%)	Repeated keratoplasty (19%)	Pseudophakic or aphakic endothelial failures and traumatic changes (both 18%)	Only PKP
	FH Brno	Czech Republic	FH Brno	2008-2012		236	Corneal transplant failure (33.05%)	Bullous keratopathy (21.19%)	Keratitis Keratokonus (both 14.41%)	Only PKP
America	Galvis	Columbia	Fundación Oftalmológica de Santander Bucamaranga	2004-2011	2013	402	Bullous keratopathy (34.6%)	Corneal scar (15.7%)	Keratoconus (12.7%)	
	Boimer	Canada	Eye Bank of Canada – Ontario division	2000-2009	2011	7755	Corneal edema (28.3%)	Corneal transplant failure (21.5%)	Fuchs's dystrophy (16.6%)	
Asia	Zare	Iran	Labbafinejad Medical Centre Tehran	2004-2009	2012	1859	Keratoconus (38.4%)	Bullous keratopathy (11.7%)	Corneal transplant failure (10.6%)	
	Wang	China	Shandong Eye Institute	2005-2010	2011	875	Infectious keratitis (37.1%)	HSK (19.1%)	Keratoconus (11.2%)	Only PKP
Australia and Oceania	Cunningham	New Zealand	New Zealand National Eye Bank	2000-2009	2011	2205	Keratoconus (41.1%)	Corneal transplant failure (17.0%)	Bullous keratopathy (13.9%)	
Africa	Tilahun	Ethiopia	Menilik II. Hospital	2001-2006	2010	111	Post-inflammatory corneal opacities (48.6%)	Keratoconus (22.5%)		Only PKP

Tab. 4 Other indications for perforating keratoplasty

Indication	n=
Auto transplantation	1
Corneal scar	5
Corneal leukoma	8
Corneal maculas affected by keratitis in childhood	6
Keratectasia	3
Keratoglobus	1
Keratocele in Stevens-Johnson syndrome	1
Mucopolysaccharidosis	2
Total	27

life. A total of 97 right and 109 left eyes were operated on, in which PKP was performed on both eyes in 9 patients within the observed period. There were 61 combined procedures during the stated 5 year period, of these the majority were connected with cataract surgery. A precise overview of the combined procedures is presented in table 5.

Of the total number of 236 perforating keratoplasty procedures, the largest proportion of 33.05% was due to corneal transplant failure following previous PKP (n = 78/236), of these 65.38% (n = 51/236) were due to rejection (table 1, graph



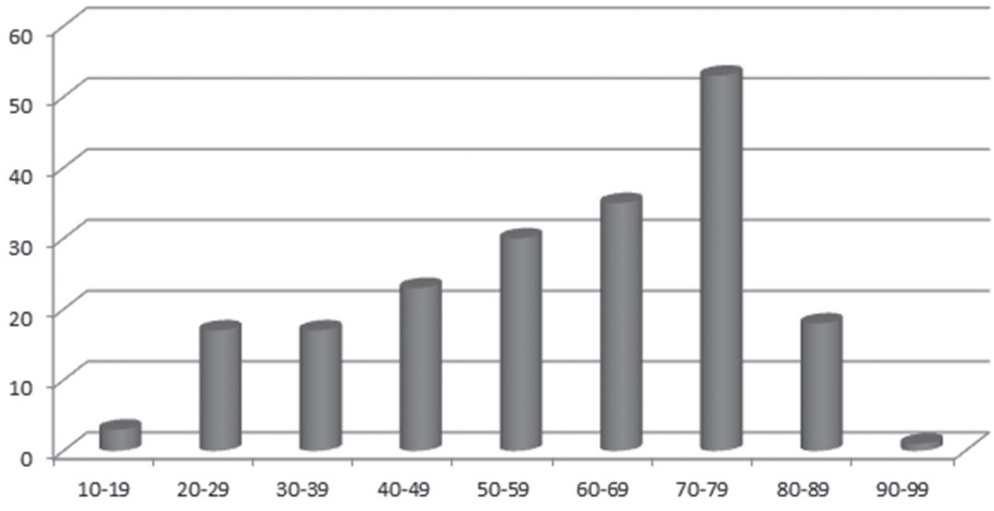
Graph 1

Tab. 5 Summary of combined procedures (n=66)

