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Penetrating keratoplasty in Africa: graft survival and visual outcome

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Abstract

***Aim*—To study the survival and visual outcome of penetrating keratoplasty in an African setting.**

***Methods*—A retrospective analysis of 216 corneal grafts, performed on 203 eyes of 186 patients, at Kikuyu Hospital, Kenya over a 5 year period.**

***Results*—Half of the transplants were carried out for keratoconus with only 5% of the grafts being undertaken for corneal scarring caused by trachoma or measles. The average follow up was 27.3 months. The probability of graft survival at 2 years was 87.4% (95% CI 80.6%–94.3%) for keratoconus and 64.7% (95% CI 54.8%–74.6%) for other corneal pathologies. Forty seven grafts (21.8%) in 36 patients (17.7%) are known to have become opaque. The commonest causes of graft opacification were bacterial keratitis (6.0%), endothelial failure (6.0%), and graft rejection (5.1%). Preoperatively 55% of keratoconus eyes and 75.7% of non-keratoconus eyes were blind. Postoperatively, 5% of keratoconus eyes and 41.7% of the non-keratoconus eyes were blind. Normal vision was achieved in 53.7% of operated eyes. Grafts carried out for keratoconus had a better visual outcome than grafts performed for other corneal pathologies. Preoperatively, 12.4% of keratoconus and 48.5% of non-keratoconus patients were blind in their better eye. Postoperatively, 1.1% of keratoconus patients and 25.7% of non-keratoconus patients were blind. The number of patients with normal vision in the better eye increased from 32 (17.2%) to 106 (57.0%). Sight was restored to 34 blind patients, but two patients with severe visual impairment preoperatively were blind at their last follow up. There was therefore a net reduction of 32 in the number of blind patients after 216 keratoplasties.**

***Conclusions*—Penetrating keratoplasty can be successful in Africa, particularly for keratoconus and other corneal dystrophies. However, penetrating keratoplasty has a limited role in the treatment of blindness from corneal scarring due to trachoma, measles, and vitamin A deficiency for which community based preventive measures must remain the priority.**

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The prognosis for penetrating keratoplasty in the industrialised world has improved greatly during the past 20 years. However, relatively little is known about the effectiveness and role of penetrating keratoplasty in countries of the developing world, particularly sub-Saharan Africa.[1] In the UK, corneal blindness accounts for 2% of blind registrations,[2] while in Africa corneal disease is responsible for at least 25% of all blindness.[3] Studies have shown that the most important causes of corneal blindness in Africa are vitamin A deficiency associated with measles and trachoma, diseases which are amenable to preventive measures.[3–6] Unfortunately many of the eyes blinded by these conditions are unsuitable for keratoplasty. This study investigates the indications and outcome of keratoplasty in Africa.

Methods

A retrospective review of the records of all patients who received a corneal graft at Kikuyu Hospital in Kenya before 1 January 1993 was undertaken in January 1994. All patients no longer attending the clinic were written to at their last known address and invited to attend for an eye examination.

The measurements of outcome were graft transparency, visual acuity in the operated eye, and visual acuity in the better eye of the patient. The method of Kaplan and Meier, for estimating survival from incomplete data, was used to analyse the probability of graft survival. Visual acuity was classified according to the World Health Organisation's recommended categories of visual loss.[7] Blindness is defined as a vision of less than 3/60 to NPL. The term *visual acuity* is used to refer to the vision in an eye. The term *visual status* is used to refer to the vision of the patient (that is, vision in the better eye).

Results

DEMOGRAPHICS

Altogether 216 grafts were carried out on 203 eyes of 186 patients during the period under review. Fifteen eyes had more than one graft. Of the 89 keratoconus patients, 61.8% were male, compared with 51.5% of 97 non-keratoconus patients ($p>0.1$). The mean age for the keratoconus grafts was 17.8 years (95% confidence interval (CI) 15.8–19.8) compared with 43.3 years (95% CI 38.9–47.7) for the non-keratoconus patients.

