

Outcomes of penetrating keratoplasty at a tertiary institution in South Africa

YM Theron MBChB (UP), Dip Ophth (SA), FC Ophth (SA); Registrar, Groote Schuur Hospital, Department of Ophthalmology, University of Cape Town, South Africa.

ORCID: <https://orcid.org/0009-0004-8635-966X>

N du Toit MBChB (UCT), Dip Ophth (SA), FRCS (Ed), MMed (UCT), FC Ophth (SA), PhD(UCT), Mauerberger Chair of Ophthalmology and Head of Division of Ophthalmology (Dept of Surgery) Faculty of Health Sciences, University of Cape Town, Groote Schuur Hospital and Red Cross Children's Hospital.

ORCID: <https://orcid.org/0000-0003-1167-2796>

M Gajjar MBChB (UCT); Medical Officer, Potchefstroom Hospital, Division of Ophthalmology.

ORCID: <https://orcid.org/0009-0006-4071-0383>

Corresponding Author: Dr Yolande Maryna Theron, debeeryol@gmail.com

Abstract

Aims: To determine corneal graft survival rates and visual outcomes of penetrating keratoplasty (PKP) in a South African setting.

Methods: A retrospective review of 99 penetrating keratoplasties performed at Groote Schuur Hospital, South Africa over a three-year period between February 2016 and February 2019.

Results: The mean age of study participants was 38 years (14-85). The study included 60% females and 40% males. The main indications for surgery were keratoconus (58%), corneal scar (21%), re-grafts (8%), pseudophakic bullous keratopathy (6%), corneal dystrophies (3%) and pellucid marginal degeneration (1%). The overall graft survival at 1-year follow up was 86%. A higher one-year graft survival rate of 94% was seen in patients with keratoconus. The total number of patients diagnosed with graft failure at one year was 13. The Kaplan-Meier survival analysis was used to assess time to graft failure. The estimate was 11.7 months (mean time to graft failure) with a 95%

confidence interval from 11.4 to 12 months. In our study, best corrected Snellen acuity in the category of 6/6-6/18 was found in 59.2% of patients one year post-operatively, compared with 1% of patients in the same BCVA group pre-operatively. Patients with a BCVA equal to 3/60 or less reduced from 56% pre-operatively to 20% postoperatively at one year.

Conclusion: Penetrating Keratoplasty is an effective long term treatment option to restore visual acuity in certain corneal disorders in a middle to low-income country. Our results demonstrated a comparable one-year graft survival rate to high-income countries.

Keywords: penetrating keratoplasty, South Africa, graft failure, cornea, outcomes.

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Introduction

According to World Health Organisation, corneal opacity is one of leading causes of global blindness and visual impairment.^{1,2} Bilateral blindness affects roughly 45 million people globally. In low-income countries, an estimated 10 million people are affected by corneal blindness.^{1,2} Children and young adults are commonly affected by corneal disease resulting in monocular and bilateral blindness. In some areas in Asia and Africa, it has been reported that the incidence of vision loss in children and young adults due to corneal disease is 20 times higher than in high-income countries.⁴

Corneal transplant surgery, where the diseased host cornea is replaced by healthy donor cornea, can restore visual potential in such patients and is the most commonly transplanted tissue/organ worldwide.^{5,6} Different methods of corneal transplant surgery exist, and these include penetrating keratoplasty (full-thickness corneal transplant) and anterior or posterior lamellar keratoplasty (partial thickness corneal transplant). Lamellar graft surgery has gained popularity during the past 10 years, especially in high-income countries.^{6,7}

Low-income countries face many challenges when attempting to resolve the

burden of disease associated with corneal blindness. Barriers include amongst others, poor eye bank infrastructure (resulting in shortage of donor tissue), limited number of trained corneal surgeons and socio-economic factors (e.g. poor post-operative follow up).^{1,8-11,25}

Long-term graft survival is an important objective in order to improve visual acuity in these patients.² Groote Schuur Hospital is a tertiary institution situated in Cape Town, Western Cape Province, which offers general and specialist ophthalmic services. The aim of this study was to evaluate corneal transplant surgery outcomes at Groote Schuur Hospital, to identify causes

of graft failure and to subsequently use this data to implement changes where possible to improvements in long-term graft survival in our patients.

