

A Clinical Study of Factors Influencing Graft Success after Repeat Penetrating Keratoplasty and their Management

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ABSTRACT

Introduction: Corneal disease ranks 5th among the causes of blindness and it forms 7.1% of total blindness and is a serious public health problem resulting in medical and economic burden to the nation. A study was carried out to evaluate re-grafts with emphasis on factors which caused failure of original graft and factors influencing graft success after repeat PK.

Material and methods: The prospective study consisted of cases of graft failure attending Eye Bank Clinic at Command Hospital, Kolkata, from Jan 2017 to Dec 2018. Interval between primary graft and repeat PK was minimum of 06 months. All the surgeries were performed by a single surgeon.

Results: Out of 164 PK, 28 re-graft (17.07%) were performed. The re-grafting were carried out on cases of graft failure due to endothelial failure (39.3%), allograft rejection (17.8%), recurrence of disease (14.2%), secondary glaucoma (10.7%), ocular surface disorder and dry eye (10.7%), Pseudomonas infection (3.6%) and unknown (3.6%). In 13 cases simple repeat keratoplasty and in rest 15 cases combined procedures were done. 17 cases (60.7%) had clear re-grafts and in 11 cases the re-graft became opaque during follow up period of 06 months to 2 years (average 12.6 months). Pseudophakic bullous keratopathy had greater rate of clear re-grafts (71.4%). 09 out of 11 cases of failure had one of the preoperative factors like raised IOP, anterior synechiae, corneal vascularization and younger recipient age group. Vascularization of recipient bed was associated with greater rate of graft failure (60%).

Conclusions: Better visual outcome and graft survival in re-graft can be achieved by understanding the underlying pathology and formulating a preoperative plan.

Keywords: Cornea, Graft failure, Penetrating Keratoplasty, Re-graft, Repeat PK.

requires a thorough examination to determine the cause of graft failure, a prediction of post-re-graft visual potential and rational surgical approach to maximize graft survival. It is important to identify complications and factors responsible for success of re-grafts. The time interval when re-graft can be carried out after primary graft failure needs to be evaluated. Understanding the causes of graft failure may help reduce the risk of failure. In order to address to all these area a study is undertaken in repeat penetrating keratoplasty.

MATERIAL AND METHODS

The study population consisted of consecutive cases of penetrating keratoplasty attending Eye Bank Clinic, during study period from Jan 2017 to Dec 2018, with graft failure and significantly reduced vision requiring repeat penetrating keratoplasty (repeat PK). This included patients of all age groups and both sexes.

All patients were evaluated preoperatively as follows:

- Detailed history was taken to ascertain the etiology leading to corneal disease whether traumatic, infective, dysgenesis, dystrophic or degeneration.
- Detailed history elicited with regards to date of primary penetrating keratoplasty, follow up period, medical treatment history and progression of graft from date of surgery to the time when patient first came to Eye Bank clinic.
- Study of medical document of each patient to extract relevant information about previous surgery, operative notes, post-operative complication and follow up.
- Details of associated systemic diseases such as diabetes, hypertension, tuberculosis, and bronchial asthma were noted.

INTRODUCTION

Corneal transplant still remains a valuable procedure to restore sight in our country. Corneal grafting results in twentieth century are reported as 85-90% by various studies.^{1,2,3} These 10-15% of grafts failures due to various factors (Fig 1) that affects the success of modern day penetrating keratoplasty have resulted in repeat penetrating keratoplasty which offers hope especially if affected eye is the patient's only eye with useful vision. Repeat penetrating keratoplasty especially in large center where penetrating keratoplasty are being done regularly, continues to be one of the leading indication for penetrating keratoplasty.

