



## Rejection and Failure in Corneal Graft: Single Centre Experience

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**Abstract**

**Purpose:** Early presentation of rejection facilitates early initiation of treatment which can favor a reversible rejection and better outcome. We analyzed the etiologies, incidence, clinical features, including rejection-treatment period and outcomes following graft rejection in different corneal grafts.

**Materials and methods:** The study is an Ambi-directional cohort. Data collected between 2010 and 2017. Case records of different penetrating keratoplasty (PK) were reviewed, and parameters noted demographic profile, indication of surgery, rejection-treatment interval, graft outcome, and complications.

**Results:** Eighty eyes were collected with an average age of 48 years. Males represent 52.5% of the sample. Penetrating keratoplasty (PKP) represents 70.0 %, and deep anterior lamellar keratoplasty (DALK) 22.5 %, and decement stripping automated endothelial keratoplasty (DSAEK) was 6.3%. Keratoconus was the primary etiology by 30 %, followed by pseudophakic bullous keratopathy 17.5%. The endothelial rejection was the commonest cause of rejection 25%. The primary complications were vascularization with a record of 26.3%, and suture-related complications were 8.8%. The overall median survival time without any complication was 49 months. PKP had the higher complication with a percentage of 55.3%, and DALK had 23.5%.

**Conclusion:** This study showed PKP is the main procedure and keratoconus is the main etiology. Vascularization of the graft was the major complication, and endothelial rejection is the main type of rejection, as in most of the studies. These data will guide us for future studies.

**Keywords:** Cornea, Keratoplasty, Keratoconus, Graft rejection, Graft failure

## Introduction

Corneal transplant is considered one of the essential surgical procedures commonly done worldwide. Corneal transplantation refers to the surgical replacement of a full-thickness or lamellar portion of the host cornea with a donor's cornea. In 2011, 46,196 corneal transplants were performed, representing an 8.3% increase from the previous year. The number of full-thickness or penetrating keratoplasties (PKP) in 2011 was 21,620. (1) Locally, a total number of thirteen PKP done in xxx Hospital. (2)

Etiologies of corneal transplantation varies; in one study, Trauma-related corneal scarring 113(26.2%) was the leading cause of PKP, followed by keratoconus 74(17.1%), redo graft 56(13%), infection-related corneal opacity 46(10.6%), corneal dystrophy 44(10.2%) and bullous keratopathy 36(8.3%). (3) In another study, the predominant indications for PKP were pseudophakic bullous keratopathy (32%), Fuchs' dystrophy (23%), and graft failure (10%) of the eyes. (4)

The success of any transplantation procedure depends on the availability and quality of corneal tissue. A complete eye examination is necessary before corneal transplantation; the assessment should include a detailed social history. Simple clinical tests, such as those for colour recognition or an afferent pupillary defect, can be essential in evaluating patients with media opacity. Ocular surface problems such as dry eye, trichiasis, exposure, blepharitis, and rosacea must be recognized and treated before transplantation. Furthermore, any retina disease, macular disease, glaucoma should be identified before PKP.

Routine postsurgical care using topical antibiotics, tapering topical corticosteroids, and frequent office visits are directed at preventing and allowing early recognition of the complications that can occur after PK and optimizing postoperative wound healing, facilitating rapid visual rehabilitation.

According to one study, graft complications can vary; the most common causes of secondary graft failure were an endothelial failure (29%) or immunologic endothelial rejection (27%). (4) Survival of first-time grafts was 90% at five years and 82% at ten years. (3) Initial regrafts had significantly lower five years and ten years survival rates, 53% and 41%, respectively. (4) In the local study (uncited source), two patients had endothelial graft rejection, and three patients developed high IOP; their final visual acuity has improved in 77% of cases with 0.37 of average the best corrected visual acuity (BCVA). (2)

In Conclusion, this study is aimed to identify the ocular condition that led to corneal transplant, short and long-term complications after transplant, visual acuity, long-term graft survival rates, and the outcome (rejection and failure) of different types of keratoplasty. The results of this might add new protocols for the management of patients post PKP.

## **Material and Methods**

The study is an Ambi-directional cohort. Data of patients collected from the computerized system which saves the patient who underwent different types of keratoplasty, and patients been analyzed in terms of causes for the keratoplasty, visual acuity, intraocular pressure changes, and complications. The study aims to explore in detail the incidence of rejection and failure in keratoplasty.