Materials and methods

This is a retrospective review of patients who underwent optical penetrating keratoplasty at Groote Schuur Hospital, Cape Town, South Africa between 1 February 2016 and 1 February 2019. All patients older than 13 years who received penetrating keratoplasty surgery during the specific time period were included. During the time period of this study, tectonic penetrating keratoplasty and glycerol graft corneal transplants were excluded. This study was approved by the University of Cape Town Research Ethics Committee and was in accordance with the tenets of the Declaration of Helsinki.

Data variables:

Data collected included patient demographics, namely: age, gender and their current area of residence (within 50km of Cape Town or beyond). Pre-operative variables that were recorded were best corrected Snellen visual acuity (pinhole, spectacles or contact lenses), indications for PKP and intraocular pressure (IOP). The different categories for BCVA were based on similar categories used in other studies.^{11,13,18} The intra-operative data obtained included surgery performed (PKP alone or combined PKP-cataract procedure) and complications encountered. Post-operative data reviewed consisted of BCVA, IOP, graft rejection, graft failure and complications that occurred. Post-operative data was obtained at the one-month, six-month and 12-month follow-up visits.

Outcome measures:

The primary outcome measure was graft success. This was defined by BCVA of 6/6-6/18 the lack of graft rejection and the absence of graft failure at the different time intervals. Secondary outcomes consisted of assessing the complications that were recorded.

Surgical technique:

All patients who underwent penetrating keratoplasty received a general anaesthetic. Donor corneas were obtained from National Medical Supplies (Visionshare) and prepared using a manual trephine. The donor graft was oversized by 0.25-0.5 mm compared with the recipient. The corneal donor button was sutured to the host bed with sixteen interrupted 10-0

Nylon sutures. Intracameral cefuroxime as well as subconjunctival betamethasone given at the end of surgery. All surgeries were performed either by one of the corneal consultants or by a supervised senior registrar. The post-operative regime included prednisolone acetate 1% eye drops six times daily and ofloxacin eye drops four times daily for one month. This was then changed to dexamethasone 0.1% eye drops four times daily for six months and three times daily for another six months. Loose sutures were removed when encountered and the remainder of sutures were removed at approximately 12-18 months post-op.

Post-operative care:

Patients were seen day one, week one, week two, then one, three, six and 12 months from the date of surgery, then subsequently at six-monthly intervals. At each routine follow-up visit, BCVA was measured using a Snellen Chart. IOP was measured using puff tonometry. The graft was evaluated by slit-lamp microscopy for clarity, signs of rejection or failure and any complication that might have occurred.

Evaluation criteria:

Graft rejection was considered if there was endothelial or epithelial rejection lines and keratic precipitates.^{8,9} Early graft rejection was defined as graft rejection occurring at or before six months. Graft failure was defined as an existing graft with irreversible loss of clarity as a result of oedema, neovascularization or scarring.¹⁰ Early graft failure was defined as graft failure occurring at or before six months.

Statistical analysis:

IBM SPSS version 28 was used to analyse the data. A *p* value <0.05 was considered as statistically significant. Categorical variables were described using frequency

tables and percentages. Continuous variables were summarised using mean and standard deviation. Comparisons between proportions were made using Fisher's exact and Chi-square tests. Comparisons between two independent means were made using t-tests. Kaplan-Meier survival analysis was used to analyse time to graft rejection. Repeated measures ANOVA was used to compare overall change in IOP over time as well as specific time points.

Results

A total of 112 PKP surgeries were performed during the three-year study period and data of 99 PKP were included for analysis. Thirteen patients did not attend their one-year follow up visit and were therefore excluded from the study.