Many a times re-grafts are more successful than original graft because knowing the cause of failure of first graft special precaution can be taken to avoid failure of graft. A patient who is considered for repeat penetrating keratoplasty

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- e) Complete general and systemic examination was done.
- f) Ocular examination included: -
- Assessment of visual acuity by Snellens chart at 6 meters in an adequately lighted room.
 - Examination in diffuse illumination.
 - Examination by oblique illumination using Slit.
 - Tear film assessment by Schirmers test and tear film break up time.
 - Intraocular pressure measurement by applanation tonometry.
 - Direct and indirect ophthalmoscopy where possible.
 - A and B ultrasonographic scan.

Donor tissue procurement and processing

All donor eyes were procured and processed by Eye bank. An existing, active hospital cornea retrieval programme was utilized to procure donations from the hospital. Relations of the diseased were counseled and written consent was obtained from the next of kin prior to removal of eye. Donor blood samples were subjected to serological tests for HIV and HbsAg.

Preoperative preparation: All patients were started on oral Tab Ciprofloxacin 500mg 12 hourly prior to surgery.

Surgical technique: All the surgeries were performed by a single surgeon using standard surgical techniques. Peribulbar anaesthesia was used. A donor graft of same size as original was used unless the first graft had been particularly large, when a graft size of more usual proportion was used. The graft size varied from 7-8 mm (avg 7.5 mm) with a .5 mm over size. Donor corneal button was prepared prior to cutting of recipient bed. Donor corneal button was trephined with a hollow hand held disposable trephine under microscope. The section was then completed with a pair of curved corneo-scleral scissors using plenty of viscoelastic substance to prevent irido-corneal and lenticulo-corneal touch. The button was then transferred to a bowl containing a coating of viscoelastic substance and placed on it epithelial side down. In case corneo-scleral buttons stored in MK media, the donor button was obtained by the posterior punch method using Teflon block and punch. The Teflon block was coated with a thin layer of viscoelastic and corneo-scleral button placed on its epithelial side down. The corneal button was then punched with the help of disposable trephine and punch with endothelial side up. The operative part was cleaned with betadine and draped under strict aseptic precautions. Vessels, if any, extending deep into the opaque cornea were cauterized at the limbus using bipolar cautery and peritomy done. Recipient cornea was trephined using a hand held hollow disposable trephine up to 80 % of thickness. AC entered with 26 G needle and viscoelastic injected to form the AC. Recipient bed was then cut with the help of a pair of curved corneo-scleral scissors along the trephined wound to produce a circular bed with vertical edges. Synaechiolysis, anterior synaechiotomy, removal of anterior chamber membrane, iridoplasty or pupilloplasty and meticulous open sky vitrectomy to remove incarcerated vitreous was done if required. Viscoelastic substance was then injected into open

anterior chamber and the donor graft placed on top. Four cardinal fixation sutures were given at 12, 6, 3 & 9 O' clock respectively using 10-0 suture. After this 2 more 10-0 suture were given in between above suture. Knots of interrupted suture were rotated into graft side and buried. At the end of procedure all patients were given 2 mg of Dexamethasone and 20 mg of Gentamycin subconjunctively (Fig-2).

Post-operative regimen: Topical Dexamethasone 1% every 2 hourly and antibiotic eye drops were given to all from first post-operative day onwards and tapered over 6 months. Post-operative oral Ciprofloxacin 500 mg BD and analgesics were continued for 5 days.

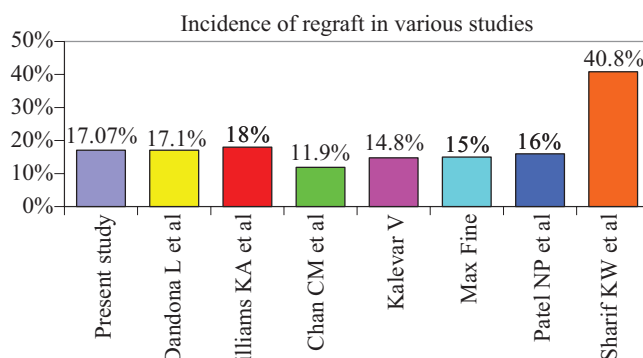
RESULTS

The results were compiled and analyzed at the end of two years of study. The duration of follow up ranged from minimum of 06 months to 2 years, (avg 12.6 months). The results were analyzed under the following heads: -