In the beginning, the demographic data collected, including patient numbers, age, sex, and the date of surgery identified, and the date of the first visit, also added. The Types of keratoplasty were also defined in the study as penetrating keratoplasty (PKP), Descemet stripping automated endothelial keratoplasty (DSAEK), deep anterior lamellar keratoplasty (DALK), Descemet membrane endothelial keratoplasty (DMEK).

Besides, the data collected includes the best-corrected visual acuity before keratoplasty and during the follow-up period, which is one month, six months, one year, and two years. The intraocular pressure was recorded in the same follow-up period. Furthermore, the pathology or the indications behind keratoplasty have been identified in the study to be either keratoconus, keratoglobus, pseudophakic bullous keratopathy, infections related to keratitis, corneal dystrophy, graft failure, and others including trauma, cornea scar, etc.

In terms of complications, vascularization, suture-related complications (including loose sutures, suture abscess, broken sutures), graft rejections (epithelial, stromal, and endothelial graft rejection), graft failure also was mentioned in the study. Timing of sutures removal was also identified.

Collection of data included all cases from 2010 until 2017 as Ambi-directional, consent taken from patient verbally for the prospective group. This study was approved by the xxx-research committee, approval code RC 8/2018. Data collection started in 2016 and included all patients who were sent for keratoplasty abroad and had a follow-up period in our hospital. The Age range of participants from ten to eighty years. The inclusion criteria necessitate at least three visits post keratoplasty, including the first-month follow-up visit. Each eye is considered as a case separately.

The Exclusion criteria were for any case which has less than three follow-up post-surgery, any child at the age of less than ten years, and any cases with severe comorbidity in the eye adding to the visual disability such as retinal detachment or advanced glaucoma.

Sample size calculated through the Raosoft system with a Confidence interval of 95% and an error of 5 %. The population has been estimated using 20000 population size with sample size calculated to be eighty Patients.

### **Statistical analysis**

There was no statistically significant difference in the survival distribution between the four types of surgeries ( $p= 0.449$ ). The median survival time was estimated to be 49.0 months. The median survival time were 45, 70, 49 months, respectively, for PKP, DALK, and DAESK. The quality of survival distributions for the different levels of the type of surgery had a Chi-square of 2.647 using the log Rank Mantel-Cox. There was no statistically significant association between complications and type of surgery ( $p= 0.075$ ).

### **Results**

The data collected in the study in the period between 2010 and 2017 includes eighty eyes. The age was ranged between ten years to eighty-five years old. The mean age in the study was 48.3 years. The percentage of males in the study was 52.5%, and the number of females was 47.5 %. When referring to the type of surgery, 70.0 % had PKP, 22.5 % had DALK, and 6.3% had DSAEK. 85.5% of eyes had a visual acuity of less than 0.1. The majority (49.4%) had their visual acuity between 0.1-0.4 in their first follow-up period. That percentage remained almost the same in the rest of the follow-ups period. 8.8% of patients had their vision of hand motion (HM) and less at the end of two years follow-up period. Intraocular pressure reading had a lot of missing data. The indications for the surgeries varied; 30 % of the cases had keratoplasty because of keratoconus, 17.5% had pseudophakic bullous keratopathy, infection-related such as keratitis recorded as 12.5 %, and corneal dystrophy and corneal scarring recorded as 30 % of cases. Certain eyes had redo-graft, which was recorded as 13.8 %.

In terms of complications and outcome, it was recorded to be 47.5%. Graft failure was recorded in eight eyes. The endothelial rejection was the commonest among all types of rejection and recorded as 25% compared with epithelial rejection, which was 12.5 %, and stromal rejection, which was 18.8 %.

Vascularization, including deep and superficial, was found to be 26.3 %. Suture-related complications such as suture abscess, broken sutures, or loose sutures were found in seven eyes.

The overall median survival time without any complication was 49 months. The overall two years of survival was 79%. The overall three years of survival was 62%. The overall five years of survival was 40%.

In terms of the rate of complications within the different types of surgery, 55.3% of PKP cases had complications, 23.5 % of DALK cases had complications, and 40 % of DAESK had complications.

