



Received: 10 February 2026

Reviewed: 10 March 2026

Revised: 28 March 2026

Accepted: 30 March 2026

ผลลัพธ์ระยะยาวและปัจจัยในการพยากรณ์ ความล้มเหลวของการผ่าตัดปลูกถ่ายกระจกตา: การศึกษาแบบย้อนหลัง ณ โรงพยาบาลขอนแก่น

นิจวรรณ วีรธิกุล

กลุ่มงานจักษุวิทยา โรงพยาบาลขอนแก่น จังหวัดขอนแก่น ประเทศไทย 40000

Long-term Outcomes and Prognostic Factors of Graft Failure in Penetrating Keratoplasty: A Retrospective Study at Khon Kaen Hospital

Nichawan Teerittikul

Department of Ophthalmology, Khon Kaen Hospital, Khon Kaen,
Thailand 40000

DOI: <https://doi.org/10.64960/srimedj.v41i3.270716>

บทคัดย่อ

ภูมิหลังและวัตถุประสงค์: การผ่าตัดปลูกถ่ายกระจกตา ในบริบทของภูมิภาคที่กำลังพัฒนา ประสบปัญหาหลายประการ เช่น ความรุนแรงของโรคกระจกตาดำที่ติดเชื้อซึ่งทำให้ต้องใช้ขนาดกระจกตาบริจาคที่ใหญ่ หรือความแตกต่างของการดูแลตนเองของผู้ป่วยหลังผ่าตัด เป็นต้น การศึกษานี้มีวัตถุประสงค์เพื่อประเมินผลลัพธ์อัตราการรอดของกระจกตาที่ปลูกถ่ายในระยะยาว สาเหตุของความล้มเหลวและค้นหาปัจจัยในการพยากรณ์ที่มีผลต่อความสำเร็จของการผ่าตัดปลูกถ่ายกระจกตา ณ ศูนย์ส่งต่อระดับตติยภูมิในภาคตะวันออกเฉียงเหนือ

วิธีการศึกษา: เป็นการศึกษาแบบย้อนหลัง ในผู้ป่วย 82 ราย (82 ตา) ที่ได้รับการผ่าตัดปลูกถ่ายกระจกตาครั้งแรกโดยจักษุแพทย์ท่านเดียวกัน ช่วงเดือนสิงหาคม 2563 ถึงพฤศจิกายน 2568 ณ โรงพยาบาลขอนแก่น ซึ่งเป็นศูนย์รับส่งต่อผู้ป่วยทั้งโรคกระจกตาทั่วไปและโรคกระจกตาดำที่ติดเชื้อ แบ่งผู้ป่วยเป็นกลุ่มที่ผ่าตัดเพื่อการมองเห็น (Optical, n=31) และกลุ่มที่ผ่าตัดเพื่อการรักษา (Therapeutic, n=51) วิเคราะห์อัตราการรอดของกระจกตาด้วยวิธี Kaplan-Meier และหาปัจจัยเสี่ยงอิสระต่อความล้มเหลวด้วยสถิติ Cox proportional hazards regression

ผลการศึกษา: อัตราการรอดสะสมของกระจกตาในภาพรวมที่ 1 และ 2 ปี เท่ากับร้อยละ 53.9 และ 49.0 ตามลำดับ กลุ่มที่ผ่าตัดเพื่อการมองเห็นมีอัตราการรอดที่ 1 ปี (ร้อยละ 75.0) สูงกว่ากลุ่มที่ผ่าตัดเพื่อการรักษา (ร้อยละ 40.4) อย่างมีนัยสำคัญ (Log-rank $p = 0.002$) สำหรับกลไกของความล้มเหลวหลังการผ่าตัด พบว่าการติดเชื้อเป็นสาเหตุอันดับหนึ่ง (ร้อยละ 39.4) ในส่วนของปัจจัยพยากรณ์ความเสี่ยงขณะผ่าตัดนั้น พบว่า การใช้กระจกตาบริจาคขนาดใหญ่กว่า 8.0 มม. เป็นปัจจัยเสี่ยงของความล้มเหลวได้มากที่สุด (Hazard Ratio [HR] 6.48; 95% CI 2.66–15.79; $p < 0.001$) รองลงมาคือปัจจัยด้านผู้บริจาค ได้แก่ อายุที่มากขึ้น (HR 1.035; 95% CI 1.01–1.06; $p = 0.006$)

Citation example: Teerittikul N. Long-term outcomes and prognostic factors of graft failure in penetrating keratoplasty: A retrospective study at Khon Kaen hospital. Srinagarind Med J 2026;41(3):303-15. doi:10.64960/srimedj.v41i3.270716.