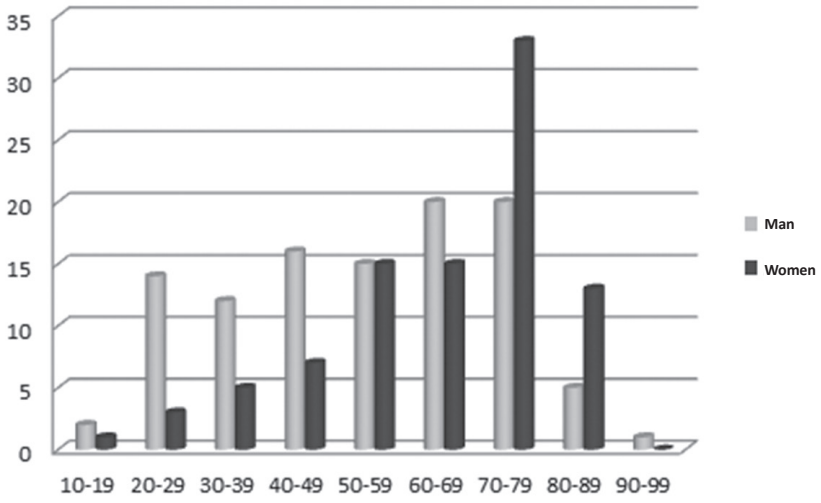
Combined procedure	n=	%
Phaco + impl. of PC IOL	39	59.09%
Phaco + impl. of PC IOL	1	1.52%
Secondary impl. of AC IOL	1	1.52%
Explantation of AC IOL + impl. Artisan Aphakia	1	1.52%
Explantation of PC IOL + impl. Artisan Aphakia	1	1.52%
Secondary cataract surgery	3	4.55%
Pupilloplasty	7	10.61%
Peripheral iridectomy	1	1.52%
Removal of cyclitic membrane	1	1.52%
Anterior vitrectomy	1	1.52%
Dislocation of anterior adherences	4	6.06%
Plastic adjustment of fornices and eyelids	5	7.58%
Extraction of corneal suture	1	1.52%

1). The second most common indication was bullous keratopathy (21.19%, n = 50/236), most frequently pseudophakic (n = 35/236). In third place were keratoconus and keratitis (both groups 14.41%, n = 34). No statistically significant differences were demonstrated in the group of male and female patients in the distribution of diagnoses requiring PKP. During the observed period, there was a reduction in the total number of PKP procedures from 56 in 2008 to 31 in 2012, which can be explained by the progressive extension of indications of lamellar keratoplasty. Graph 4 illustrates the increase in the number of corneal transplant failures and the slight reduction in the number of PKP due to other causes over the course of the five year observation period (table 2).

As table 2 illustrates, observation of the trend in indications for PKP confirmed an increasing but statistically insignificant occurrence of indications due to corneal transplant failure. This increase was contributed to above all by the increase in life expectancy of patients, and this has been recorded in re-



Graph 2

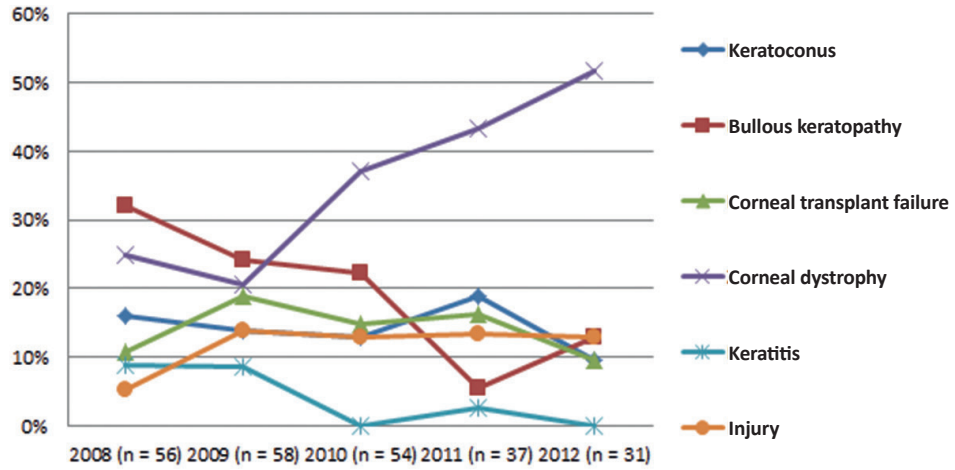


Graph 3

cent years also in other studies (1). By contrast, there was a decreasing trend in the case of bullous keratopathy. The number of perforating keratoplasty procedures for keratoconus, keratitis and for other reasons was stable within the observed period. The prevalence of bullous keratitis and Fuchs's endothelial dystrophy decreased slightly during the observation period. This can be explained by means of the progressive increase in the number of lamellar keratoplasty procedures in the case of these indications.

DISCUSSION

Our study sample comprised 206 eyes of 197 patients, who altogether underwent 236 perforating keratoplasty procedures during the period 2008-2012. A slight predominance of men (53.3%) was confirmed amongst the patients, which is described also by the authors of other studies (1, 2, 11, 14, 16, 19). Study cohorts with a predominance of women have been described within our region by Jirásková et al. (1999, n = 100) (7), and in Canada by Boimer et al. (2011, n = 7755) (1). The average age of our patients was 59.0 ± 18.62, the median 63. A group of 100 patients following PKP performed in Hradec Králové had a similar age composition (average age 58 years, range 18-84 years) (7). Also from the region of Central Europe is the study cohort described by Wang et al. (2013, n = 1200), in which the average age was 57.9 and 55.62 respectively, which correlates with our results (17). A group of patients with a markedly lower average age was described by Zare et al. (2012, n = 1859) (19) in Iran, and by Cunninghm et al. (2012, n = 2205) (2) in New Zealand. This difference can be explained by the low incidence of Fuchs's endothelial dystrophy afflicting older patients, and conversely by the high incidence of keratoconus in younger patients. The comparison with the literature is influenced by the fact that our study sample is composed of adult patients, whereas the majority of other studies also include children from the age of a few months old. The largest number of patients in our study sample were within the age group of 70-79 years (n = 53). The bimodal curve of the age distribution of the study sample, with a second peak in the age group of 20-29 years, as can be