Demographics:

Table 1 summarises the patient's demographics. The mean age was 38 years (range 14-85; SD = 20). The majority of patients (85%) lived within 50km radius of the hospital, where they underwent PKP and attended followed-up visits.

		Count	%
Sex	Male	40	40.4%
	Female	59	59.6%
	Total	99	100.0%
Residence: Local or country	C	14	14.1%
	L	85	85.9%
	Total	99	100.0%
Age (years)	Mean (SD)	38 (20)	

C = Country ; L = Local; SD = Standard variation

Indications:

The main indications for corneal transplant were keratoconus (58%). Refer to Table II for other indications.

		Count	Column %	
Indications	Bullous keratopathy	6	6.1%	
	Corneal dystrophy	Lattice	1	1.0%
		Fuch's	4	4.0%
	Corneal scar	Trauma	6	6.1%
		IK	13	13.1%
		Unspecified	2	2.0%
	Failed graft	8	8.1%	
	Keratoconus	58	58.6%	
	Pellucid marginal degeneration	1	1.0%	
Total	99	100.0%		

IK = Infective keratitis

Table III: Best corrected visual acuity outcomes

BCVA category	Pre-op		1 month		6 months		1 year	
	n	%	n	%	n	%	n	%
6/6-6/18	1	1.0%	34	35.4%	47	50.0%	58	59.2%
<6/18-6/36	26	26.5%	34	35.4%	25	26.6%	17	17.3%
<6/36-6/60	16	16.3%	6	6.3%	4	4.3%	3	3.1%
<6/60-3/60	0	0.0%	0	0.0%	0	0.0%	0	0.0%
<3/60	55	56.1%	22	22.9%	18	19.1%	20	20.4%

Visual outcome:

During the study period, best corrected Snellen acuity (BCVA) was evaluated pre-operatively, at one month, six month and a year follow up visits. Pre-operatively BCVA of <3/60 was seen in 55 patients (56.1%) in the affected eye. Post-operative BCVA in the operated eye at one-year in the 6/6-6/18 group was seen in 58 patients (59.2%)

The distribution of BCVA at different time intervals is summarised in Table III.

Intraocular pressure:

Repeated measures ANOVA was used to compare overall change over time as well as specific time points. IOP increased significantly over the entire time period (Wilk’s lambda = 0.792, p = 0.004) and also significantly between each time period and the pre-operative value. However, when comparing each time point to the one preceding it, the only statistically significant increase was between pre-op and one month.

Figure 1 summarises mean and 95% CI IOP over time.

Graft outcomes:

The Kaplan-Meier survival analysis was used to assess time to graft failure. The

estimate was 11.7 months (mean time to graft failure) with a 95% CI from 11.4 to 12 months. The cumulative survival probability at one year was 86%.

The total number of patients diagnosed with graft failure at one-year was 13. Among these patients, the pre-operative indications included pre-existing corneal scar (46%), keratoconus (23%), regrant (15%) and pseudophakic bullous keratopathy (15%).

Early graft failure (occurring before six months) was seen in 30% of patients which had graft failure.

Complications which contributed to graft failure were graft rejection 30% (n = 4), persistent central epithelial defect 15% (n = 2), infective keratitis 15% (n = 2), graft dehiscence 7% (n = 1), post-avastin endophthalmitis 7% (n = 1) and poor compliance and follow up was seen in 23% (n = 3) patients. .

In our study 24% (n = 24) of patients experienced at least one episode of graft rejection over a follow-up period of one-year. Early graft rejection (occurring before six months) was detected in 18 patients and 83% (n = 15) of these episodes occurred most frequently in the one-month post-operative time period. The progression to graft failure following an

episode of graft rejection was seen in 16% of patients.

Table IV summarises the complications seen at different follow up visits.