*Corresponding author: Nichawan Teerittikul, E-mail: nichawan.tee@gmail.com

สรุป: แม้ว่าการผ่าตัดเพื่อการมองเห็นจะให้ผลลัพธ์อัตราารรอดที่สูงกว่า แต่ในการผ่าตัดเพื่อการรักษาโดยเฉพาะผู้ป่วยที่มีความจำเป็นต้องใช้กระจกตาบริจาคขนาดใหญ่ยังคงมีอัตราการรอดที่ต่ำ ผลการศึกษาชี้ว่า ขนาดกระจกตาที่ใหญ่และกระจกตาจากผู้บริจาคที่อายุนมาก เป็นปัจจัยกำหนดความล้มเหลวที่สำคัญกว่าข้อบ่งชี้ในการผ่าตัด แนวทางการรักษาควรเน้นการจำกัดขนาดแผลให้เล็กที่สุดเท่าที่จะทำได้ ทำห้ที่สุดการส่งต่อผู้ป่วยเพื่อรับการรักษาอย่างรวดเร็วเป็นสิ่งจำเป็นเพื่อป้องกันการลุกลามจนต้องใช้กระจกตาขนาดใหญ่ในการผ่าตัดที่มีความเสี่ยงสูง

คำสำคัญ: การผ่าตัดปลูกถ่ายกระจกตา, อัตราการรอดของกระจกตา, การผ่าตัดปลูกถ่ายกระจกตาเพื่อการรักษา, กระจกตาขนาดใหญ่, ภาวะตะวันออกเฉียงเหนือ

Abstract

Background and objectives: Penetrating keratoplasty (PKP) in developing regions face unique challenges, including a high prevalence of severe infectious keratitis that often requires large-diameter grafts, as well as disparities in patient health literacy. This study aimed to evaluate the long-term graft survival outcomes, causes of failure and independent prognostic factors of PKP at a tertiary referral center in Northeastern Thailand.

Methods: A retrospective cohort study was conducted in 82 patients (82 eyes) who underwent primary PKP by a single surgeon between August 2020 and November 2025. The study was carried out at Khon Kaen Hospital, a regional tertiary center in Northeastern Thailand. Patients were classified into optical (n=31) and therapeutic (n=51) groups. Graft survival rates were estimated using the Kaplan-Meier method. Cox proportional hazards regression analysis was performed to identify independent risk factors for graft failure.

Results: The overall cumulative graft survival rates at 1 and 2 years were 53.9% and 49.0%, respectively. The optical group achieved significantly higher 1-year survival (75.0%) compared to the therapeutic group (40.4%) (Log-rank $p = 0.002$). Regarding the mechanisms of failure, post-operative infection was the leading direct cause (39.4%). In terms of baseline predictors, intra-operative factors, specifically a large graft size (> 8.0 mm), emerged as the strongest independent risk factor for graft failure (Hazard Ratio [HR] 6.48; 95% CI 2.66–15.79; $p < 0.001$), followed by donor factors, specifically older donor age (HR 1.035; 95% CI 1.01–1.06; $p = 0.006$).

Conclusions: While Optical PKP achieves higher survival outcomes, the prognosis for Therapeutic PKP is significantly compromised by the necessity of large-diameter trephination. Large graft size and advanced donor age, rather than therapeutic indication, are the primary determinants of failure. Strategies should aim to minimize graft size, alongside public health initiatives for early referral to prevent the need for high-risk, large-diameter keratoplasty.

Keywords: penetrating keratoplasty, graft survival, therapeutic keratoplasty, large graft size, northeastern Thailand

Introduction

Corneal blindness persists as a major cause of visual impairment worldwide [1-3]. Corneal transplantation, particularly penetrating keratoplasty (PKP), remains the gold standard for restoring vision in patients with full-thickness corneal pathology [1]. Globally, graft survival rates have improved significantly over the decades, with reports from developed countries showing 1-year survival rates exceeding 85% for low-risk indications [2,3]. However, these optimistic statistics are often derived from specialized university centers or national registries in developed nations, where the majority of cases are elective optical procedures performed on quiet, non-inflamed eyes [3,4].

In contrast, the landscape of corneal transplantation in developing regions, particularly in Northeastern Thailand, presents different challenges. This region is an agricultural hub where corneal trauma and aggressive infectious keratitis especially fungal ulcers, are endemic [5-7]. Consequently, a significant proportion of PKP procedures are performed for therapeutic indications (tectonic or therapeutic grafts) to save the eye globe, rather than for purely optical purposes [5,8]. These high-risk eyes often present with severe inflammation, large perforations and delayed medical attention, factors known to compromise graft survival [9].

Despite the high volume of surgeries, there is a paucity of data regarding long-term graft survival and prognostic factors specifically within the context of a regional tertiary referral center. Unlike university-based settings, patients in this “real-world” context often face unique barriers, including lower health literacy, difficulties in accessing follow-up care and delayed presentation due to socioeconomic constraints [5]. Furthermore, the interplay between surgical factors, such as the necessity for large-diameter grafts in severe infections, and the clinical indication itself has not been adequately explored in this specific population.

Therefore, this study aimed to evaluate the long-term outcomes and identify independent prognostic factors for graft failure in patients who underwent PKP at Khon Kaen Hospital, Thailand. By analyzing data from this distinct setting, we sought to bridge the knowledge gap regarding the true survival expectations of corneal grafts in Northeastern Thailand and to determine whether the high failure rates were driven by the disease biology or modifiable surgical factors.

Methods

Study design and population

This retrospective cohort study was conducted at the Department of Ophthalmology, Khon Kaen Hospital, a tertiary referral center in Northeastern Thailand. The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Khon Kaen Hospital Ethics Committee for Human Research (No. KEXP68106, Date: December 11, 2025). Following approval, we reviewed the medical records of all patients who underwent penetrating keratoplasty (PKP) between August 1, 2020, and November 30, 2025. Inclusion criteria comprised patients aged 18 years or older who received PKP for either optical or therapeutic indications. To ensure independence of observations, only the first operated eye (first graft) of each patient during the study period was included. Exclusion criteria included incomplete medical records and the use of glycerol-preserved corneas or grafts performed solely for tectonic purposes without visual potential.