DIAGNOSES

The preoperative diagnoses for all 216 penetrating keratoplasties are shown in Table 1. Keratoconus accounted for 50%, scar 11%,

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and herpetic disease 8%. Of 14 repeat grafts for graft failure nine were for keratoconus.

SURGERY

Within 7 days of surgery there were 28 complications in 22 grafts (10.2%). Nine patients had a shallow anterior chamber, of which six had a leaking wound and three had aqueous leaking from a suture track. There were eight postoperative hyphaemas, seven grafts had a persistent epithelial defect, three had fibrinous uveitis, and there was one case of vitreous haemorrhage in a graft with a hyphaema.

DONOR MATERIAL

Out of 216 grafts performed, 210 donor corneas came from eye banks in the USA and Sri Lanka (mainly preserved in Optisol) and six from local donations.. The interval from donation to graft ranged from 2 to 14 days. The mean donor age was 64.6 years (range 1–92 years).

FOLLOW UP

The mean length of follow up was 27.3 months (range 1–94 months). There was no difference in the mean follow up for keratoconus and non-keratoconus grafts. Out of 203 eyes, 128 (63.1%) were currently being seen at the eye clinic of which 111 were clear and 17 opaque. Nineteen had been discharged with an opaque graft. Patients were counted as lost to follow up if they either had a clear graft at their last visit and had not attended the clinic for 6 months; or in patients whose grafts had been performed over 3 years previously, if they had not attended for 12 months. Altogether 56 (27.6%) eyes were lost to follow up, of which 35 attended for at least 6 months with a clear graft, but had not been seen during the last 6–12 months. All grafts were included in the calculation of graft survival.

Table 1 Preoperative diagnoses on 216 eyes undergoing penetrating keratoplasty at Kikuyu, Kenya, 1987–92

Diagnosis	*Number*	*Aetiology*
Keratoconus	108 (50.0%)	
Corneal scar	24 (11.0%)	
Herpes simplex keratitis	17 (7.9%)	
Corneal dystrophy	16 (7.4%)	
		Lattice dystrophy 6
		Macular dystrophy 3
		Other dystrophies 7
Opaque corneal graft	14 (6.5%)	
		Primary graft failure 5
		Delayed graft failure 5
		Rejection 4
Bullous keratopathy	14 (6.5%)	
		Aphakic 10
		Pseudophakic 4
Trachoma	7 (3.2%)	
Measles	4 (1.9%)	
Bacterial keratitis	4 (1.9%)	
Other diagnoses	8 (3.7%)	
Total	216 (100%)	

Table 2 Causes of corneal graft opacification in 216 penetrating keratoplasties, Kikuyu, Kenya

Cause of opacity	*Keratoconus (n=108)*	*Non-keratoconus (n=108)*	*Total (n=216)*
Bacterial infection:	3	10	13 (6.0%)
Bacterial ulcer	1	8	9
Bacterial ulcer and endophthalmitis	2	2	4
Graft failure:	7	6	13 (6.0%)
Primary graft failure	5	1	6
Delayed graft failure	2	5	7
Graft rejection	1	10	11 (5.1%)
Recurrent disease:	0	7	7 (3.2%)
Herpes simplex keratitis		3	3
Mooren's ulcer		3	3
Pseudophakic bullous keratopathy		1	1
Persistent epithelial defect	1	1	2 (0.9%)
Vitreous touch	0	1	1 (0.5%)
Total	12	35	47 (21.8%)

