

Penetrating Keratoplasty in the Singapore National Eye Centre and Donor Cornea Acquisition in the Singapore Eye Bank

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Abstract

We analyzed all penetrating keratoplasties performed in the Singapore National Eye Centre from 1 January 1991 to 31 December 1995, using records of the Singapore Eye Bank Registry, evaluating the indications, complications, causes of graft failure, visual outcome and graft survival rate. We also looked into donor cornea acquisition in the Singapore Eye Bank and its influence on the development of corneal transplantation in the Singapore National Eye Centre.

A total of 327 penetrating keratoplasties were performed during the 5-year period. Bullous keratopathy was an indication in 26.3% of cases. Of these, aphakic bullous keratopathy accounted for 11.6% of all cases, while pseudophakic bullous keratopathy accounted for 11.3%. Other indications were re-grafts (11.9%), corneal dystrophies (10.4%), traumatic corneal scarring (10.1%) and keratoconus (9.8%). Graft rejection was a complication in 20% of all cases. Of these, 40.9% led to graft failure. Other major complications were raised intraocular pressure (18%), epithelium-related problems (7.3%), wound dehiscence (4.3%), cataract (3.3%) and microbial keratitis (3.1%). The main causes of graft failure were graft rejection (8.2%), endothelial failure (2.4%), infection (2.4%) and glaucoma (2.1%). Of the 327 grafts, 40.3% achieved best corrected visual acuity of 6/12 or better; 70.8% achieved vision of 6/24 or better. The overall graft survival rate was 82.3% after a mean follow-up period of 2 years. Donor corneas for the penetrating keratoplasties were obtained from foreign eye banks as well as locally, with the local donation rate steadily increasing from 1991 to 1996, with the establishment of proper eye banking facilities and the Singapore Eye Bank.

These results show that the indications and outcome of penetrating keratoplasty in the Singapore National Eye Centre are similar and comparable to that of other centres with established corneal grafting programmes. The establishment of the Singapore Eye Bank has ensured the proper co-ordination of acquisition of donor material which has been vital to the development of corneal transplantation in the Singapore National Eye Centre.

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Key words: Bullous keratopathy, Corneal transplantation, Eye banking, Eye donation, Graft rejection

Introduction

Penetrating keratoplasty is the removal and replacement of a diseased cornea by a full thickness donor cornea (i.e. full thickness corneal grafting). The disease indications for penetrating keratoplasty are many, and these can be broadly classified into optical, tectonic, therapeutic or cosmetic. Like all other organ transplantations, an important problem is that of allograft rejection. Other significant complications of penetrating keratoplasty include post-keratoplasty glaucoma, infection, epithelial problems and recurrence of the primary disease.¹ Significant advances in penetrating keratoplasty have been achieved over the past few decades, including improved surgical techniques and

new immunosuppressive therapies, resulting in the broadening of indications and improved graft survival.¹

The Singapore Eye Bank Registry was established in 1993 and included in the Registry are details of all corneal grafts done in the Singapore National Eye Centre from 1 January 1991 onwards. The aim of the Registry is to collect and collate information on the practice of corneal grafting (both penetrating and lamellar keratoplasty) in the Singapore National Eye Centre, with emphasis on the clinical auditing of all grafts done.

We analyzed all penetrating keratoplasties performed in the Singapore National Eye Centre during a five-year period from 1 January 1991 to 31 December 1995, using records of the Singapore Eye Bank Registry. The indica-

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tions for grafting, the complications encountered, the causes of graft failure, the overall visual outcome and graft survival rate, as well as the source of donor corneas were analyzed. Our results were collated and directly compared to a similar study of penetrating keratoplasty done in the Singapore General Hospital in the 1980s, carried out by Tseng et al in 1991.² We also evaluated our results in comparison to the Australian Corneal Graft Registry 1994 Report,” which is a good example of corneal grafting in a country with an established corneal grafting programme.

Materials and Methods

All penetrating keratoplasties performed at the Singapore National Eye Centre between 1 January 1991 and 31 December 1995 were included in our study. Data for analysis were obtained from the computer records of the Singapore Eye Bank Registry, which included preoperative data, donor data, postoperative data, complications data and graft survival data.