Data collection and variables

Data were extracted from electronic medical records and paper charts using a standardized case record form. To systematically analyze the risk factors for graft failure, the variables were categorized chronologically into three main phases.

First, pre-operative factors included demographic data (age, sex, systemic comorbidities and domicile distance), pre-operative ocular

characteristics (pre-existing glaucoma, lens status, presence of peripheral anterior synechiae, and extent of corneal vascularization), and the primary indications for surgery, which were categorized into the Optical PKP group and the Therapeutic PKP group (active infectious keratitis).

Second, intra-operative and donor factors were recorded. Operative data comprised graft size, which was classified into three subgroups (≤ 7.5 mm, 7.6–8.0 mm, and > 8.0 mm), and the surgical technique performed (PKP alone or a combined procedure). Donor characteristics included donor age and pre-operative donor endothelial cell density (ECD).

Finally, post-operative factors were collected to evaluate the direct clinical mechanisms of graft failure. These encompassed post-operative complications leading to an irreversible loss of graft clarity, specifically infection, allograft rejection, endothelial decompensation and glaucoma.

Surgical technique and post-operative management All surgeries were performed under general anesthesia by a single cornea specialist using a standard PKP technique.

Donor tissue source

All donor corneas used in this study were procured exclusively from the Thai Red Cross Eye Bank. In accordance with the national allocation policy, donor tissues were stratified into two grades: ‘Optical grade’ for elective procedures and ‘Emergency grade’ for urgent therapeutic indications. Consequently, patients in the Therapeutic PKP group predominantly received ‘Emergency grade’ grafts, which are generally characterized by lower endothelial cell density or older donor age compared to the ‘Optical grade’ tissues allocated for elective surgery. The post-operative medication protocols were tailored to the surgical indication: (i) Optical PKP Group: Patients received topical corticosteroids, alternating between 1% prednisolone acetate and 1% methylprednisolone every 2 hours, combined with topical antibiotics (0.5% moxifloxacin or 1.5%

levofloxacin) four times daily. A combination antibiotic-steroid ointment (Maxitrol®) was applied at bedtime. (ii) Therapeutic PKP Group: Patients received intensive topical antimicrobial agents (tailored to the identified or suspected pathogen) every 1 hour. Topical corticosteroids were withheld in the early post-operative period until the infection was controlled. Suture removal was performed based on graft healing and refractive status.

Primary outcome measures

The primary outcome was graft failure, defined as an irreversible loss of optical clarity due to any cause (e.g., rejection, endothelial decompensation, recurrence of infection) requiring regrant or resulting in a permanently opaque cornea. A reversible loss of clarity, such as an allograft rejection episode that was successfully treated with medical therapy resulting in the full restoration of corneal transparency, was considered a post-operative complication rather than a graft failure. In such cases, the graft was still classified as a “success” in the survival analysis. The survival time was calculated from the date of surgery to the date of failure or the last follow-up visit (censored data).

Secondary outcomes measures

Secondary outcomes included visual acuity, endothelial cell density (ECD), and post-operative complications. Best-corrected visual acuity (BCVA) was measured using the Snellen chart and converted to LogMAR units for analysis. The percentage of endothelial cell loss (ECL) was calculated at the last follow-up for clear grafts. Post-operative complications included graft rejection episodes, elevated intraocular pressure (IOP), persistent epithelial defect (PED), suture-related complications, and graft infection (classified as new microbial keratitis or recurrence of primary infection). Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were

described as mean $\pm$ standard deviation (SD) or median and interquartile range (IQR), depending on data distribution. Categorical variables were presented as frequencies and percentages.

Comparison between groups was performed using the Independent T-test or Mann-Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. Visual improvement (pre- vs. post-operative) was analyzed using the Wilcoxon signed-rank test.

Graft survival rates were estimated using the Kaplan-Meier method and differences between groups were compared using the Log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were conducted to identify independent risk factors for graft failure. Variables with a p -value < 0.20 in the univariate analysis or those with clinical significance were included in the multivariate model. A p -value < 0.05 was considered statistically significant.

Results

Study population

During the study period, a total of 104 eyes underwent corneal transplantation. Based on the exclusion criteria, 22 eyes were excluded from the analysis: 11 eyes were excluded as they were either repeat grafts or the second operated eye of the same patient, 8 eyes underwent surgery using glycerol-preserved corneas for tectonic purposes, 2 eyes underwent Descemet Membrane Endothelial Keratoplasty (DMEK), and 1 eye was excluded due to incomplete follow-up data. Consequently, a total of 82 eyes of 82 patients were included in the final analysis.

Baseline characteristics

The cohort comprised 43 right eyes (52.4%) and 39 left eyes (47.6%). The mean age was 58.1 ± 14.1 years (range, 19–89 years), and the majority were male (64.6%). Geographically, most patients resided within Khon Kaen province (91.4%), comprising 15.8% from the Mueang district and 75.6% from other districts. The remaining patients came from other provinces within Health Region 7 (3.7%) or outside the region (4.9%). Regarding systemic health, diabetes mellitus was the most common comorbidity (17.1%), followed by autoimmune diseases (3.6%).

