

Original Article

Comparison of Penetrating Keratoplasty and Deep Anterior Lamellar Keratoplasty Post-Operative Results among Keratoconus Patients

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Abstract

Purpose: To compare post-operative results among keratoconus patients undergoing penetrating keratoplasty (PKP) in comparison with deep anterior lamellar keratoplasty (DALK) and to study the risk factors for transplant rejection.

Patients and Methods: In this retrospective cross-sectional study, the records of all keratoconus patients referred to Labbafinezhad Eye Hospital, Tehran, Iran, who underwent penetrating keratoplasty (PKP) or deep anterior lamellar keratoplasty (DALK) from 2006 to 2016, were investigated. For all patients entering the study information related to surgical corneal transplantation techniques, post-operative follow-up and post-operative results were recorded.

Results: In total the records of 216 patients (106 in the PKP and 110 in the DALK group) were included. The rate of graft rejection was 13 % and 34.3 % in DALK and PKP groups respectively ($P < 0.001$). The graft failure rate was 7.8 % in DALK and 2.4 % in PKP group ($P = 0.12$). No statistically significant difference in post-operation BCVA or the number of patients with astigmatism of more than 4 diopters was observed when comparing the study groups. The higher age of patients at the time of transplant, the presence of post-surgical vascularization, and interface complications were correlated with a higher chance of transplant rejection.

Conclusion: The rate of graft rejection is significantly higher after PKP than DALK among keratoconus patients undergoing corneal transplant. The higher age of patients at the time of transplant, the presence of post-surgical corneal vascularization and interface complications were the observed risk factors for graft failure in both groups.

Keywords: Corneal Transplant; Keratoconus; Penetrating Keratoplasty; Deep Anterior Lamellar Keratoplasty; Surgical Results.

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Introduction

Keratoconus is a relatively common disease with a frequency of about 50 patients per 100,000 people¹. In this disease, the central or paracentral part of the cornea becomes progressively thinned, followed by a corneal bulge resulting in a cone-shaped cornea². Most patients have mild illnesses and their eyesight is corrected with eyeglasses. In some cases, such as those with irregular corneal astigmatism, which cannot be corrected by eyeglasses, hard contact lenses can be used^{2,3}. If initial treatments to reduce progress and improve vision are not successful, which happens in 10% - 15% of patients corneal transplantation will be needed^{4,5}.

Over the past half century penetrating keratoplasty (PKP) has been the preferred surgical procedure for advanced keratoconus disease^{6,7}. According to a study in Iran, keratoconus is the most common indication for PKP surgery⁸. Another method for treating keratoconus is deep anterior lamellar keratoplasty (DALK), in which the endothelium and the Descemet membrane of the host are preserved and the rest of the corneal stroma is transplanted^{9,10}.

Corneal transplant rejection reports have increased since the 1960s as the number of surgeries has increased¹¹⁻¹³. Despite the progress made in improving corneal transplant success rates, the most common cause of transplant rejection is still the host immune system response¹²⁻¹⁵.

Transplant rejection, if not reversible, is considered the most significant cause of transplant failure. Several factors have been reported to cause transplant rejection in previous studies. These factors include the age of the host, the ABO group mismatch, a previous history of transplantation, anterior iris adhesion, the number of host vascular

quadrants, the large size of the graft, suture-related complications like vascularization, suture relaxation, corneal epithelial defect, history of glaucoma, history of herpes simplex, and donor-related factors¹⁶⁻²⁰.

In recent years, DALK has evolved to become a serious contender for the PKP transplant method. Although this surgical technique has existed for many years, it has not been widely adopted due to poor visual results. With the introduction of the big-bubble method by Anwar et al., and the use of cutting-edge surgical instruments to improve visual and refractive outcomes, the popularity of this method has increased²¹⁻²⁴. In this method, only the abnormal stroma of the host cornea is replaced by healthy graft tissue²⁵. It is hoped that by preservation of deep immunogenic corneal layers and endothelium, this method could reduce corneal transplant rejection. Since host endothelial cells remain intact in the DALK operation, the number of endothelial cell deaths caused by surgical manipulation and transplant rejection is low²⁵⁻²⁷.

Several studies have compared DALK and PKP regarding their clinical outcomes and transplant rejection rates with different results²⁸⁻³³. Considering the high rate of corneal transplantation in referral centers, which are expensive and time-consuming for both patients and these centers, it is imperative to investigate the factors affecting corneal transplant rejection. Therefore, this study aims to compare post-operative results among keratoconus patients undergoing PKP in comparison with DALK and to study the risk factors for transplant rejection.