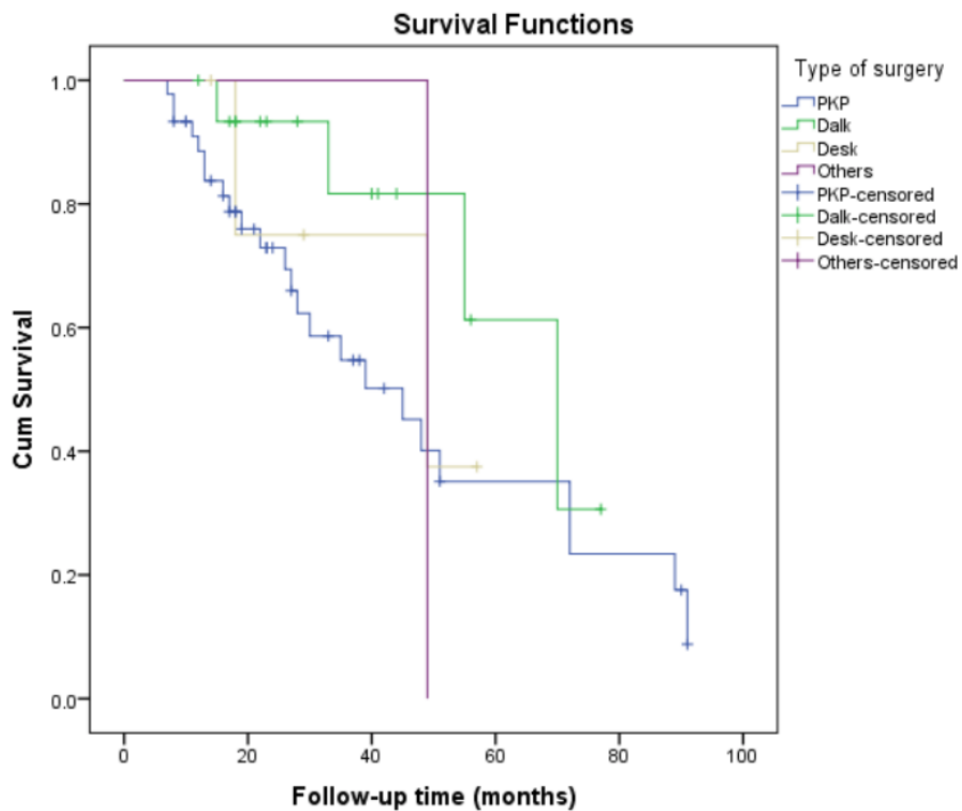


Figure 1: The survival of each type of graft in months.

Mean				Median			
Estimate	Std. Error	95% confidence interval		Estimate	Std. Error	95% confidence interval	
		Lower Bound	Upper Bound			Lower Bound	Upper Bound
51.192	4.077	43.200	59.184	49.000	3.725	41.700	56.300

Table 1: Means and medians of survival time

**Table 2: Type of surgery**

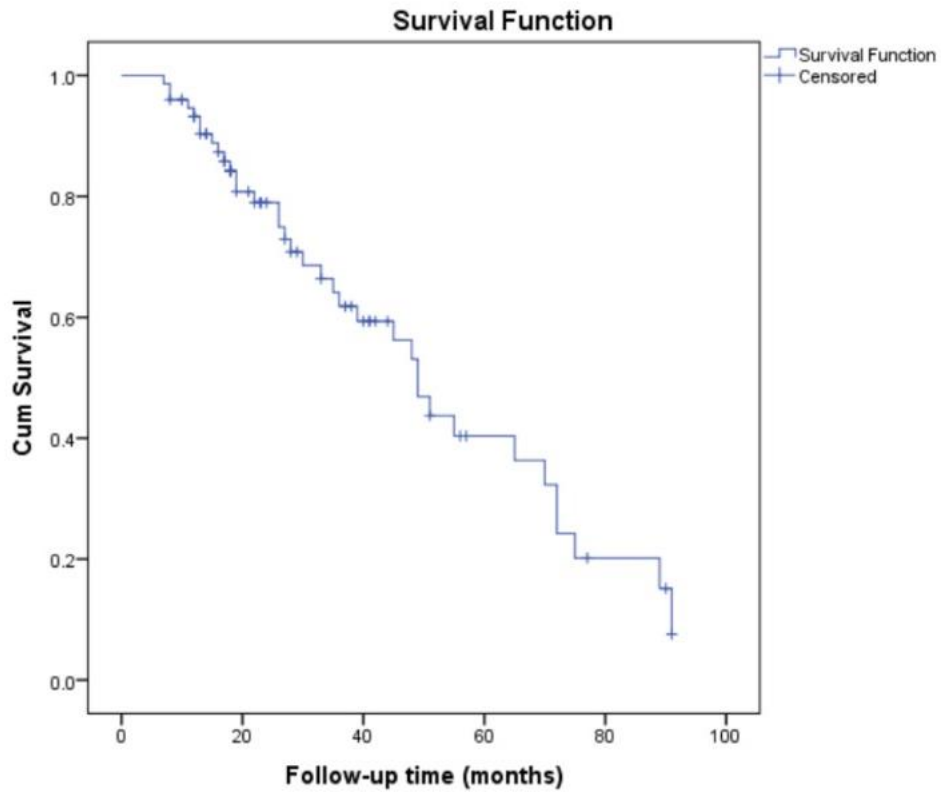
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	PKP	56	70.0	70.0	70.0
	DALK	18	22.5	22.5	92.5
	DESK	5	6.3	6.3	98.8
	Others	1	1.3	1.3	100.0
	Total	80	100.0	100.0	