In terms of ocular characteristics, the most common indication for PKP was active infectious keratitis (Therapeutic group), accounting for 62.2% (51 eyes), followed by the Optical group 37.8% (31 eyes) which included corneal scarring, bullous keratopathy, dystrophy, and re-grafts. The specific distribution of causative pathogens is detailed in Table 1. Most eyes were phakic (74.4%) at the time of surgery, while 23.2% were pseudophakic and 2.4% were aphakic.

Regarding operative factors, the majority of procedures were PKP alone (89.0%), with 11.0% requiring combined procedures. The median waiting time for donor tissue was 210.5 days (range 40–553) for the Optical group and 6 days (range 2–35) for the Therapeutic group. Baseline demographic and pre-operative risk factors are summarized in Table 1.

Table 1 Baseline Characteristics and Univariate Analysis of Risk Factors Associated with Graft Failure.

Characteristics	Total (n=82)	Success Group (n=49)	Failure Group (n=33)	p-value
Demographics				
Age (years), Mean ± SD	58.12 ± 14.14	57.43 ± 14.37	59.15 ± 13.96	0.592
Sex , n (%)				0.208
Male	53 (64.6)	29 (59.2)	23 (69.7)	
Female	29 (35.4)	20 (40.8)	9 (27.3)	
Pre-operative Ocular Factors				
Purpose of Surgery , n (%)				0.006*
Optical group	31 (37.8)	25 (51.0)	6 (18.2)	
Therapeutic group	51 (62.2)	24 (49.0)	27 (81.8)	
· Fungal Keratitis	36 (43.9)			
· Bacterial Keratitis	14 (17.1)			
· Mixed Infection	1 (1.2)			
Corneal Vascularization , n (%)	2 (2.4)	2 (4.1)	0 (0)	0.513
Pre-existing Glaucoma , n (%)	13 (15.9)	9 (18.4)	4 (12.1)	0.448
Peripheral Anterior Synechiae (PAS) , n (%)	4 (4.9)	3 (6.1)	1 (3.0)	0.645
Pre-operative VA (LogMAR) , Median (IQR)	2.3 (1.86 - 2.3)	2.3 (1.78 - 2.3)	2.3 (2.3 - 2.7)	<0.001*
Operative & Donor Factors				
Surgical Procedure , n (%)				0.077
PKP alone	73 (89)	41 (83.7)	32 (97.0)	
Combined Procedure	9 (11)	8 (16.3)	1 (3.0)	
Recipient Graft Size (mm) , n (%)				<0.001*
≤ 7.5	56 (68.3)	41 (83.7)	15 (45.5)	
7.6-8.0	9 (11.0)	5 (10.2)	4 (12.1)	
>8.0	17 (20.7)	3 (6.1)	14 (42.4)	
Donor Age (years), Mean ± SD	49.04 ± 18.33	44.27 ± 18.34	56.15 ± 16.10	0.003*
Pre-op Donor Endothelial Cell Density (cells/mm ²) Mean ± SD	2,411.268 ± 688.897	2,624.796 ± 525.931	2,094.212 ± 737.667	<0.001*

Note: Data are presented as mean ± SD, median (IQR), or number (percentage). Abbreviations: PKP, Penetrating Keratoplasty; VA, Visual Acuity; LogMAR, Logarithm of the Minimum Angle of Resolution. *Statistically significant difference (p< 0.05).

There were no statistically significant differences between the success and failure groups regarding age, sex, domicile, laterality, lens status, systemic comorbidities, or surgical procedure ($p > 0.05$ for all). Although the proportion of active infection cases was higher in the failure group (81.8%) compared to the success group (49.0%), this difference was further explored in the multivariate analysis.

Surgical and visual outcomes

Graft survival (clear graft) was achieved in 49 eyes (59.8%). Visual outcomes and post-operative complications are presented in Table 2. Patients with successful grafts achieved significantly better visual outcomes compared to the failure group. The median final BCVA in the success group was 0.78 logMAR (approx. Snellen 6/36), significantly better than the 2.30 logMAR (hand motion) in the failure group ($p < 0.001$). Notably, the success group experienced a median visual improvement of 11.8 Snellen lines, whereas the failure group showed no improvement (median 0.0 lines; $p < 0.001$). Among clear grafts, the mean astigmatism at the last follow-up was 4.65 ± 2.65 diopters.

Table 2 Visual Outcomes and Post-operative Complications

Outcomes	Total (n=82)	Success Group (n=49)	Failure Group (n=33)	p-value
Visual Outcomes				
Final BCVA (LogMAR), Median (IQR)	1.48 (0.78-2.30)	0.78 (0.60-1.33)	2.30 (1.86-3.0)	<0.001*
Visual Improvement (lines), Median (IQR)	6.4 (0.0 – 13.0)	11.8 (5.6 – 15.2)	0.0 (-3.0 – 4.2)	<0.001*
Astigmatism at Last Follow-up (Diopter), Mean $\pm$ SD	-	4.65 $\pm$ 2.65 (n=29)	N/A ^a	-
Post-operative Complications, n (%)				
Allograft Rejection Episode	14 (17.1)	5 (10.2)	9 (27.3)	0.044*
Elevated Intraocular Pressure / Glaucoma	30 (36.6)	16 (32.7)	14 (42.4)	0.368
Persistent Epithelial Defect (PED)	8 (9.8)	5 (10.2)	3 (9.1)	0.868
Suture-related Complications	3 (3.7)	3 (6.1)	0 (0)	0.270
Microbial Keratitis (Post-op Infection), n (%)				<0.001*
None	59 (72.0)	41 (83.7)	18 (54.5)	
Recurrence of Primary Infection	12 (14.6)	1 (2.0)	11 (33.3)	
New Microbial Keratitis	11 (13.4)	7 (14.3)	4 (12.1)	