Patients and Methods

This retrospective cross-sectional study was conducted after approval from the Medical

Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran. The study included patients with corneal keratoconus referred to the Eye Department of Labbafinezhad Eye Hospital in Tehran, Iran. All patients underwent corneal transplant surgery between 2006 and 2016.

The data for this study were collected from patients' files using a researcher-designed form. The form included information such as the patient's sex, age at the time of transplantation, corneal diameter of the host and donor, freshness of the donor cornea, history of severe ocular allergy, corneal vascularization in different quadrants of the host cornea, re-transplantation, rejection of the transplanted cornea, timing of the first rejection, time interval until all sutures were removed, best corrected visual acuity (BCVA), refractive errors at the last examination, complications (epithelial problems associated with sutures, cataracts, and increased intraocular pressure), secondary surgical interventions, transplant transparency, other eye diseases, dry eye, presence of associated illnesses such as glaucoma or diabetes, duration of steroid drop use, causes of transplant rejection, type of corneal transplant rejection (epithelial, stromal, endothelial), and the patients' immune system state.

The diagnosis of corneal keratoconus was based on clinical findings and slit lamp examination (corneal ectasia, stromal thinning, Fleischer's ring, and Vogt's striae). The diagnosis was confirmed using topographic findings (TMS-4 Topography Modeling System, Tomey) and corneal tomographic findings (Orbscan II, Bausch & Lomb, Rochester, NY, USA). After a keratoconus diagnosis, patients qualified for corneal transplantation if they did not achieve adequate vision with glasses, could not use contact lenses for any reason, or were

unsuitable for corneal ring insertion.

The patients underwent deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty (PKP) surgery. Postoperative examinations were performed on the first and third days after surgery. They were followed by periodic exams until complete epithelial healing at 30 days postoperative, and then every 2 months for 18 to 24 months. After surgery, betamethasone eye drops 1 % (Sina Daro, Tehran, Iran) were prescribed four times a day and gradually tapered off within three months. Removal of stitches started four months after surgery based on astigmatism developed. Eventually, all sutures were removed within two years postoperatively. Complications and rejection of the transplant were confirmed by two ophthalmologists during follow-up visits. In this study, transplant rejection was confirmed based on epithelial, subepithelial, and stromal immune reactions in patients undergoing the DALK procedure. For PKP patients, endothelial immune reactions were also considered. These reactions were either controlled using steroid drops or autoimmune modulators, or resulted in transplant failure. Transplant failure was defined as corneas with intense opacity, high astigmatism, irregular edema, vascularization, Transplant failure was defined as corneas with intense opacity, high astigmatism, irregular edema, vascularization, or infection. These corneas caused low visual acuity and were irreversible within 3-6 months. Corneal vascularization was defined as superficial or deep vascularization in one or more quadrants. Infiltration was defined as the presence of superficial inflammation, bacterial or sterile keratitis, or deep inflammation (ulcers and abscesses caused by sutures). Graft opacity was graded from clear (grade 0) to completely opaque (grade 4).

The severity of dry eye after transplantation

was determined based on the reduction of the height of the lacrimal layer, extent of punctate epithelial erosions (normal cornea, less than 1/3 of corneal surface, between 1/3 and 1/2 of corneal surface, and more than 1/2 of corneal surface), and the presence of filamentary keratitis on the corneal surface, which required closure of lacrimal punctum, tarsorrhaphy, or blepharorrhaphy during postoperative follow-up.

Statistical analysis was performed using SPSS version 23 (IBM Inc., Chicago, USA). Percentages were used to describe qualitative data, while means and standard deviations were employed to describe quantitative data. A non-inferiority comparison was conducted between the two groups to determine the margin of effect. Qualitative results were analyzed using Chi-square or Fisher exact tests, and quantitative variables were analyzed by t-tests or the Mann-Whitney method. Regression analysis was also performed. P-values less than 0.05 were considered statistically significant.

Results

In total 216 patients (106 in PKP and 110 in the DALK group) were followed up for at

Table 1: Demographic findings of patients entering the study

Variable	PKP	DALK	P value
Age	29.06 ± 9	27.9 ± 19	0.14
BCVA	0.8 ± 0.31	0.73 ± 0.34	0.43

least six months after complete removal of the sutures. There was no statistically significant difference between the PKP and DALK groups regarding patients' preoperative mean age or mean BCVA (Table 1).