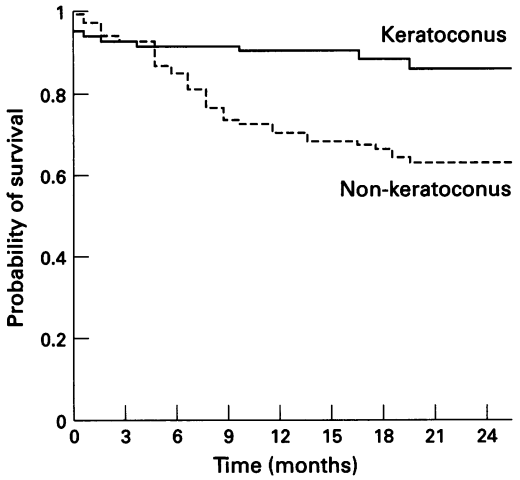

Figure 1 Probability of graft survival in 108 penetrating keratoplasties for keratoconus and 108 penetrating keratoplasties for other corneal pathologies.

GRAFT SURVIVAL

The probability of graft survival was determined using the method of Kaplan and Meier. Grafts lost to follow up were treated as censored data, and survival time was taken from their last clinic attendance. The probability of survival at 24 months among the keratoconus grafts was 87.4% (95% CI 80.6–94.3%) and in the non-keratoconus grafts 64.7% (95% CI 54.8–74.6%). The survival curve is shown in Figure 1.

CAUSE OF GRAFT OPACIFICATION

Altogether 47 of 216 grafts (21.8%) were known to fail in 36 of 203 eyes (17.7%). The causes of graft opacification are given in Table 2. Infection refers to a bacterial keratitis. This occurred in 34 grafts (15.7%) and led to permanent graft opacity in 13 (6.0%). Herpes virus infections were classified as recurrent disease. Primary graft failure was defined as graft oedema present from the time of surgery. Delayed graft failure referred to graft oedema occurring in a previously clear graft in the absence of signs of rejection. Graft rejection was defined as graft oedema, occurring in a previously clear graft, accompanied by keratic precipitates and/or uveitis.

REJECTION

There were 54 episodes of rejection in 46 grafts of 43 patients (Table 3). Eleven grafts (5.1%) became permanently opaque as a result of graft rejection. A total of 21 rejection episodes occurred in keratoconus grafts, one of which led to permanent graft failure, and 33 rejection episodes occurred in non-keratoconus grafts, of which 10 led to permanent graft failure. An episode of graft rejection was more likely to

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Table 3 Graft rejection in 216 penetrating keratoplasties, Kikuyu, Kenya

Diagnosis	Total	Number with graft rejection	Number with graft failure due to rejection
Trachoma	7	4 (57.1%)	1 (14.3%)
Bacterial keratitis	4	2 (50.0%)	0 (0%)
Graft failure	14	6 (42.9%)	2 (14.3%)
Corneal scar	24	7 (29.2%)	3 (12.5%)
Measles	4	1 (25.0%)	1 (25%)
Corneal dystrophy	16	3 (18.8%)	0 (0%)
Keratoconus	108	19 (17.6%)	1 (0.9%)
Other	8	1 (12.5%)	1 (12.5%)
Herpes simplex keratitis	17	2 (11.8%)	1 (5.9%)
Bullous keratopathy	14	1 (7.7%)	1 (7.1%)
Total	216	46 (21.3%)	11 (5.1%)

lead to permanent graft failure in non-keratoconus grafts than in keratoconus grafts (Fisher's exact test, p=0.02).The mean time to first rejection in grafts for keratoconus was 9.9 months, and 12.0 months in grafts for other corneal pathologies.

FURTHER OPERATIONS

A total of 47 grafts required further surgery (not including repeat penetrating keratoplasty), of which 22 (46.8%) became opaque. Eleven patients required resuturing of the graft following traumatic wound dehiscence of which 10 were in keratoconus eyes. Six patients required trabeculectomy and four had cataract extractions.

VISUAL ACUITY

The preoperative visual acuities in both keratoconus and non-keratoconus eyes are shown in Table 4. Non-keratoconus eyes were more likely to have a preoperative visual acuity of <3/60 than keratoconus eyes (75.7% versus 55.0%, $\chi^2 = 9.6$, $p<0.01$). Out of the total of 203 eyes undergoing keratoplasty, 176 (86.7%) had a preoperative visual acuity of less than 6/60.