Note: Data are presented as median (IQR) for visual outcomes, mean $\pm$ SD for astigmatism, and number (percentage) for complications. Abbreviations: BCVA, Best-Corrected Visual Acuity; LogMAR, Logarithm of the Minimum Angle of Resolution; N/A, Not Applicable. ^a Astigmatism could not be measured in the failure group due to corneal opacity, evisceration, or surface irregularity. *Statistically significant difference ($p < 0.05$).

Post-operative complications

Post-operative complications were common, with elevated IOP/glaucoma being the most frequent (36.6%), followed by allograft rejection (17.1%) and persistent epithelial defect (9.8%). Allograft Rejection was significantly associated with graft failure; 27.3% of patients in the failure group experienced a rejection episode compared to 10.2% in the success group ($p = 0.044$). Furthermore, infectious Complications were strongly associated with poor outcomes ($p < 0.001$). Specifically, recurrence of the primary infection occurred in 12 eyes, of which 11 (91.7%) resulted in graft failure. In contrast, new microbial keratitis occurred in 11 eyes, with a failure rate of 36.4%.

Endothelial cell density (ECD)

Analysis of clear grafts at the last follow-up (Table 3) revealed that the Therapeutic group received donor corneas with significantly lower baseline ECD compared to the Optical group (2,249 vs. 2,943 cells/mm²; $p = 0.005$). However, the rate of endothelial cell loss was comparable between the two groups (43.1% vs. 45.4%; $p = 0.877$), suggesting similar long-term endothelial survival among successful cases.

Table 3 Endothelial Cell Density (ECD) Outcomes in Clear Grafts at Last Follow-up

Parameters	Optical PKP (n = 10)	Therapeutic PKP (n = 13)	p-value
Duration to Last Follow-up (months) Median (IQR)	10.4 (5.4 – 19.4)	15.7 (10.2 – 38.3)	0.083
Pre-operative Donor ECD (cells/mm ²) Mean ± SD	2,943 ± 255	2,249 ± 508	0.005*
Last Post-operative ECD (cells/mm ²) Mean ± SD	1,597 ± 613	1,230 ± 422	0.182
Endothelial Cell Loss (%) Mean ± SD	45.4 ± 21.5	43.1 ± 22.9	0.877

Note: Data are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]). **Abbreviations:** ECD, Endothelial cell density; PKP, Penetrating keratoplasty. *Statistically significant difference ($p < 0.05$). Should be interpreted cautiously due to small sample size.

Graft survival analysis

The overall cumulative graft survival rates were 64.2% at 6 months, 53.9% at 1 year, and 49.0% at 2 years. When stratified by indication, the Optical PKP group demonstrated significantly superior survival compared to the Therapeutic PKP group (Log-rank test, $p = 0.002$). Specifically, the Optical group

maintained a high survival rate of 92.4% at 6 months, whereas the Therapeutic group showed a rapid decline to 49.0% during the same period. By the 1-year and 2-year marks, the cumulative survival rates for the Optical group were 75.0% and 50.0%, respectively, compared to 40.4% at both time points for the Therapeutic group (Table 4).

Table 4 Kaplan-Meier Survival Analysis of Corneal Grafts by Risk Group

Group	N	6-month Survival (%) (SE)	1-year Survival (%) (SE)	2-year Survival (%) (SE)	Log-Rank p-value
Overall	82	64.2 (5)	53.9 (6)	49.0 (7)	
Risk Stratification					
Optical PKP (Low Risk) ^a	31	92.4 (5)	75.0 (10)	50.0 (21) ^c	
Therapeutic PKP (High Risk) ^b	51	49.0 (7)	40.4 (7)	40.4 (7)	0.002*

Note: Data are presented as cumulative survival percentage (standard error). Abbreviations: PKP, Penetrating Keratoplasty; SE, Standard Error. ^aOptical PKP group comprises indications including keratoconus, corneal dystrophy, scar, bullous keratopathy (PBK/ABK), and non-infected regrafts. ^bTherapeutic PKP group comprises active infectious keratitis and therapeutic indications. ^cSurvival estimates at this time point are limited by the small number of patients at risk (n < 5) and should be interpreted with caution.