All penetrating keratoplasties were performed by corneal subspecialists or senior ophthalmologists and all data were entered by the attending ophthalmologists.

The classification of indications in the Registry was designed according to Brightbill’s classification.’ Unaided and best corrected visual acuity were entered at 1 month, 3 months and 6 months postoperatively, then at 1 year and 18 months postoperatively, and subsequently at yearly intervals. Complications detected at each follow-up were noted and the eventual outcome (i.e. failed graft or clear graft) entered.

For purposes of our study, “post-keratoplasty glaucoma” is defined as raised intraocular pressure of more than or equal to 22 mmHg, with or without accompanying optic disc and visual field changes. A “failed corneal graft” is defined as an irreversibly oedematous or opaque graft, resulting in visual acuity of counting fingers or worse. Conversely, “graft survival” refers to an optically clear graft at the time of last follow-up.

Results

During the five-year period, 327 penetrating keratoplasties were performed. Fifty-five cases were performed in 1991, 49 cases in 1992, 72 cases in 1993, 91 cases in 1994 and 60 cases in 1995.

Demographics

The mean age of the patients was 54.7 years with a range of 1 to 92 years. There were 206 males (63%) and 121 females (37%) giving a male to female ratio of 1.7:1. Of the 327 cases, 241 (73.7%) patients were Chinese, 34 (10.4%) were Malays, 41(12.5%) were Indians and 12 (3.7%) were classified as other races. The distribution among the various races was consistent with the racial distribution in Singapore.

Indications (Table I)

In our series, bullous keratopathy was the most frequent indication, accounting for 26.3% of all cases. Aphakic bullous keratopathy accounted for 11.6% of cases, while pseudophakic bullous keratopathy accounted for 11.3%. The other causes of bullous keratopathy (3.4%) were secondary to glaucoma and uveitis and following laser treatment.

The next major group of indications was regrafts, accounting for 11.9% of cases. Graft failure secondary to allograft rejection accounted for 56.4% of cases in the regraft group. Other indications for regrafting included post-penetrating keratoplasty glaucoma (17.9% of regraft cases), late endothelial failure (10.3%), post-keratoplasty microbial keratitis (7.7%), recurrence of corneal dystrophy (5.1%) and primary tissue failure (2.6%).

TABLE I: INDICATIONS FOR PENETRATING KERATOPLASTY SINGAPORE NATIONAL EYE CENTRE 199 1- 1995

Indications	Number of grafts	Percentage
Bullous keratopathy	86	26.3
Regrafts	39	11.9
Corneal dystrophies	34	10.4
Trauma	33	10.1
Keratoconus	32	9.8
Acute/Chronic ulceration	31	9.5
Interstitial keratitis	26	8.0
Corneal scarring	20	6.1
Herpetic keratitis	13	4.0
Chemical		1.2
Congenital		1.0
Others	6	1.8
Total number	327	100

Corneal dystrophies accounted for 10.4% of all cases. Of these, Fuchs endothelial dystrophy accounted for 52.9% of the cases (5.5% of all cases). Other corneal dystrophies in our series included lattice dystrophy (1.5% of all cases), granular dystrophy (0.6%) and dystrophy associated with the irido-corneal-endothelial (ICE) syndrome (0.9%).

Traumatic scarring, was an indication in 10.1% of cases. The majority of these cases were industrial accidents with penetrating ocular injuries.

Keratoconus accounted for 9.8% of cases. Interestingly, of the 34 cases of keratoconus in our series, 18 cases (52%) were Indian patients and 24 cases (70.6%) were males. The mean age was 26.9 years.

Acute and chronic ulcerative diseases accounted for 9.5% of cases. Of the 31 cases, 13 cases were bacterial corneal ulcers, 10 cases were fungal ulcers and 5 cases were due to trachoma. There was one case each of Acanthamoeba keratitis, Mooren’s ulcer and exposure keratitis.

Interstitial keratitis was an indication in 8.0% of cases.