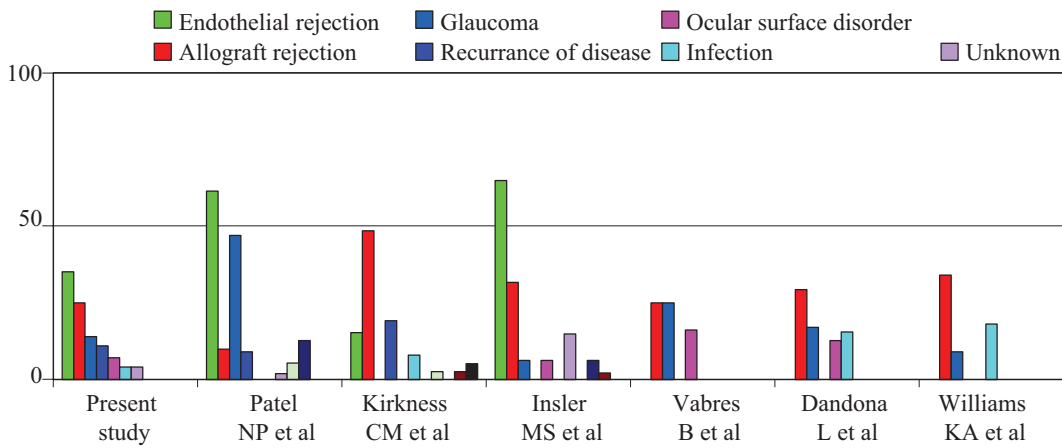
1. General results and incidence of regrant.
2. Indications of primary graft.
3. Indications of regrant.
4. Donor age and condition of donor cornea
5. Surgical procedure before regranting
6. Surgical procedure at time of regranting
7. Graft clarity
8. Preoperative factors present before regranting effecting the outcome
9. Visual recovery
10. Post operative complications

An overall 28 regrant were done out of 164 penetrating keratoplasty performed at Command Hospital, Kolkata from Jan 2017 to Dec 2018. The incidence rate of regranting for this study is 17.07%. The study population consisted of 16 male patients and 12 female patients. The average age of study population was 48 yrs (33 to 63 yrs). Interval between primary graft and repeat keratoplasty was minimum of 06 months to 2 yrs (average 13 months). The study brought out that a regrant should not be done earlier than six months after primary surgery to allow for eye to become quite, except when tectonic graft is required to preserve the anatomical integrity of the eye.

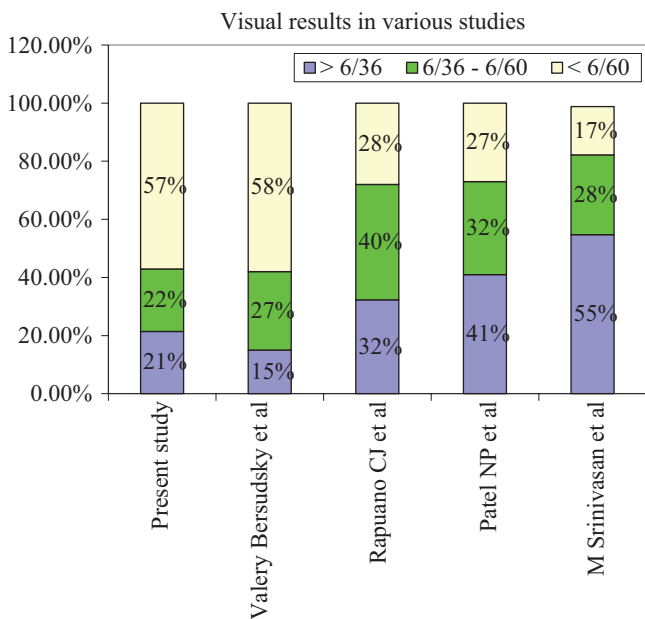
In all cases enucleation was done before six hours and transplanted before 24 hours. The average age of all donors for this study was 47.9 yrs (25% - 39.5 yrs, 42.8% - 47.9