Further subgroup analysis revealed distinct survival patterns among the four diagnostic categories (Log-rank test, p = 0.012; Figure 1). The Good Prognosis group (Keratoconus/Dystrophy) demonstrated the most favorable outcomes, achieving a 100% survival rate at both 1 and 2 years, followed by the Corneal Scar/Edema group (PBK/ABK), which showed intermediate rates of 70.1% at 1 year and 46.7% at 2 years. In contrast, the Active Infection (Therapeutic) group faced greater challenges, maintaining a survival rate of 40.4% at the 1- and 2-year marks. Notably, this group was characterized by a steep decline within the first 3 months due to early recurrence; however, long-term data revealed that the survival curve eventually stabilized at a plateau of 33.6% (SE 0.09) from approximately 26.9 months through the 4-year mark. This suggests that high-risk grafts surviving the critical first 2.5 years tend to maintain favorable long-term viability. Finally, the Regraft group exhibited the poorest prognosis, with all cases (n=3) failing within the first year (0% survival).

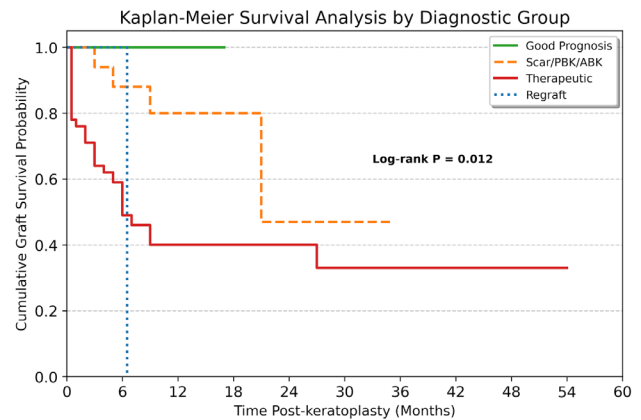


Figure 1 Kaplan-Meier survival analysis of corneal grafts stratified by pre-operative diagnostic group. The graph illustrates the cumulative survival probability over time for four distinct categories: Good Prognosis (Keratoconus/Dystrophy; green line), Scar/PBK/ABK (Corneal Scar, Pseudophakic, or Aphakic Bullous Keratoplasty; orange dashed line), Therapeutic (Active Infectious Keratitis; red solid line), and Regraft (blue dotted line). Statistical comparison was performed using the Log-rank test (p = 0.012).

Post-operative causes of failure

Among the 33 eyes that failed, infection was the leading primary cause, accounting for 39.4% of failures. This was followed by allograft rejection (24.2%), while endothelial decompensation and glaucoma each contributed to 18.2% of failures

(Figure 2). Notably, 8 cases of recurrent infection were severe enough to require evisceration.

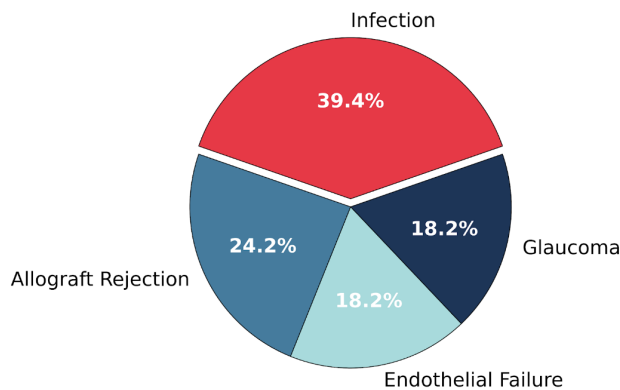


Figure 2 Post-operative causes of graft failure. The pie chart shows the distribution of post-operative etiologies leading to graft failure among 33 eyes. The segments represent infection (red), allograft rejection (blue), glaucoma (dark navy), and endothelial failure (light teal), with each color corresponding to a distinct cause.

Risk factors for graft failure

Univariate analysis (Table 1) identified therapeutic indication, larger graft size, and older donor age as potential risk factors associated with graft failure. However, after adjusting for confounding factors in the multivariate Cox proportional hazards regression model (Table 5), the pre-operative diagnosis (Optical vs. Therapeutic) was no longer a significant predictor (HR 1.14; 95% CI: 0.38–3.42; $p = 0.817$). Instead, the analysis identified two independent risk factors significantly associated with graft failure. A large graft size (> 8.0 mm) was associated with a 6.48-fold increased risk of failure compared to small grafts (HR 6.48; 95% CI: 2.66–15.79; $p < 0.001$). Furthermore, for every 1-year increase in donor age, the risk of failure increased by 3.5% (HR 1.035; 95% CI: 1.01–1.06; $p = 0.006$).

Table 5 Multivariate Cox proportional Hazards Regression Analysis for Risk Factors of Graft Failure

Risk Factors	Hazard Ratio (HR)	95% CI	p-value
Pre-operative Diagnosis			
Optical PKP (Low Risk)	Reference	-	-
Therapeutic PKP (High Risk)	1.14	0.38 – 3.42	0.817
Graft Size			
≤ 7.5 mm	Reference	-	-
7.6 – 8.0 mm	1.6	0.49 – 5.21	0.432
> 8.0 mm	6.48	2.66 – 15.79	$< 0.001^*$
Donor Age (per year increase)	1.04	1.01 – 1.06	0.006*

Note: Abbreviations: CI, Confidence Interval; PKP, Penetrating Keratoplasty. *Statistically significant predictor ($p < 0.05$).

