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Outcomes of Penetrating Keratoplasty After Open Globe Injury

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Purpose: The purpose of this study was to investigate the clinical features, surgical outcomes, and prognostic factors of penetrating keratoplasty (PKP) after open globe injury (OGI).

Methods: A retrospective review of all patients treated for OGI between January 2000 and July 2017 was conducted. Demographic, preoperative, perioperative, and postoperative data were collected for those who underwent PKP after OGI. The predictive value of each preoperative variable on graft failure was assessed using univariate and multivariable Cox proportional hazards models, and the predictive value of variables on post-PKP visual outcome was assessed using both univariate and multivariable logistic regression models. All eyes that underwent PKP after OGI were included unless they had less than 365 days of follow-up.

Results: Forty-six eyes that underwent PKP met inclusion criteria. The median age was 46 years (interquartile range = 23.00–61.25), median follow-up was 78.5 months (interquartile range = 38.63–122.02), and 37 of 46 subjects (80.4%) were male. The observed 1- and 5-year graft survival estimates were 80.4% and 41.7%, respectively. Factors statistically associated with graft failure in multivariable analyses were rejection episode, hazard ratio (HR) = 3.29; retinal detachment (RD), HR = 3.47; and endophthalmitis, HR = 6.27. Fifteen of 42 eyes (35.7%) regained ambulatory vision (20/200 or better). The strongest predictors of vision worse than 20/200 at the last follow-up were RD, odds ratio (OR) = 43.88; graft rejection, OR = 12.42; and injury outside the workplace, OR = 25.05.

Conclusions: Despite a high graft survival at 1 year, most of the patients did not regain ambulatory vision. Graft rejection, RD, and endophthalmitis were risk factors for graft failure. These factors should be considered when counseling patients regarding PKP after OGI.

Key Words: trauma, cornea, penetrating keratoplasty, open globe

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Open globe injury (OGI) has an estimated global incidence of 200,000 cases per year.[1,2] Nearly 50% of cases result in permanent visual impairment.[3] Visual acuity (VA) after OGI is often limited by corneal scarring and irregular corneal astigmatism.[4] In select cases, rigid gas permeable contact lenses can correct irregular astigmatism and provide a nonsurgical option to improve VA.[5] However, significant corneal scarring after OGI may require surgical management with penetrating keratoplasty (PKP).[6]

A paucity of data exists in the literature regarding PKP after OGI.[6,7] The literature suggests that final VA is often poor, graft survival is low, and frequent postoperative complications occur compared with non–trauma-related transplants.[8–11] In the past 2 decades, improvement in surgical techniques and careful preoperative selection of patients have improved surgical outcomes in keratoplasty after OGI.[12] To optimize patient selection, preoperative counseling, and postoperative care, it is necessary to determine the preoperative characteristics that put patients at risk for graft failure and poor VA after transplantation. The purpose of this study was to identify the prognostic factors for graft failure and ambulatory vision posttransplantation as well as the survival rates of PKP after OGI over a 17-year period at the University of Michigan.

MATERIAL AND METHODS

A retrospective chart review of all patients undergoing PKP after OGI at a nonurban academic center between January 2000 and July 2017 was conducted. This study was approved by the Institutional Review Board of the University of Michigan and adhered to the tenets of the Declaration of Helsinki. The research was conducted in compliance with the

Health Insurance Portability and Accountability Act, and all patient data were deidentified on review.

Data Collection

A total of 586 eyes with OGI, defined as a full-thickness wound to the cornea and/or sclera,[13] were diagnosed and surgically managed over the study period. Fifty-four eyes underwent corneal transplantation after OGI. Inclusion required subsequent PKP after OGI. Eyes were excluded if they underwent partial thickness corneal transplantation (4 eyes) or had PKP with less than 365 days of follow-up (4 eyes). This resulted in 46 eyes that were included in the final data set for receiving PKP and having at least 365 days of follow-up afterward. The following variables were collected from the electronic medical record (Epic Systems Corporation, Verona, WI): demographics, mechanism of injury, associated ocular surgeries, status of the lens and retina, concurrent surgeries at the time of PKP, best-corrected preoperative and postoperative VA, and postoperative complications such as episodes of allograft rejection. Contact lens trials, refractive, and keratometric data were also collected. The Ocular Trauma Classification Group criteria were used to characterize the zone of injury. The zone of injury was classified as zone I (confined to the cornea), zone II (limbus to 5 mm posterior into the sclera), or zone III (more than 5 mm posterior to the limbus).[13]