Graph 4

observed in countries with a geographically higher incidence of keratoconus (2), was not confirmed. In the distribution according to sex, statistically significant differences were demonstrated in the age of group of 20-29 years in favour of men (p = 0.026) and in the age group of 80-89 years in favour of women (p = 0.04). This difference in the group of younger patients is probably conditioned by the more frequent incidence of keratoconus in men, favour of men (p = 0.026) and in the age group of 80-89 years in favour of women (p = 0.04). This difference amongst young patients is probably caused by the more frequent incidence of keratoconus in men, which in our group, however, was not demonstrated to be statistically significant (p = 0.138). In the age category of 80-89 years it is possible to explain the predominance of women with reference to the higher incidence of systemic pathologies and corneal dystrophies in women, as well as by the longer average length of life.

During the course of the observed 5 year period, the most common indication for perforating keratoplasty was corneal transplant failure following previous keratoplasty (33.05%). With regard to the increase in the total number of transplants over the course of recent decades, this finding is to be expected. It is linked to greater life expectancy of patients and an improvement in the availability and quality of donated corneas. Even when none of the studies in the available literature state corneal transplant failure as the most common reason for perforating keratoplasty, in the majority of the most significant studies in developed countries it is possible to identify this trend at the end of the observation period (1, 2, 9, 11, 14). In Ontario, Boimer et al. also recorded an increase in the number of PKP procedures for corneal transplant failures, and in the last observed year of 2009 corneal transplant failure became the most common indication for PKP. The authors explain this fact with reference to the longer life expectancy of the recipients and the increase in the number of PKP procedures (1, 11). By contrast, authors from developing countries describe a low number of corneal transplant failures, as demonstrated by studies by Zare et al. in Iran (10.6%, n = 1859) and Galvis et al. in Columbia (7.7%, n = 402). Zare et al. attribute this fact to the sufficient number of donated corneas from young donors (9). One of few European studies to record a decline in the number of PKP procedures for corneal transplant failure (7.0%, n = 1200) was the histopathological study by Wang et al. in Germany (16). They see the reason for this in thorough systemic medication using acyclovir for at least 1 year following PKP for herpetic keratitis and systemic administration of cyclosporine A and mycophenolate mofetil in high risk keratoplasty procedures. The efficacy of administration of cyclosporine A in the treatment of high risk keratoplasty procedures is confirmed also by the study conducted by Sundmacher et al. (12).

The second most common indication for perforating keratoplasty at our centre was bullous keratopathy (21.19%, n = 50/236), predominantly pseudophakic (n = 35/236). Pseudophakic and aphakic bullous keratopathy has been the most common indication for PKP since 1980 in the USA and selected European countries, which is attributed to the developing availability of cataract surgery for a wide spectrum of patients (4, 8, 11). Bullous keratopathy was one of the three most common indications for corneal transplant in virtually all the published studies (1, 2, 11, 16, 19, 9, 10). In recent years, however, it is possible to observe a slightly declining trend of bullous keratopathy, and a subsequent increase in corneal transplant failure (1). The large number of patients with bullous keratopathy in our study sample is also influenced by the high prevalence of Fuchs's endothelial dystrophy in our population.

Keratoconus (14.41%) is the most common indication for PKP worldwide, in countries with a high occurrence such as the Middle East and New Zealand, which is confirmed also by the studies of Zare and Cunningham (2, 19). In studies by European authors published in recent years, keratoconus has always been amongst the first two indications for PKP (7, 9, 10, 14, 16). Even despite the progressive promotion of deep anterior lamellar keratoplasty (DALK) in this indication, there are still a number of patients for whom DALK is inappropriate due to the late stage of the pathology.

Together with keratoconus, keratitis was the third most common indication in our study sample (14.41%, n = 31). In the literature from developing countries and countries with large social inequality amongst the population, keratitis is currently one of the most common indications for PKP (3, 17, 18). The large number of patients with keratitis in comparison with developed countries is explained by the relatively large catchment area and the seriousness of the finding upon the first examination at our clinic.

According to the retrospective analysis of perforating keratoplasty procedures performed at our clinic during the period 2008-2012, the most common indications were corneal transplant failure following previous keratoplasty, bullous keratopathy, keratoconus and keratitis. Our results correspond with the data in the foreign literature with regard to the varying prevalence of hereditary corneal pathologies within our geographical expanses (table 3). The slight discrepancies in the results are caused also by the inclusion of lameallar keratoplasty procedures by the authors of certain studies.

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