The incidence of transplant failure was 7.4 % and 2.8 % in the DALK and PKP groups respectively (P = 0.12) (Table 2). The incidence of transplant rejection was 13 % and 34.3 % in the DALK and PKP groups, respectively (P < 0.001) (Table 2). The mean best corrected visual acuity (BCVA) before and after corneal transplantation in the DALK group were 0.73 ± 0.34 LogMAR and 0.28 ± 0.25 LogMAR, respectively. The mean BCVA change was 0.47 LogMAR. The mean BCVA before and after transplantation in the PKP group were 0.8 ± 0.31 LogMAR and 0.3 ± 0.26 LogMAR, respectively. The mean BCVA change was 0.52 LogMAR. No statistically significant difference in post-

Table 2: Comparison of post-surgical outcomes in patients undergoing DALK and PKP transplants

Event	PKP	DALK	P value
Transplant failure	2.8 %	7.4 %	0.12
Transplant rejection	34.3 %	13 %	< 0.001
Post-surgical BCVA (LogMar)	0.0 ± 3.26	0.0 ± 28.25	0.66
Post-surgical Astigmatism (More than 4 diopter)	29.6 %	32.4%	0.65
Post surgical vascularization	25 %	10.2 %	0.004
Steril infiltration	15 %	12 %	0.4
Transplant opacity	14.8 %	30.6 %	0.006

Table 3: Assessment of factors associated with transplant rejection among all patients

Value	No Transplant rejection	Transplant rejection	P
Mean age at transplant (year)	27.8 ± 2	31.5±10	0.005
Mean duration of using topical steroids (months)	13.5 ± 3.8	15.1 ± 1	0.2
Prevalence of post surgical dry eye	19.7 % (30)	32.8 % (21)	0.37
Post-surgical corneal vascularization	15.7 % (28)	60.5 % (23)	< 0.001
Transplant infiltration	18.8 % (35)	53.2 % (16)	0.16
Interface complications	35.8 % (25)	34.2 % (13)	0.026

surgical BCVA was observed when comparing the study groups (Table 2).

The final total astigmatism after complete removal of sutures was more than 4 diopters in 36 eyes (32.4 %) in DALK group versus 32 eyes (29.6 %) in PKP group. This difference was not statistically significant ($P = 0.65$) (Table 2).

Post-surgical vascularization was significantly higher in PKP group ($P = 0.004$), while transplant opacity was significantly higher in DALK group (0.006) (Table 2).

Table 3 shows the probable risk factors for transplant rejection among all patients. According to our results, patients' age, post-surgical corneal vascularization, and interface complications were the factors associated with transplant rejection among all patients.

Discussion

In the present study 110 patients undergoing DALK (mean age: 27.9 ± 19) and 106 patients undergoing PKP (mean age 29.06 ± 9 years) were evaluated.

Among our patients the transplant rejection rate in the DALK (13 %) group was significantly

lower than in the PKP (34.3 %) group ($P < 0/001$). Transplant rejection rates reported in various studies are very different^{32, 33}. Cohen et al.,³⁰ found a lower transplant rejection rate than our study. However, similar to the present study, the rejection rate in the DALK group was less than in the PKP group. The difference was statistically significant. The rejection rate in the Stulting et al.,¹⁴ study was 23 %, which is similar to the present study. Gilbert et al.,¹⁸ reported an overall graft rejection rate of 19.3 %, which is lower than our results. Both studies, consistent with our finding, found a higher rate of transplant rejection in PKP than in DALK^{14,18}. This wide difference in reported outcomes may be due to differences in rejection definition. Other reasons for the difference in transplant rejection rate can be the duration of post-operative follow-up or the initial cause of grafting.

We observed no statistically significant difference in post-surgical BCVA when comparing the study groups. Similar to our results in a study by Fallahi Motlag et al.,³⁴ there was no significant difference between the post-operative BCVA in the two groups of patients undergoing DALK or PKP. Also,

Cohen et al.,³⁰ reported a slightly better BCVA after PKP, but the difference between the two groups was not statistically significant. BCVA results in DALK might be less favorable when the surgeon is in the early stages of experience. However, with more experience the results will improve and be equal to PKP²⁸.

We observed that patients with transplant rejection had a higher average age (31.5 ± 10) versus (27.2 ± 8) years for non-occurrence ($P = 0.005$). Therefore, in the present study, the higher age of the recipient at the time of transplantation was correlated with an increased rate of transplant rejection. Similar to our results Rahimzadeh et al.,³⁵ have reported a higher rate of transplant rejection among older keratoconus patients undergoing a corneal transplant.

Other risk factors for transplant rejection observed in the present study were the rate of post-surgical corneal vascularization and interface complications, which is in line with the results of previous studies³⁶⁻³⁸.

Conclusion

The rate of graft rejection is significantly higher after PKP than DALK among keratoconus patients undergoing corneal transplant. The higher age of patients at the time of transplant, the presence of post-surgical corneal vascularization and interface complications were the observed risk factors for graft failure in both groups.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.