Outcome Measures

Graft survival was the primary outcome measure. Graft clarity was defined as a clear cornea with an unimpaired view of iris details. Corneal haze or intermediate clarity was defined as having good or partial view of iris details. Graft rejection was defined by signs of corneal inflammation. Graft failure was defined as an irreversible loss of graft clarity.

Snellen VA was recorded from measurements of best-corrected VA with refraction at follow-up. For statistical calculations, Snellen VA was converted to the logarithm of the minimum angle of resolution (logMAR) equivalent. Subjects with count fingers, hand motion, light perception, or no light perception were assigned values of 1.85, 2.3, 2.75, and 3.2, respectively.[14] The 7 eyes that did not have VA at the time of presentation after OGI and the 4 eyes that did not have VA at the final follow-up because of enucleation were not included in the analysis of this outcome measure. An ambulatory VA was defined as final VA of 20/200 or better, whereas poor VA was defined as final VA of less than 20/200. Improvement in VA was defined as improvement of at least 1 line compared with pretransplant vision.

Statistical Analysis

For categorical variables, significant differences between and within groups were analyzed using the χ^2 test of independence. For continuous variables, comparisons were performed with the Mann–Whitney *U* test. Continuous variables that were not normally distributed were expressed as median and interquartile range (IQR).

Kaplan–Meier estimates were used to determine the long-term probability of graft survival and compare group success rates with the log-rank test. Univariate Cox proportional hazards regression was conducted to assess associations between graft failure and individual predictors. Multivariate Cox proportional hazards regression was then performed, including variables that were significant at a univariate level ($P < 0.05$), and a final multivariable model was selected using backward selection methods.

Univariate logistic regression analysis was used to analyze a set of variables considered predictive for blindness, defined as VA worse than 20/200. Multivariable logistic regression analysis was then conducted, including variables that were significant at a univariate level ($P < 0.05$) and using the backward selection method to determine a final multivariable model. The odds ratio (OR) and 95% confidence interval (CI) were calculated for all variables. A 2-tailed, $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Patient Population

Forty-six eyes of 46 patients that underwent PKP after OGI over a 17-year period were included in this study. Most of the patients, 37 of 46 (80.4%), were male. The median age at the time of keratoplasty was 46 years (IQR = 23.00–61.25). The median logMAR VA at the time of presentation was 2.3 (IQR = 2.30–2.75), a Snellen equivalent of hand motion vision in the 39 eyes that had measurable VA at the time of trauma. The median length of follow-up was 78.5 months (IQR = 38.63–122.02). Patients had an average of 2.3 additional trips to the operating room after initial globe closure, with 13 eyes (28.3%) having 1 additional surgery, 15 eyes (32.6%) having 2 additional surgeries, 11 eyes (23.9%) having 3 additional surgeries, 14 eyes (10.9%) having 4 additional surgeries, 1 eye (2.2%) having 5 additional surgeries, and 1 eye (2.2%) having 6 additional surgeries. Characteristics and presenting features of open globe injuries were recorded for all patients (Table 1). Causes of injury included tools, metal shards, falls, potato guns, exploding garbage, thumbs, fights, and motor vehicle accidents.

Pretransplant Characteristics

In this study, first keratoplasty after trauma (henceforth referred to as "first graft") was with PKP in all cases. The median time from injury to first graft was 4.4 months (IQR = 1.61, 12.51). A shorter time interval between the onset of trauma and performance of keratoplasty was not a risk factor for graft failure, $P = 0.29$.