Scarring with or without inflammation accounted for 6.1% of cases. These included scarring secondary to blepharitis, previous pterygium surgery, bee sting injury, lipid keratopathy and scarring from unknown cause.

The other indications were herpetic keratitis (4.0%), chemical injury (1.2%) and congenital causes (1.0%). The congenital causes included Peter's anomaly, buphthalmos and sclerocornea. The indications for 1.8% of cases were not clearly defined in the casenotes and were classified as "others".

Complications (Table II)

Graft rejection occurred in 20% of cases. Of these 40.9% lead to graft failure. Glaucoma was the next most frequently encountered complication (18%). Of these, 11.8% lead to graft failure. 2.4% had recurrence of primary disease. Endothelial failure occurred in 2.4% of cases. All these grafts failed. Two cases (0.6%) developed postoperative endophthalmitis.

Graft Failure (Table III)

Fifty-eight of our 327 cases (17.7%) ended in graft failure. Of the failed grafts, 46.6% were due to graft rejection. Other important causes of graft failure in our study were endothelial failure (13.8% of graft failure cases), infection (8.6%) and glaucoma (12.1%). The other causes of graft failure (18.9%) included epithelium-related problems, recurrence of primary disease, uveitis and reactivation of herpetic disease.

Visual Outcome (Table IV)

Table IV shows the postoperative best corrected visual

TABLE III: LEADING CAUSES OF GRAFT FAILURE

	SNEC 1991-1995 *	ACGR 1985-1994 **
Graft rejection	8.2%	5.1%
Endothelial failure	2.4%	2.4%
Infection	2.4%	2.2%
Glaucoma	2.1%	1.2%
Others	2.4%	3.1%
Total	17.7%	14.1%

* Percentage of 327 grafts

** Percentage of 4499 grafts

SNEC: Singapore National Eye Centre

ACGR: Australian Corneal Graft Registry

acuity of 234 of our cases with more than 6 months follow-up. Other pre-existing causes of poor visual acuity have not been excluded in this list. 40.3% of cases achieved visual acuity of 6/12 or better, 70.8% achieved 6/24 or better and only 24.8% achieved 6/60 or worse.

Overall Graft Survival Rate

The overall graft survival rate (based on graft clarity) was 82.3%, with a mean follow-up period of 2 years.

Source of Donor Corneas (Table V, Figure 1)

From 1991 to 1995, donor corneas were obtained from Sri Lanka, Queensland, Australia as well as from local donors. In 1996, a significant number of donor corneas came from Florida, USA as well. Table V shows the donor sources from 1991 to 1996. The numbers include all corneas used for both penetrating and lamellar keratoplasty in the Singapore National Eye Centre. There was a significant increase in the number of local donors from 1991 to 1996. In 1991, 53 out of 57 donor corneas (93%)

TABLE II: COMPLICATIONS OF PENETRATING KERATOPLASTY

Complication	Number	% of all grafts	Leading to graft failure	
			Number*	%**
Graft rejection	66	20.0	27	40.9
Glaucoma	59	18.0	7	11.8
Epithelium-related problems	24	7.3	1	0.04
Wound dehiscence	14	4.3	0	0.0
Cataract	11	3.3	0	0.0
Microbial keratitis	10	3.1	3	30.0
Recurrence of primary disease	8	2.4	5	62.5
Uveitis / Peripheral anterior synechiae	6	1.8	1	10.4
Late endothelial failure	5	1.5	5	100.0
Suture abscess	4	1.2	1	25.0
Primary endothelial failure		0.9	3	100.0
Reactivation of herpetic disease	2	0.6	1	50.0
Endophthalmitis	2	0.6	1	50.0
Retinal detachment	2	0.6	0	0.0
Others	12	3.6	3	25.0

* Number of grafts with the specified complication that failed

** Percentage of grafts with the specified complication that failed

Note: More than one complications may occur in each graft

TABLE IV: BESTCORRECTEDVISUALACUITY (WITHMORETHAN 6 MONTHS FOLLOW UP)