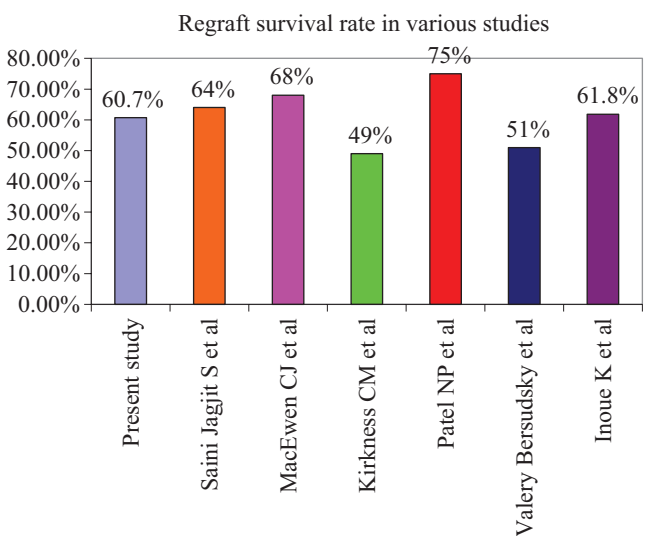
Graph-1: Incidence of regrant in various studies



Graph-2: Indications of regraft/causes of primary graft failure in various studies.



Graph-4: Visual results in various studies



Graph-3: Regraft survival rate in various studies

yrs and 32.2% - 56.4 yrs). In 46.5% donor cornea were of grade A type and 53.5% were of grade B+ type. This study

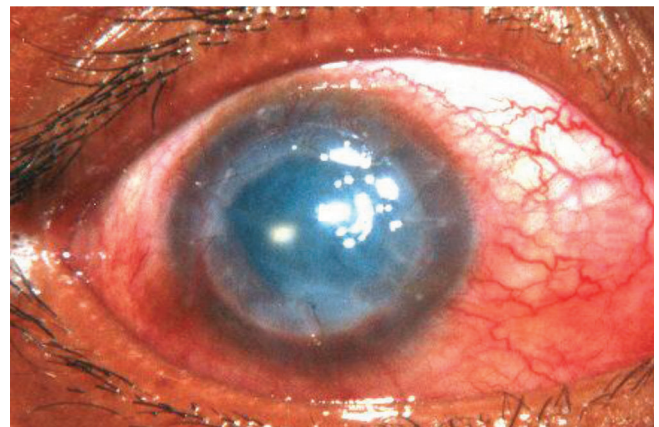


Figure-1: Primary corneal graft failure

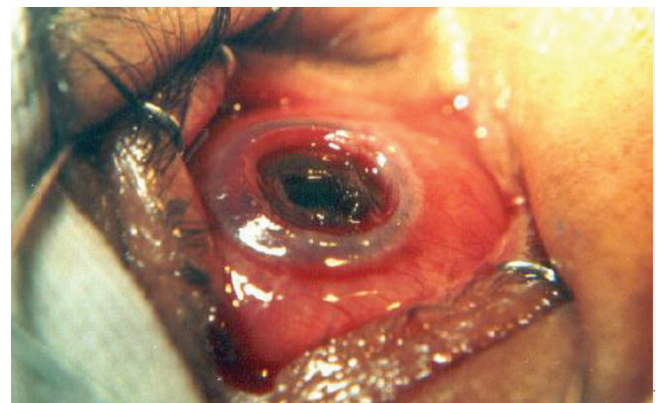


Figure-2: Repeat PK

failed to established any relation between type of donor material and regraft outcome as all donor cornea were of good quality and time of enucleation (median 3.5 hours) to time of transplantation (median 12.5 hours) was kept less in order to give better outcome to visually handicapped patients. Moreover the study population is small to arrive at any conclusion.