The median pretransplant logMAR VA (recorded at the last follow-up before PKP) was 2.08 (Q1 = 1.30, Q3 = 2.39), with 9 of 46 eyes (19.57%) having vision 20/200 or better. Thirty-five eyes (76.1%) were phakic, 10 of 46 (21.7%) were pseudophakic, and 1 of 46 (2.2%) was aphakic at the time of grafting. Common indications for PKP were corneal scarring

TABLE 1. Risk of Graft Failure as a Function of Different Variables Examined in Eyes Undergoing Penetrating Keratoplasty After Ocular Trauma

Variable N Included in Analysis	Univariate Analysis	Hazard Ratio (95% CI)	*P**
Eye N = 46	Left (N = 25, 54.3%) vs. right (N=21, 45.7%)	1.26 (0.57, 2.77)	0.573
Sex N = 46	Female (N = 9, 19.6%) vs. male (N = 37, 80.4%)	1.15 (0.46, 2.87)	0.771
Age N = 46 Median age = 46 years (IQR = 23.00–61.25, 3 min–84 max)	18 years and older (N = 37, 80.4%) vs. younger than 18 years (N = 9, 19.6%)	2.08 (0.83, 5.20)	0.119
Location of injury N = 46	Workplace (N = 31, 67.4%) vs. nonworkplace (N = 15, 32.6%)	2.03 (0.92, 4.47)	0.079
Injury mechanism N = 15	Rupture (N = 5, 10.9%) vs. perforating (N = 10, 21.7%)	0.99 (0.39, 2.51)	0.989
Injury mechanism N = 41	Penetrating (N = 31, 67.4%) vs. perforating (N= 10, 21.7%)	0.46 (0.09, 2.28)	0.340
Pretransplant corneal neovascularization N = 46	Yes (N = 4, 8.7%) vs. no	1.04 (0.25, 4.42)	0.957
Transplant before trauma N = 46	Yes (N = 13, 28.3%) vs. no	1.18 (0.51, 2.71)	0.705
Fuchs dystrophy N=46	Yes (N =6, 13.0%) vs. no	1.13 (0.39, 3.30)	0.821
Herpes simplex keratitis N = 46	Yes (N = 4, 8.7%) vs. no	0.22 (0.03, 1.66)	0.143
Ocular surgery before trauma N = 46	Yes (N = 16, 34.8%) vs. no	1.25 (0.57, 2.73)	0.575
Cataract surgery before trauma N =46	Yes (N = 10, 21.7%) vs. no	0.90 (0.26, 3.11)	0.869
Injury zone N =46	Zone I (N = 30, 65.2%) vs. zone II (N = 8, 17.4%) and III (N=8, 17.4%)	0.55 (0.26, 1.20)	0.136
Time to presentation N = 46	> 24 hours (N = 4, 8.7%) vs. ≤ 24 (N = 42, 91.3%) hours	0.45 (0.06, 3.29)	0.428
Intraocular foreign body N = 46	Yes (N = 4, 8.7%) vs. no	0.31 (0.04, 2.29)	0.252
Relative afferent pupillary defect N = 26	Yes (N = 6, 13.0%) vs. no	0.85 (0.24, 3.05)	0.801
Traumatic cataract N = 46	Yes (N = 27, 58.7%) vs. no	1.38 (0.61–3.09)	0.439
Uveal prolapse N = 46	Yes (N = 31, 67.4%) vs. no	2.09 (0.84–5.23)	0.114
Lens status at globe repair N = 45	Pseudophakic (N = 10, 21.7%) vs. phakic (N = 35, 76.1%)	1.22 (0.51, 2.90)	0.661
Lensectomy at globe repair N = 46	Yes (N = 6, 13%) vs. no	0.45 (0.11, 1.91)	0.279
Silicone oil use N = 46	Yes (N = 11, 23.9%) vs. no	1.98 (0.88, 4.45)	0.097
Vitrectomy at the time of globe repair N = 45	Weck-cel (N = 11, 23.9%) vs. none	1.28 (0.54–3.06)	0.577
Indications for transplant N = 28	Corneal edema (N = 8, 17.4%) vs. corneal scar (N = 20, 43.5%)	1.24 (0.38, 4.05)	0.718
Indications for transplant N = 33	Failed graft (N = 13, 28.3%) vs. corneal scar (N = 20, 43.5%)	1.54 (0.61, 3.89)	0.360
Corneal glue N = 46	Yes (N = 5, 10.9%) vs. no	1.22 (0.36, 4.07)	0.752
Endophthalmitis N = 46	Yes (N = 3, 6.5%) vs. no	3.50 (0.97–12.66)	0.056
Pretransplant visual acuity N = 46	Median logMAR VA = 2.08 (IQR = 1.30, 0.10 min- 2.75 max)	2.38 (1.27, 4.45)	0.007
Retinal detachment N = 46	Yes (N = 19, 41.3%) vs. no	3.29 (1.48, 7.32)	0.004
Vitreous hemorrhage N = 46	Yes (N = 15, 32.6%) vs. no	2.45 (1.13, 5.31)	0.023
Keratoconus N = 46	Yes (N = 4, 8.7%) vs. no	4.33 (1.25, 14.95)	0.021
TKP at the time of PKP N = 46	Yes (N = 19, 41.3%) vs. no	2.34 (1.07, 5.09)	0.032