Discussion

The overall graft survival at one-year was 86% in our study group. This is comparable to studies done in other low-income African countries. Chen *et al.* in Kenya reported one-year graft survival rate as 85.8%.¹¹ Ayalew *et al.* in Ethiopia and Yorston *et al.* in Kenya reported the two-year graft survival as 80% and 87% respectively. ^{10,13}

In high-income countries a comparable one-year graft survival rate was reported. The Corneal Transplant follow up study in the UK reported one-year graft survival as 88% and the Australian Corneal Graft registry reported it as 91%.¹⁹

The pre-operative indications for PKP greatly influence graft outcomes. Keratoconus most often has a higher graft survival rate as seen in a number of previous studies.^{14,15}

In our study group, keratoconus made up the greatest proportion of patients (58%). This is comparable to studies done in other African and high-income Western countries.¹⁵ Khan *et al.* (2015) reported the commonest indication for PKP in South Africa was keratoconus (64%).² Similar reports were noted by Chen *et al.* indicating the total percentage of patients with keratoconus in their study as 66.1%.¹¹

In other low-income countries such as Pakistan and India, studies have reported their main indication for PKP to be corneal scarring. This generally influence graft survival which may explain the lower graft survival rates in these countries.^{16,17} Dandona *et al.* in India reported graft survival rates at one-year as 79.6%.¹⁸ Moin-ud-Din in Bangladesh reported the leading indication for PKP to be corneal scarring (41%).¹⁷

Looking at the different subgroups, the one-year graft survival rate for keratoconus in our study was 94%. This is comparable to other studies in low-income countries. In Kenya and India the graft survival rates for keratoconus at one-year was reported as 89.9% and 96.4% respectively.^{11,18}

In our study, best corrected Snellen acuity in the category of 6/6-6/18 was seen in 59.2% of patients at one-year post-operatively. This was much higher compared to the percentage of patients in the same BCVA group pre-operatively.

The overall graft failure rate was 13% in our study group and the majority

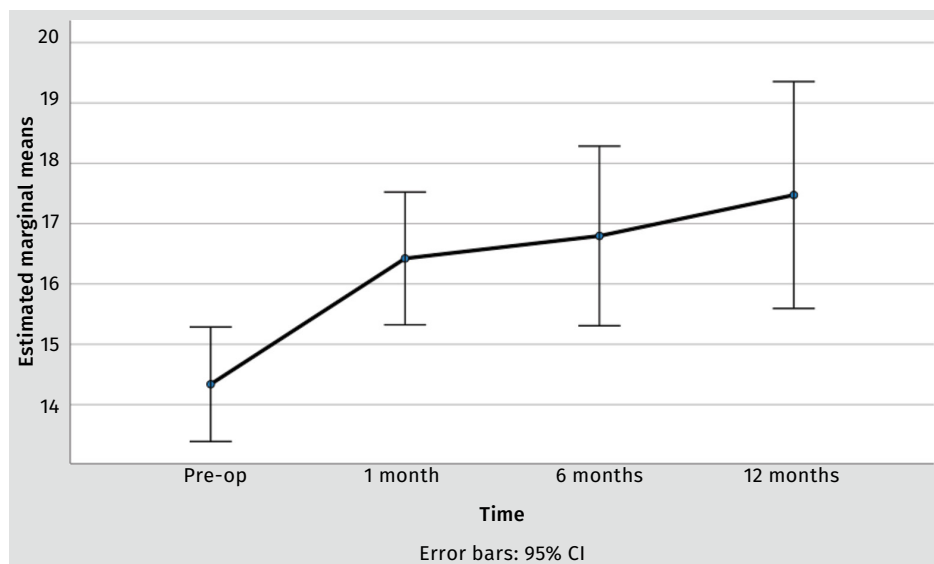


Figure 1: Mean and 95% CI IOP over time

IOP = Intraocular pressure; CI = Confidence interval

Table IV: Complications at various time intervals

		Count	Column %
Intra-op complications	Aqueous misdirection	2	2.0%
	Hyphaema	1	1.0%
	Leucoma adherens	1	1.0%
	None	88	88.8%
	Suture tract leak	2	2.0%
	Thin peripheral host corneal tissue	5	5.1%
	Total	99	100.0%