Out of 28 regrafts, 17 cases had clear regrafts and in 11 cases the regraft became opaque and resulted in failure during follow up period. The success rate of this study is 60.7%. Pseudophakic bullous keratopathy had greater rate of clear regrafts (71.4%). Regraft failure are more common in patients having preoperative factors like raised IOP, anterior

synechiae, corneal vascularization and younger recipient age group. Failure of regrant was not related to size of graft, host age, and host sex 09 out of 11 cases of regrant failure had one of the above factors present before regranting in this study. Among all factors vascularization of recipient bed was associated with greater rate of graft failure and rejection episodes. Vascularization > 2 quadrant was present in 05 cases out of which 03 failed (60%). IOP> 21 mmHg was present in 07 cases out of which 03 failed (42.8%). Anterior synechiae was present in 05 cases out of which 02 failed (40%). Two patients had age lower than 35 yrs out of which one developed allograft rejection (50%).

Pre operative visual acuity ranged from PL / PR +ve to 6/60 in all cases. Out of 11 cases of regrant failure, 06 cases had acuity of HM close to face and 05 cases had PL/PR +ve forming 39.3% of cases with poor acuity. 32.1% cases had visual acuity between 1/60 to 6/60 (moderate acuity). 28.6% cases achieved visual acuity 6/36 or better (good acuity). Regrafting did not produce significant visual improvement in 03 cases of trauma, 02 cases of regranting and 01 case of fungal keratitis.

DISCUSSION

Incidence of regranting (graph-1)

The incidence was 17.07% of this study. Dandona L et al⁴ in Indian setting reported incidence of regrant as 17.1%. According to Australian Corneal Graft Registry⁵ incidence was 18% and as per Singapore National Eye Centre⁶ it is 11.9%. The rate of regrants reported by Kalevar V⁷ was 14.8%; Max Fine⁸ reported 15%, whereas Patel NP et al⁹ reported 16% regrants. Sharif KW et al¹⁰ reported that regranting was the most common indication overall, accounting for 40.8%. Repeat penetrating keratoplasty especially in large center where penetrating keratoplasty are being done regularly, continues to be one of the leading indication for penetrating keratoplasty. These data have shown that indication of keratoplasty as regrant has increased over the past decade.

Indications of regrant/causes of primary graft failure (graph-2)

The indications for regranting in this study were endothelial failure without signs of rejection (39.3%), allograft rejection (17.8%), recurrence of disease (14.2%), secondary glaucoma (10.7%), ocular surface disorder & dry eye (10.7%), Pseudomonas infection (3.6%) & unknown (3.6%). The major causes of graft failure as per Dandona L et al¹¹ were allograft rejection (29.2%), increased intraocular pressure (16.9%), infection excluding endophthalmitis (15.4%), and surface problems (12.7%). The three most common causes of graft failure as reported by Williams KA et al¹¹ were rejection (34%), infection (18%) and glaucoma (9%). As per Vabres B et al⁵ the leading causes of graft failure are: graft rejection (25%), endothelial consequences of a non-controlled elevated intra ocular pressure (25%) and ocular surface disorders (16%). As per Inslar MS et al¹³ indications for regrant were endothelial rejection (64.8%), unknown (14.8%), descemetocoele (6.2%), glaucoma (6.2), epithelial defect (6.2%) and wound dehiscence

Interval between primary and repeat penetrating keratoplasty

Interval between primary graft and repeat keratoplasty was minimum of 06 months to 2 yrs (average 13 months) for this study.