Postoperatively 109 eyes (51.7%) had a latest visual acuity of 6/18 or better (Table 4) of which 73 were in keratoconus eyes, and 36 were in non-keratoconus eyes (73.0% versus 35.0%, $\chi^2 = 29.5$, $p<0.001$). Fifty seven eyes (28.1%) had a postoperative visual acuity of less than 6/60, of which 50 were in non-keratoconus eyes and seven in keratoconus eyes (48.5% versus 7%, $\chi^2=37.9$, $p<0.001$). The non-keratoconus eyes with severe scarring and visual acuity less than 3/60 tended to do badly.

Table 4 Pre- and postoperative visual acuities in 100 keratoconus and 103 non-keratoconus eyes undergoing penetrating keratoplasty at Kikuyu Hospital

	Preoperative		Postoperative	
Acuity	Keratoconus	Non-keratoconus	Keratoconus	Non-keratoconus
6/6–6/18	0 (0%)	0 (0%)	73 (73%)	36 (35.0%)
<6/18–6/60	18 (18%)	9 (8.7%)	20 (20%)	17 (16.5%)
<6/60–3/60	27 (27%)	16 (15.5%)	2 (2%)	7 (6.8%)
<3/60–NPL	55 (55%)	78 (75.7%)	5 (5%)	43 (41.7%)
Total	100 (100%)	103 (100%)	100 (100%)	103 (100%)

Table 5 Pre- and postoperative visual status (acuity in better eye) of 89 keratoconus and 97 non-keratoconus patients undergoing penetrating keratoplasty at Kikuyu Hospital

	Preoperative		Postoperative	
Acuity	Keratoconus	Non-keratoconus	Keratoconus	Non-keratoconus
6/6–6/18	22 (24.7%)	10 (10.3%)	69 (77.5%)	37 (38.1%)
<6/18–6/60	38 (42.7%)	27 (27.8%)	16 (18.0%)	24 (24.7%)
<6/60–3/60	18 (20.2%)	13 (13.4%)	3 (3.4%)	11 (11.3%)
<3/60–NPL	11 (12.4%)	47 (48.5%)	1 (1.1%)	25 (25.7%)
Total	89 (100%)	97 (100%)	89 (100%)	97 (100%)

Table 6 Change in visual status of 186 patients undergoing keratoplasty, Kikuyu, Kenya*

	Better	Same	Worse
Keratoconus	55 (61.8%)	34 (38.2%)	0
Non-keratoconus	41 (42.3%)	53 (54.6%)	3 (3.1%)
Total	96 (51.6%)	87 (46.8%)	3 (1.6%)

* Visual status = visual acuity in the better eye.

VISUAL RECOVERY

A total of 118 eyes (79 keratoconus, 39 non-keratoconus) achieved a best visual acuity postoperatively of 6/18 or better (of which nine subsequently deteriorated). The average time to 6/18 was 7.2 months for keratoconus eyes, and 6.7 months for non-keratoconus eyes.

VISUAL STATUS

The preoperative and latest postoperative visual status of both keratoconus and non-keratoconus patients is shown in Table 5. Before surgery, 58 patients were blind (<3/60 in the better eye). Of these the majority (81%) were non-keratoconus patients.

Postoperatively, 26 (14.0%) patients were blind (non-keratoconus 25.7% versus keratoconus 1.1%). A total of 34 patients who were blind preoperatively improved so that they were no longer blind after surgery. However, two patients who were not blind before surgery had become blind at their last follow up visit. Therefore, from a total of 216 penetrating keratoplasties performed, there was a net reduction in the number of blind patients of 32.

The number of patients with normal vision increased by 74, from 32 to 106. Most of these (77.5%) were keratoconus patients. Keratoconus patients were more likely than non-keratoconus patients to achieve normal visual status postoperatively (77.5% versus 38.1%, $\chi^2= 29.3$, $p<0.001$).