Variable	Multivariable Analysis	Hazard Ratio (95% CI)	*P*†
Rejection episode	Yes vs. no, N = 17	3.29 (1.47, 7.35)	0.004
Retinal detachment	Yes vs. no, N = 19	3.47 (1.51, 7.99)	0.003
Endophthalmitis	Yes vs. no, N = 3	6.27 (1.62, 24.38)	0.008

*Univariate Cox proportional hazards regression model.
†Multivariable Cox proportional hazards regression model.

in 20 of 46 eyes (43.5%), failure of a preexisting corneal graft after the OGI in 13 of 46 eyes (28.3%), and corneal edema in 8 of 46 eyes (17.4%). Three eyes (6.5%) underwent PKP for a combination of scarring and edema, and 2 eyes (4.3%) underwent PKP as treatment for corneal ulcers. Thirty-three of 46 eyes had additional surgical procedures at the time of

PKP, including temporary keratoprosthesis (TKP) in 19 of 46 eyes (41.3%). In eyes undergoing TKP, all 19 underwent subsequent pars plana vitrectomy (PPV) for a variety of indications including retinal detachment (RD) repair, intraocular foreign body removal, pars plana lensectomy, pars plana tube placement, or membrane peeling. Other surgeries commonly performed with PKP included lensectomy in 9 of 46 eyes (19.6%), intraocular lens insertion in 8 of 46 eyes (17.4%), and synechiolysis in 7 of 46 eyes (15.2%).

Outcomes

The overall first graft survival rate was 80.4% (95% CI, 65.8%–89.3%) at 1 year, 73.7% (95% CI, 58.4%–84.2%) at 2 years, and 41.7% (95% CI, 26.1%–56.6%) at 5 years (Fig. 1A). For the 12 eyes that required repeat grafting, survival was 61.9% at 1 year and 18.6% at 5 years (Fig. 1B). First grafts without any history of immunologic rejection had a 3-fold higher survival rate compared with those with at least 1 rejection episode, 59.7% versus 17.6% at the 5-year follow-up, respectively, P = 0.001 (Fig. 1C). Seventeen eyes (37.0%) experienced at least 1 rejection episode after first graft. Five of 17 rejection episodes (29.4%) occurred within the first 6 months after grafting and the remaining 12 episodes (70.6%) occurred within the first 2 years. The survival rate for first grafts was significantly higher if TKP was not performed compared with those with TKP at the time of PKP, 55.1% versus 22.7% at the 5-year follow-up, P = 0.028 (Fig. 1D). Interestingly, eyes with no history of grafting before trauma did not have significantly higher survival rates compared with those that had received previous grafting before trauma, 81.8% versus 76.9% at the 1-year follow-up, respectively, P = 0.704. Regarding lens status, phakic and pseudophakic eyes' graft survival rate did not differ significantly from those of aphakic eyes, 50.9% versus 34.2% survival rate at the 5-year follow-up, P = 0.160. First grafts for eyes with zone I injury had a comparable survival rate to those with zone II and III injury, 45.7% versus 35.0% at the 5-year follow-up, respectively, P = 0.130. Graft failure occurred at a median of 26.5 months (IQR = 6.32, 40.87) after primary grafting. Twenty grafts (43.5%) eventually failed by last follow-up. Rejection was the most common cause of graft failure and accounted for 12 of 20 failed grafts (60.0%). Other causes of graft failure were phthisis in 4 of 20 eyes (20.0%) and failure secondary to silicone oil fill in 2 of 20 eyes (10.0%). Among the failed grafts, 12 of 20 cases (60.0%) were regrafted during our follow-up period (Fig. 1B). The final clarity of these regrafts was determined to be clear in 5 of 12 (41.7%) and failed in 7 of 12 cases (58.3%).