Best Corrected Visual Acuity	Number	%	Cumulative %
6/6	16	7.2	7.2
6/9	29	13.0	20.2
6/12	45	20.2	40.3
6/18	25	11.2	51.6
6/24	43	19.3	70.8
6/36		3.1	74.0
6/60	15	6.7	80.7
6/120	10	4.5	85.2
Counting Fingers	25	11.2	96.4
Hand Movement	4	1.8	98.2
Light Perception	2	0.9	99.1
No Light Perception	2	0.9	100.0
Total Number	234		

Note: Cases with other pre-existing causes of poor visual acuity have not been excluded in this list

TABLE V: SOURCES OF DONOR CORNEAS (1991-1996)

Country	1991	1992	1993	1994	1995	1996
Sri Lanka	53	39	35	35	18	42
Queensland	0	0	36	21	28	1
USA	0	0	0	0	0	37
Singapore	4	13	2	40	26	45
Yearly Total	57	52	73	96	72	125

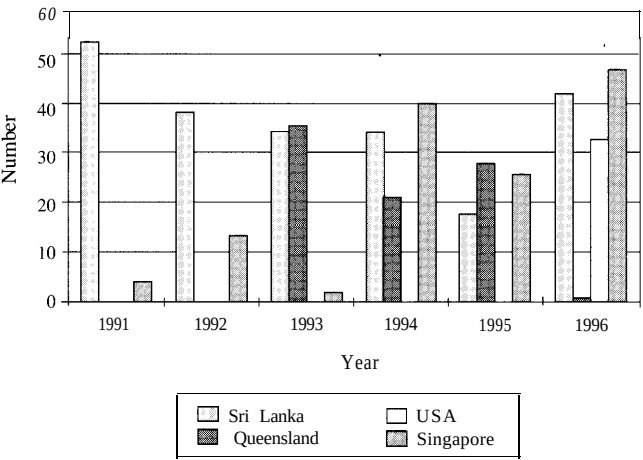


Fig. 1. Source of donor corneas (1991-1996).

were obtained from Sri Lanka with only 4 corneas contributed by local donors. In 1994, there were 40 local donor corneas and in 1996, there were 45.

Discussion

The majority of corneal transplants carried out in the world today are done in developed Western countries where keratoconus, pseudophakic bullous keratopathy and corneal dystrophy are relatively common indica-

tions.⁴

For many years, corneal disease from infection and malnutrition has been a major cause of blindness in Asia. Corneal transplantation in Asia as a whole has been poorly developed due to a combination of factors including the lack of donor material and limited financial and manpower resources. One of the outstanding exceptions in Asia is the efforts of a single-minded doctor, Hudson Silva, who is responsible for the existence and success of the Sri Lanka International Eye Bank, an important source of donor material in Asia. (Lim A S M, Balakrishnan V. The importance of corneal transplantation in Asia. Keynote address: Ninth Lions Eye Bank Lecture, Ninth Annual Lions Eye Bank Meeting, Adelaide, 4-6 March 1992.)

With growing affluence and advances in medicine and ophthalmology, there is a higher expectation of good vision in previously untreatable corneal diseases, making penetrating keratoplasty increasingly important in Asia in the 1990s.⁵

The Singapore Eye Bank of the Ministry of Health was established by Dr Robert C K Loh in March 1966 following the introduction of the Medical (Therapy) and Education Act (1965). The primary function of the Eye Bank then was very much to serve as a relay station for the despatch of donor eyes from Sri Lanka, Australia and New Zealand to countries like Malaysia, Indonesia, Philippines and Singapore itself.⁶ Despite the existence of such a set-up, acquisition of donor material at that time was still a major constraint, due to limited resources.

Proper co-ordination of donor material acquisition is vital to the success of the corneal grafting programme in Singapore today. The establishment of eye banking facilities for donor tissue acquisition in the Singapore National Eye Centre began in 1993 and the Singapore Eye Bank of today was officially opened on 2 December 1995. The Singapore Eye Bank is responsible for the procurement, storage and utilization of donated corneas in the Singapore National Eye Centre. It plays an important role in procuring high quality donor tissue, which is vital to the development and success of the corneal transplantation programme in the Singapore National Eye Centre.