Changes in visual status are shown in Table 6. Ninety six patients (51.6%) had an improvement in their visual status and three patients (1.6%) had a worse visual status postoperatively. Of the keratoconus patients, 61.8% showed some improvement in their visual status as opposed to 42.3% of the non-keratoconus patients ($\chi^2= 7.1$, $p<0.01$).

ASTIGMATISM

Postoperative astigmatism was worse in keratoconus grafts. The mean cylinder was 4.2 D in the keratoconus eyes and 2.7 D in non-keratoconus eyes.

POOR VISUAL OUTCOME

Fifty seven operated eyes had a latest visual acuity of <6/60 (seven keratoconus and 50 non-keratoconus). The causes of the poor visual acuities are shown in Table 7. Graft opacification accounted for 54.4% and glaucoma 14.0%. Retinal disease was the cause in

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Table 7 Causes of postoperative visual acuity less than 6/60, in 203 eyes undergoing keratoplasty, Kikuyu, Kenya

Cause of low vision	*Non-keratoconus (n=103)*	*Keratoconus (n=100)*
Graft opacity	27	4
Glaucoma	8	0
Retinal disease	5	1
Amblyopia	3	1
Cataract	3	0
Not known	4	1
Total	50 (48.5%)	7 (7%)

10.5% and included two eyes with cystoid macular oedema, two with hereditary maculopathy, and one each with albinism and optic atrophy.

Discussion

AGE

The average age of grafting patients with keratoconus was 17.8 years which is younger than reported in other series.[8] This may be due to the shortage of facilities in Kenya for fitting hard contact lenses. It is also possible that keratoconus may have an earlier onset in this population, owing to the high prevalence of vernal conjunctivitis.

DIAGNOSIS

The most frequent diagnosis was keratoconus, which was the indication for grafting in 50% of the patients. The proportion of grafts performed for herpes simplex keratitis (7.8%) is higher than in recent series from Western countries,[9] reflecting the greater severity of the disease in Africa,[10] and the relative unavailability of effective treatment. It is striking that only 11 out of 216 grafts were performed for the major causes of corneal blindness in Africa—measles and trachoma. The grafts that were performed for measles or trachoma did badly, as six out of the 11 grafts became opaque. This suggests that penetrating keratoplasty has a very limited role in eliminating blindness from measles, vitamin A deficiency, and trachoma in Africa.

DONOR MATERIAL

It was encouraging to see that out of 210 grafts using overseas material, there were only six cases (3%) of primary graft failure. This confirms that it is possible to send donor corneas thousands of kilometres from their place of origin.

GRAFT SURVIVAL

Overall survival rates were lower than those reported from developed countries.[11–14] In most of these series, the 2 year survival rate for keratoconus grafts was well over 90% compared with 87% in our series. Among the keratoconus grafts, the younger age of the patients, and the coexisting severe vernal disease may play a part in reducing graft survival. If the five keratoconus grafts that failed because of primary graft failure are excluded, the 2 year survival improves to 91.7%.The overall rate of 64.7% survival of non-keratoconus grafts at 2 years is lower than would be expected in an industrialised country.

The major reason for the poorer prognosis is inadequate follow up. Nearly one third of patients with corneal grafts that were clear at their last follow up visit are no longer attending the clinic. Failure to attend for follow up, despite intensive preoperative counselling, is due to the cost involved in travelling to attend the clinic, and different cultural attitudes to health and disease leading to poor patient compliance.

GRAFT FAILURE

Suppurative keratitis was the leading cause of graft failure. The incidence of infection (15.7%) is much higher than reported in the UK.[15] Suppurative keratitis was associated with loose sutures, increasing age, and preoperative diagnosis of bacterial keratitis or trachoma. Secondary endothelial failure often followed traumatic wound dehiscence or wound leaks. Acute rejection was more likely to lead to graft failure in non-keratoconus grafts than in keratoconus grafts. All patients received topical steroids for at least 6 months after surgery.