	1 month		6 months		1 year	
	Count	%	Count	%	Count	%
Non attendance	1	1.0%	4	4.0%		
Descemet folds	2	2.0%				
Graft dehiscence	3	3.0%				
Graft failure			4	4.0%	13	13.1%
Graft rejection	15	15.2%	4	4.0%	6	6.1%
Graft rupture: trauma	1	1.0%	3	3.0%	1	1.0%
Infective keratitis	1	1.0%	1	1.0%		
Loose sutures	1	1.0%	1	1.0%	1	1.0%
Non compliance	3	3.0%	1	1.0%		
None	65	65.7%	64	64.6%	68	68.7%
Ocular surface disease	1	1.0%	2	2.0%		
Other			4	4.0%	5	5.1%
Persistent CED	2	2.0%	2	2.0%		
Steroid induced ocular hypertension	4	4.0%	9	9.1%	6	6.1%
Total	99	100.0%	99	100.0%	99	100.0%

CED = Central epithelial defect

of these patients had corneal scarring pre-operatively. The causes of corneal scarring were mostly due to infective keratitis, trauma and unspecified reasons respectively. Patients with previous herpes simplex keratitis were not selected for penetrating keratoplasty at Groote Schuur Hospital due to the high risk of graft failure in these patients.

In a multivariate analysis done by Yu *et al.*, the postoperative risk factors strongly associated with graft failure were postoperative glaucoma medication, suture problems, infective keratitis, graft rejection, persistent epithelial defect and retinal surgery.²²

Graft rejection is one the most common reasons for graft failure.²⁰ The time period that constitutes the highest risk for graft rejection is 150 days post-operatively as reported by the Corneal Transplant follow up Study.¹⁹ This correlates to findings in our study where the majority of graft episodes occurred within the first six months. In contrast, Perera *et al.* reported that in their study group, 27% of patients experienced early graft rejection and 73% of patients had late graft rejection episodes.²⁰

Rahman *et al.* in the UK reported that an endothelial graft rejection episode was seen in 21% of patients over a period of five years. Of these patients, 7.4% experienced graft failure.²¹ In our study a higher percentage of patients (16%) that had a graft rejection episode progressed to graft failure.

In low-income countries, poor follow up and non-compliance with treatment remains a challenge.²³ In our study the non-attendance at one month, six month and one-year follow up was 1%, 4% and 13% respectively. Twenty three percent of graft failure cases failed to attend the six month follow up visit and therefore poor compliance and non-attendance were contributing factors. A study done in Kenya reported that 33% of patients that underwent PKP did not attend the one-year follow up visit and financial barriers were the main reason for non-attendance in 42% of these patients.²⁴ Dandona *et al.* reported that patients in poor socio-economic circumstances had a higher chance of graft failure – the relative risk was 1.28.¹

It is important to note that good

outcomes with penetrating keratoplasty were achievable despite using imported corneas travelling long distances from the USA.

Limitations to our study were the small number of patients included and the relative short follow up time. This was also a retrospective study based on the review of medical records and the information provided in patient's folders determined the quality of data.

Conclusion

In this study, the overall graft survival rate at one-year was 86%, with 59.2% of patients having BCVA of 6/6-6/18. Therefore, penetrating keratoplasty remains an effective long term treatment option to restore visual acuity in certain corneal disorders. This is comparable to other studies done in low-income and high-income countries. In South Africa, the lack of resources such as a shortage of donor corneas greatly impacts the number of PKP that can be performed.^{2,25} Socio-economic challenges also influence the post-operative care. Despite these hurdles in our system, our study reports that an effective corneal graft outcome can be achieved. Although we didn't assess donor corneal graft availability, efforts in increasing the number of graft tissue remains a high priority to address the burden of corneal blindness. Further prospective studies are required to give more information on outcomes of penetrating keratoplasty in South Africa.

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