From 1991 to 1993, there was a heavy reliance on foreign eye banks for donor material (Table V). For example, donor corneas from Sri Lanka constituted 93% of all corneas obtained in 1991 and 75% of corneas obtained in 1992. There was, however, a subsequent increase in the local donation rate from 1994, resulting in a decrease in the reliance on foreign eye banks for donor tissue.

A Hospital Eye Donation Programme was established in October 1995 by the Singapore General Hospital and the

Singapore Eye Bank. In the Singapore General Hospital, upon the death of a patient who is identified as a suitable donor, the relatives are counselled to give consent to cornea donation. With the establishment of this programme, there has been a gradual increase in the number of local donors to date. Table VI shows the source of local donors from 1991 to 1996. In 1996, the majority (71.1 %) of donor eyes obtained locally were from the Hospital Eye Donation Programme. In marked contrast, there was a significant decrease in the number of donors from the Changi Prison.

TABLE VI: SOURCE OF LOCAL DONORS (1991-1996)

Year	Prison	Multi-Organ*	HEDP**	Total
1991	2	2		4
1992	12	1		13
1993	2	0		2
1994	36	4		40
1995	22	4		26
1996	7	6	32	45

* Multi-organ donation

** Hospital Eye Donation Programme

A retrospective study of penetrating keratoplasty done in the Singapore General Hospital from 1980 to 1989 was carried out by Tseng et al in 1991.² During the 10-year period only 56 penetrating keratoplasties were performed. The small number of grafts performed reflects the problems at that time in obtaining donor tissue. Majority of the grafts were done on an emergency basis, as "there was never any warning as to when a donor eye was going to be available".² This is in stark contrast to corneal grafting today, where the majority of grafts are done on an elective basis. Co-ordination between the Singapore Eye Bank and the eye banks of Sri Lanka, Queensland and more recently that of Florida ensures the availability of donor tissue at predictable times for elective surgery to be carried out.

During the period from 1991 to 1995, 741 corneal grafts (both lamellar and penetrating keratoplasties) were performed in Singapore.⁷ Of these, 347 grafts were performed in the Singapore National Eye Centre alone, which was 46.8% of the total number of grafts done in Singapore. The other grafts were performed mainly by various ophthalmologists in the private sector.

With growing affluence comes improved hygiene, living standards and health services, resulting in a decrease in corneal blindness from infection and malnutrition. Due to this changing pattern of corneal blindness, the indications for penetrating keratoplasty in Singapore have also changed through the years.⁸

In the study carried out by Tseng et al in 1991, acute and chronic ulcerative disease was the leading indication, accounting for 27.2% of the grafts done. The major-

ity of these cases were bacterial ulcers (11 out of 13 cases), with trachoma (1 case) and measles (1 case) contributing to the list. Bullous keratopathy was an indication in only 3.6% of the cases. No regrafts were done. This is in contrast to the indications of penetrating keratoplasty in our study, in which bullous keratopathy was the leading indication, accounting for 26.3% of all cases. 11.9% of our cases were regrafts, and acute and chronic ulceration accounted for 9.5% of our cases. Bullous keratopathy (aphakic and pseudophakic) as the leading indication is largely due to the increasing number of cataract surgeries being performed today.

The Australian Corneal Graft Registry 1994 Report³ included 6031 penetrating keratoplasties done throughout Australia between 1985 and 1994. It provides an excellent insight into corneal grafting in a developed nation with an established corneal grafting programme. The leading indications in this series were keratoconus (29.5%) followed by bullous keratopathy (25.1%) and regrafts (18.2%). Infection (non-viral) was an indication in only 2.5% of cases. The major indications in our series somewhat parallel the indications in this series, except that keratoconus was an indication in only 9.8% of our cases.