VISUAL ACUITY

The preoperative visual acuities tended to be worse in the non-keratoconus eyes. This may reflect the fact that keratoconus rarely reduces the vision to hand motions. It is also likely that there is some bias, as the known better prognosis for keratoconus grafts probably encouraged earlier surgery in these patients. The final visual acuities are lower than reported for most other series, particularly for keratoconus eyes.[11 12] This is partly because of the higher graft failure rate in our series, but may also be due to the fact that in other series 20–37% of the patients were at least partly reliant on contact lens correction in order to obtain good visual acuity.[11] In a large multicentre prospective study of corneal grafts in the UK, 47% of eyes at 3 months and 61% at 12 months had a visual acuity of 6/18 or better[12]; this compares with 73% for keratoconus eyes and 35% for non-keratoconus eyes in the present study. The latest visual acuity in the operated eye was worse than the vision in the unoperated eye in 13.8% of eyes. This compares with 48.3% in the series from Australia.[16] This figure is likely to be an important factor in determining patient satisfaction with his or her graft.

ASTIGMATISM

We found that the mean astigmatism was significantly greater in keratoconus eyes than non-keratoconus eyes with an average astigmatism of 4.2 D for the keratoconus patients. Less than a quarter (23.3%) of all eyes had a cylinder greater than 5 dioptres. As contact lenses are expensive and difficult to obtain in Kenya, astigmatism was usually managed with spectacles.

POOR VISUAL OUTCOME

Fifty seven eyes (28%) had a postoperative visual acuity of less than 6/60. The commonest cause of poor vision was graft opacity (31 of 57 eyes). This indicates that the most effective way of improving visual outcome will be to improve

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graft survival. The causes of poor acuity with a clear graft are similar to those reported in other series[8] although the numbers affected are proportionately greater.

VISUAL STATUS

The non-keratoconus patients were much more likely to be bilaterally blind preoperatively than the keratoconus patients. Only one keratoconus patient remained blind after penetrating keratoplasty, but 25 (25.7%) of the non-keratoconus patients were still blind, with a vision of <3/60 in their better eye. After the 216 penetrating keratoplasties in this series, the number of blind patients was reduced by 32—that is, an average of one in seven corneal grafts restored sight to a blind person. It is currently estimated that six million people are blind from corneal disease.[4]

Compared with cataract surgery, penetrating keratoplasty is relatively ineffective at restoring sight to blind patients; however, it does result in an improved visual status in the majority of patients, which can have far reaching socioeconomic effects. Consider a teenager with keratoconus and vision of 6/60 and 2/60. He will be having serious difficulties continuing his education in a normal African school. If his vision improves to 6/12 in one eye following keratoplasty, he will be able to stay in a normal school and education system, with improved prospects for himself, and considerable savings for his community.

Conclusions

Penetrating keratoplasty in Africa is possible and, with care and attention, clear grafts can be obtained in many patients. We suggest that penetrating keratoplasty has a definite role in the treatment of keratoconus, which is non-preventable, visually disabling, usually bilateral, occurs in young people, and in which nearly three quarters of grafted eyes obtained a postoperative visual acuity of 6/18 or better. In non-keratoconus corneal disease, we recommend that surgery should only be considered if the fellow eye has a vision of less than 6/60 and the eye for surgery is suitable for penetrating keratoplasty.

We advocate the development of selected tertiary centres for penetrating keratoplasty in Africa. These centres should focus their efforts on grafting for keratoconus and other corneal dystrophies, and should seek to change cultural attitudes to tissue donation. In view of the limited role and poor results of penetrating keratoplasty in corneal scarring due to trachoma, vitamin A deficiency, and measles—currently the major causes of corneal blindness in Africa—priority must still be given to community health programmes including measles immunisation, improved nutrition, trachoma control, and eyelid surgery for trichiasis.

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