**Table 3: Gender distribution**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	42	52.5	52.5	52.5
	Female	38	47.5	47.5	100.0
	Total	80	100.0	100.0	

**Table 4: Overall comparisons of all types of surgery**

	Chi- Square	Df	Sig.
Log Rank (Mantel-Cox)	2.647	3	.449
Breslow (generalized Wilcoxon)	3.917	3	.271
Tarone -ware	3.586	3	.310



**Overall Comparisons**

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.647	3	.449
Breslow (Generalized Wilcoxon)	3.917	3	.271
Tarone-Ware	3.586	3	.310

Test of equality of survival distributions for the different levels of Type of surgery.

**Means and Medians for Survival Time**

Mean <sup>a</sup>				Median			
Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound			Lower Bound	Upper Bound
51.192	4.077	43.200	59.184	49.000	3.725	41.700	56.300

a. Estimation is limited to the largest survival time if it is censored.

## Discussion and Conclusion

In this paper, the main issues to discuss are the outcomes of different types of keratoplasty, including various types of graft rejection and graft failure with some associated complications, including vascularization and suture-related complications. Avoiding complications can be through close monitoring of the patients as outpatients visits and recording the visual acuity changes with intraocular pressure monitoring. Complete ophthalmic examination is needed, including slit-lamp examination to look for graft clarity, graft vascularization, identifying the depth of the vascularization, and the number of quadrants involved. Finding the objective of the study, including the visual acuity changes and IOP fluctuation, and long-term survival of the graft, an overall view of the keratoplasty will be achieved, which will help the ophthalmic centre in our hospital to modify the follow-up period intervals, focusing on specific findings in the graft which should not be missed while writing the notes. Knowing certain risk factors that caused graft rejection can be an excellent preventive measure. The results of this study will help to get better outcomes in future cases. As found in our study, the overall median survival time without any complication was 49 months.

Factors contributing to graft failure were evaluated in the study, vascularization was recorded to be 26.3%, and suture-related complications were recorded to be 8.8%. Vascularization is considered as one of the host factors contributing to graft rejection and failure, which can be defined as either superficial or deep. (5)

Multiple causes are responsible for the epithelial type of rejection, including loose sutures and exposed suture knots, trichiasis, and entropion. (6)

In our study, graft failure was recorded in eight eyes. The endothelial rejection was the commonest among all types of rejection and recorded as 25% compared with epithelial rejection, which was 12.5 %, and stromal rejection, which was 18.8 %. The main classification of corneal graft rejection can be either epithelial, stromal, or endothelial or combinations. (7)

The ten years cumulative risk of glaucoma, rejection, or failure was 21%, 21%, and 22%, respectively. (8) We found that 13.8 % of eyes that underwent keratoplasty had regraft due to rejection of the previous graft. It was mentioned in one article that certain types of the transplanted cornea are more predisposed to rejection, including previously failed grafts. (9)

Epithelial rejection is considered as one of the types which have a silent course and very mild symptoms. It was reported to be 10–14%. (10) The incidence of stromal rejection was recorded to be from 2.4-15%. (9) The type of rejection that was difficult to treat and considered irreversible and lead

most of the time to graft failure was endothelial graft rejection. Endothelial rejection is the most symptomatic and devastating type, and it's around 97%. Reported incidence rates of endothelial rejection vary between 2% and 44%. (10) Endothelial graft rejection is related to the extent of vascularization. The avascular graft had 3.5 % of endothelial rejection. (11)

Some limitations were noticed in the study, including the intraocular pressure measurement, which was not possible in certain visits due either to corneal oedema or uncooperative from the patients' side. One way of reducing that limitation was by measuring the intraocular pressure in two methods, either the contact method or the non-contact method (air puff). The study was limited in terms of defining the vascularization extend and depth. It was noticed that details of the number of quadrants or clock hours in identifying the extent of vascularization were missed in the follow-up visits, which needed to be stressed in the future study. Visual acuity recording for hand motion to be recorded in the future study as a numerical factor that was missed in some of the follow-up visits. This study is the first study in our centre and will help to do more studies in corneal graft and guiding us for better management.

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