Furthermore, to address the complex interrelated baseline characteristics inherent in therapeutic procedures, a supplementary subgroup analysis was performed exclusively on the Therapeutic PKP group ($n=51$). This subgroup multivariate Cox regression confirmed our primary findings: even within severe infectious cases, a large graft size (> 8.0 mm) remained

a robust and highly significant independent predictor of graft failure (HR 5.51; 95% CI: 2.21–13.72; $p < 0.001$). Donor age exhibited a continued trend toward increased risk but reached borderline significance in this smaller subgroup (HR 1.03; 95% CI: 1.00–1.05; $p = 0.058$).

Discussion

The most noticeable finding in our study is that while therapeutic PKP initially seemed to have a higher risk of failure, our multivariate analysis revealed that the pre-operative diagnosis was not an independent risk factor. Instead, large graft size (> 8.0 mm) emerged as the primary determinant, with a 6.48-fold increased risk of failure. In our practice, graft sizes larger than 8.0 mm are almost exclusively reserved for therapeutic cases requiring extensive eradication of infection, whereas optical cases typically receive smaller grafts. Consequently, the poor survival observed in the therapeutic group is intrinsically linked to the necessity of using large-diameter grafts. These grafts face a dual challenge. They are prone to immune rejection due to their proximity to limbal vessels [10]. They inherently reflect severe, aggressive disease where the risk of recurrent infection remains high. This aligns with previous findings indicating that recipient graft size > 8.0 mm is significantly associated with higher rates of post-keratoplasty glaucoma and graft failure [1,3,11,12]. This suggests that if infection control can be achieved while maintaining a smaller graft diameter, survival outcomes may improve significantly.

Therefore, it is important to understand the sequence of these clinical events. Although the need for a large graft is the main baseline factor associated with a higher risk of failure, the immediate post-operative cause that most often leads to graft loss is infection. Consistent with this burden, infection was identified as the leading primary cause of failure (39.4%), with the recurrence of the primary infection proving particularly devastating. Out of 12 patients with recurrence, 11 failed and notably, 8 ultimately required evisceration. This high rate of eye loss highlights the aggressive nature of keratitis in our regional setting, where fungal infections are endemic and difficult to eradicate. This serves as a stark reminder that in cases of recurrence, the prognosis for graft survival is extremely poor and surgeons must be prepared for the possibility of eye globe loss [13,14].

Reflecting these challenges, our overall 1-year graft survival (53.9%) is lower than reports from major university hospitals or international registries, where survival often exceeds 80% [1,2,4,15]. This disparity is likely attributable to the case mix in our tertiary center, where more than half of the procedures were performed for severe, active infectious ulcers. Furthermore, we observed significant challenges regarding patient compliance and health literacy. Many patients in the Northeastern region delayed seeking care when early signs of rejection or infection appeared, often waiting for their next scheduled appointment. This delay meant that grafts frequently reached an irreversible state before intervention could occur. Therefore, improving post-operative education to emphasize that “red eyes or blurred vision are emergencies” is as vital as the surgery itself. Recent local evidence supports this approach, demonstrating that structured self-care promoting programs based on nursing theories can significantly improve self-care behaviors, reduce anxiety and maintain graft clarity in Thai patients [16].

In terms of donor characteristics, our analysis revealed that the Therapeutic group received donor corneas with significantly lower baseline ECD compared to the Optical group, reflecting the national allocation policy. Despite this initial disadvantage, the percentage of endothelial cell loss (ECL) at the last follow-up was not significantly different between the two groups. This encouraging finding is consistent with local studies suggesting that donor endothelial cell count may not always be a significant risk factor for secondary graft failure in the multivariate context [4], implying that if the graft survives the initial infectious and inflammatory storm, its long-term physiological health is comparable to that of optical grafts.

However, donor age significantly impacted outcomes, with older donor age associated with an increased risk of failure (HR 1.035 per year). While some studies suggest donor age does not influence survival in low-risk cases or optical indications [3, 4], our findings align with research involving high-risk

recipients. In the inflamed environment of a therapeutic recipient, the functional reserve of the donor endothelium is critical. Grafts from older donors may have limited capacity to withstand the active inflammatory state and the potential toxicity of intensive antimicrobial regimens, particularly during the early post-operative period when corticosteroids are withheld.

Interestingly, unlike many published studies where glaucoma is a major risk factor for graft failure [1,7,9,11,12,17], our study did not find a significant association. We believe this discrepancy is primarily due to competing risks. Since a significant proportion of our grafts failed early due to fulminant infection or acute rejection, they may not have survived long enough to suffer the cumulative endothelial damage typically caused by chronic glaucoma, a mechanism well-documented in long-term follow-up studies [9]. Similar findings have been noted in other retrospective series where short observation times or high rates of early complications masked the long-term impact of chronic intraocular pressure elevation [14].

Strengths and limitations

A major strength of this study is that all surgeries were performed by a single surgeon, which minimizes the variability of surgical technique—a common confounding factor in multi-surgeon studies. Furthermore, this study provides valuable “real-world” data from a tertiary referral center in an endemic region for severe microbial keratitis. However, several limitations must be noted. First, as a retrospective study, there were inherent limitations in data completeness and the inability to control for all confounding variables. Second, the relatively small sample size in certain subgroups and the variable follow-up duration in the optical group limit our ability to draw definitive conclusions regarding very long-term outcomes (>5 years).

Conclusion

Our study demonstrates that while Optical PKP achieves favorable survival rates, the primary challenge lies in the management of severe infectious keratitis. The study reveals that large graft size (> 8.0 mm) and advanced donor age are the primary independent risk factors for graft failure, rather than the therapeutic indication itself.