Graft clarity and success (graph-3)

Out of 28 regrants, 17 cases had clear and in 11 cases the graft became opaque (graft that was not clear in the central visual axis was classified as opaque) and resulted in failure. The success rate of this study is 60.7%. Pseudophakic bullous keratopathy had greater rate of clear regrants (71.4%). Saini Jagjit S et al¹⁴ have reported overall success of 64% at 1 year in regrant in same eye. MacEwen CJ et al¹⁵ reported success rate over a 10-year period as 68%. Kirkness CM et al¹⁶ reported that the five-year survival of regrants was 49%. They also reported that regrant survival in bullous keratopathy was greater than herpetic keratitis and was poor in cases with original diagnosis as trauma and inflammatory disease. The reasons for regrant failure were almost same as those in the first graft except that there was greater proportion of allograft and endothelial decompensation in regrants. At Wills Eye Hospital, Rapuano CJ et al¹⁷ reported failure rate as 26%. Patel NP et al⁹ reported failure rate as 25% and 11% regrant fail during first six months and 55% fail within 18 months. Endothelial failure without evidence of allograft failure was the most common cause of regrant failure (78%). Other important cause were allograft failure (9%), and recurrence of disease (4%). The most common indication of previous grafts of the regrant failure were repeat graft (31%), pseudophakic bullous keratopathy (16%), aphakic bullous keratopathy (16%) and herpes keratitis (7.3%). Inoue K et al¹⁸ showed that the overall rates of graft survival and rejection-free graft survival at 10 years were 61.8% and 72.1% in regranting respectively. Valery Bersudsky et al¹⁹ found that 51% had clear grafts.

Pre operative factors

As per Saini Jagjit S et al¹⁴ regrant failure are more common in patients having preoperative factors like raised IOP, anterior synechiae, corneal vascularization and younger recipient age group.

Visual recovery (graph-4)

M Srinivasan et al²⁰ reported that 20% had visual acuity better than 6/12. Visual acuity was 6/24 in 34.7%, 6/60 to 6/24 in 27.5%, finger counting to 6/60 in 11.5% eyes and PL to HM in 5.7% eyes.

Visual results were slightly lower than other studies^{9,16,17} as failed regrant were also included in evaluating visual outcome. Visual acuity was reduced due to cystoid macula oedema in 01 cases where original pathology was pseudophakic bullous keratopathy, advanced glaucomatous cupping in 01 case and cataract in 01 case. High astigmatism was seen in 04 cases where it was > 3 D.

Post operative complications

The various complications encountered during study were (a) allograft rejection (25%), (b) elevated IOP (21.4%), (c) vascularization (17.8%), (d) peripheral anterior synechiae

(17.8%), (e) endothelial failure (14.2%), (f) astigmatism >3 D (14.2%), (g) persistent epithelial defect (10.7%), (h) recurrence of disease (10.7%), (i) uveitis (10.7%), (j) cystoid macular oedema (3.6%) and (k) cataract (3.6%). Commonest complication after regrant was allograft rejection occurring earlier than the primary graft. 07 cases developed allograft rejection out of which 03 regrant failed. Among these 03 failed regrant all had preoperative allograft rejection as cause of previous graft failure.

CONCLUSION

Repeat keratoplasty once believed to be inoperable is effective and successful method of achieving good visual rehabilitation especially in cases of one-eyed patients. Better visual outcome and graft survival in regrant can be achieved by understanding the underlying pathology and formulating a preoperative plan with subsequent modification during surgery if required. Excellent quality donor material, meticulous tissue handling, use of modern methods of microsurgery and advances in eye banking, adequate control of IOP and postoperative inflammation are the factors leading to success. The commonest primary indication in Indian setting is corneal scarring due to various causes and commonest indications for regrant is endothelial decompensation without sign of allograft rejection. The Interval between primary graft and regrant should be at least six months to allow eye to become quite except in primary donor failure where it can be done as early as possible. Allograft is the commonest cause of regrant failure and it effects the regrant with greater severity and earlier each time. High-risk preoperative conditions (like vascularization, raised IOP and anterior synechiae), postoperative complications, and the need for additional surgical interventions decrease graft survival. Close follow-up, extended use of anti-inflammatory, antiviral, and immunosuppressive drugs, and avoiding additional surgical interventions as much as possible decrease grafts failure and the need for repeated keratoplasties. Early recognition and immediate attention to complication minimize the risk of ultimate graft failure.

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