A series done by the Will's Eye Hospital (USA) from 1983 to 1988 revealed that pseudophakic bullous keratopathy was the leading indication accounting for 22.9% of cases, followed by Fuchs endothelial dystrophy (16.3%) and keratoconus (15.1%).⁹ A study done by the Moorfield's Eye Hospital (UK) from 1985 to 1987, however, revealed keratoconus (34.2%), regrafts (17.2%) and bullous keratopathy (12.6%) to be the main indications.¹⁰

Corneal graft failure occurs when a graft becomes irreversibly oedematous or opaque. It must be differentiated from graft rejection which is an immunological reaction mounted by the recipient to the presence of "foreign" donor tissue. Graft failure can result from various causes like infection, glaucoma or endothelial failure but graft rejection is still the leading cause of graft failure. The incidence of corneal allograft rejection ranges from 2.3% to as high as 68% of cases of penetrating keratoplasty.^{11,12} Predisposing factors for graft rejection include vascularization, inflammation, repeat grafting, bilateral grafts, anterior synechiae, lid and ocular surface disease and young age of recipient.* Graft rejection occurred in 20.0% of cases in our study and 15.1% of cases in the Australian Corneal Graft Registry Report 1994.

Maximal doses of corticosteroids do not reliably prevent corneal graft rejection. In solid organ transplantation (e.g. kidney and liver), histocompatibility matching is a fairly effective method of immunomodulation. However, in corneal transplantation, especially in high-risk cases, this has been proven to be rather disappointing.¹³

Cyclosporin A has been found to decrease the incidence and increase the reversal rate of rejection episodes. This effect has been found to continue even after cessation of treatment with cyclosporin A, suggesting that some immune-privilege had been established.¹⁴ Systemic cyclosporin A has been found to be superior to systemic corticosteroids, suggesting that selective systemic immuno-modulation with cyclosporin A may be more effective than generalized suppression with corticosteroids.¹³

Regrafting is associated with an increased risk of allograft rejection as the host is sensitized. In our study, 39 penetrating keratoplasties were regrafts. No regrafts were done in the previous study by Tseng et al. This increase in the rate of regrafting is attributed to the fact that cases previously not considered for grafting due to high risk for failure (e.g. previous failed graft, presence of vascularization or poor ocular surface) are now being undertaken. This is possible with improved surgical expertise, advances in instrumentation and corneal preservation as well as the use of immunomodulators like cyclosporin A.

Glaucoma is another complication encountered in penetrating keratoplasty. The overall incidence of glaucoma is about 30% of all grafts performed. Cases at high risk for post-keratoplasty glaucoma include aphakic eyes especially after intracapsular cataract extraction, the elderly, traumatized eyes and repeat corneal grafts.¹⁵ The incidence of post-keratoplasty glaucoma in our series was 18.0%.

Table III compares the leading causes of graft failure in our study with that of the Australian Corneal Graft Registry 1994. Allograft rejection was the leading cause of graft failure in both series. The overall graft failure rate in our study was 17.7% compared to 14.1% in the Australian Corneal Graft Registry 1994.

In penetrating keratoplasty, stable visual acuity is often not achieved until as long as 6 months to a year following surgery. In our study, 40.3% of cases with more than 6 months of follow-up achieved visual acuity of 6/12 or better. Other pre-existing causes of poor visual acuity (e.g. glaucoma, macular disease and diabetic retinopathy) have unfortunately not been excluded in this list. However, in our current data collection (for grafts done after October 1996), we have improved our database to address this deficiency.

With a mean follow-up period of 2 years, the overall graft survival rate in our study was 82.3%. This is comparable to that of the Australian Corneal Graft Registry 1994 which was 83.5%.

Conclusion

With improved eye banking facilities, improved standards of eye care and microsurgical techniques, the trends

in penetrating keratoplasty in Singapore have changed. Our results are now comparable to that of centres with established corneal grafting programmes.

The Singapore Eye Bank aims to increase the local cornea donation rate in the coming years, with a decrease in the reliance on foreign eye banks. It also aims to extend its eye banking facilities to all corneal transplants in Singapore, including those done in the private sector. This would help increase the database for the clinical auditing of corneal transplants done in Singapore. There is also a need to continue a longer follow-up of our corneal transplant patients to obtain the 5-year survival rates of local grafts and also to look into the effects of newer therapies such as systemic immunomodulation with cyclosporin A.

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