Therefore, surgical strategies should aim to minimize graft size whenever clinically feasible. Regarding donor characteristics, while tissue availability often precludes selective allocation, recognizing the adverse impact of advanced donor age is crucial for accurate prognostication and patient counseling in high-risk therapeutic cases. Finally, given the profound adverse impact of large grafts, public health initiatives focusing on early presentation and referral of corneal ulcers are essential to prevent the progression to stages requiring high-risk, large-diameter keratoplasty.

Acknowledgment

The author wishes to thank Worachart Lertitthiporn, Ph.D., M.D., for his technical support with SPSS software and his valuable feedback on the manuscript.

Conflict of Interest

The author declared none.

References

1. Reinprayoon U, Srihatrai P, Satitpitakul V, Puangsricharn V, Wungcharoen T, Kasetsuwan N. Survival outcome and prognostic factors of corneal transplantation: A 15-year retrospective cohort study at King Chulalongkorn Memorial Hospital. *Clin Ophthalmol* 2021;15:4189-99. doi:10.2147/OPTH.S336986.
2. Bidaut-Garnier M, Monnet E, Prongue A, Montard R, Gauthier AS, Desmarests M, et al. Evolution of corneal graft survival over a 30-year period and comparison of surgical techniques: a cohort study. *Am J Ophthalmol* 2016;163:59-69. doi:10.1016/j.ajo.2015.12.014.

3. Tan DT, Janardhanan P, Zhou H, Chan YH, Htoon HM, Ang LP, et al. Penetrating keratoplasty in Asian eyes: the Singapore corneal transplant study. *Ophthalmology* 2008;115(6):975-82. doi:10.1016/j.ophtha.2007.08.049.
4. Chotikavanich S, Prabhasawat P, Satjapakasit O. Ten-year survival of optical penetrating keratoplasty and risk factors for graft failure in Thai patients. *J Med Assoc Thai* 2020;103(9):883-90. doi:10.35755/jmedassothai.2020.09.8667.
5. Naranunn P, Naranunn W. Penetrating keratoplasty in regional health 8th. *Udonthani Hospital Medical Journal* 2023;31(2):153-60.
6. Booranapong W, Junsangsri C, Chirapapaisan C, Ngowyutagon P, Kengpunpanich S. Indications and current surgical techniques for keratoplasty: A 10-year review from 2011 through 2020 at a Tertiary Referral Hospital in Thailand. *Siriraj Medical Journal* 2025;77(2):146-57. doi:10.33192/smj.v77i2.268932.
7. Singh R, Gupta N, Vanathi M, Tandon R. Corneal transplantation in the modern era. *Indian J Med Res* 2019;150(1):7-22. doi:10.4103/ijmr.IJMR_141_19
8. Isipradit S, Roongpoovapatr V. Outcomes of therapeutic penetrating keratoplasty in a tertiary care hospital in Thailand. *Thai J Ophthalmology* 2019;33(1):27-39.
9. Alio JL, Montesel A, El Sayyad F, Barraquer RI, Arnalich-Montiel F, Alio Del Barrio JL. Corneal graft failure: an update. *Br J Ophthalmol* 2021;105(8):1049-58. doi:10.1136/bjophthalmol-2020-316705
10. Yin J. Advances in corneal graft rejection. *Curr Opin Ophthalmol* 2021;32(4):331-7. doi:10.1097/ICU.0000000000000767.
11. Tangpagasit W, Chea G. The incidence and risk factors of post-penetrating keratoplasty glaucoma. *Eye South East Asia* 2024;19(2):45-52.
12. Karadag O, Kugu S, Erdogan G, Kandemir B, Eraslan Ozdil S, Dogan OK. Incidence of and risk factors for increased intraocular pressure after penetrating keratoplasty. *Cornea* 2010;29(3):278-82. doi:10.1097/ICO.0b013e3181b6eb9e.
13. Thanathanee O, Sripawadkul W, Anutarapongpan O, Luanratanakorn P, Suwan-Apichon O. Outcome of therapeutic penetrating keratoplasty using glycerol-preserved donor corneas in infectious keratitis. *Cornea* 2016;35(9):1175-8. doi:10.1097/ICO.0000000000000841.
14. Szkodny D, Wroblewska-Czajka E, Wylegala A, Nandzik M, Wylegala E. Incidence of complications related to corneal graft in a group of 758 patients. *J Clin Med* 2022;12(1):220. doi:10.3390/jcm12010220.
15. Omar N, Bou Chacra CT, Tabbara KF. Outcome of corneal transplantation in a private institution in Saudi Arabia. *Clin Ophthalmol* 2013;7:1311-8. doi:10.2147/OPTH.S43719.
16. Tupcharoen K, Phinitkhajorndech N, Puangsrichareon V. A Feasibility study the effectiveness of self-care promoting program on self-care behavioral and clinical outcomes in people with corneal transplantation: a quasi-experiment study. *Pacific Rim Int J Nurs Res* 2024;28(3):645-58. doi:10.60099/prijnr.2024.268807.
17. Banitt M, Lee RK. Management of patients with combined glaucoma and corneal transplant surgery. *Eye (Lond)* 2009;23(10):1972-9. doi:10.1038/eye.2008.377.