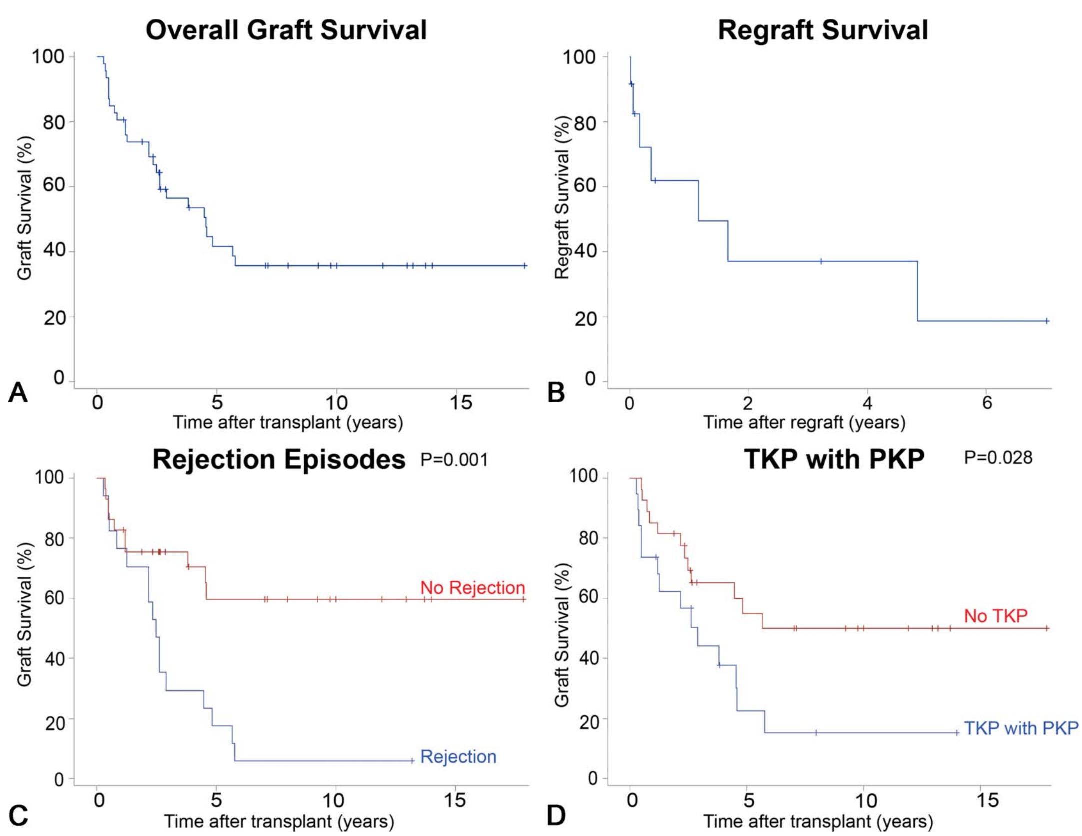

FIGURE 1. Kaplan–Meier survival data by selected group. The graft survival rate for (A) primary grafts and (B) regrafts (N = 12). C, The survival rate was significantly higher for eyes that had not experienced a rejection episode compared with those that had at least 1 rejection episode, P = 0.0012. D, The survival rate for eyes that had not received TKP was significantly higher compared with those with TKP at the time of PKP, P = 0.0277.

Nineteen eyes in this series were diagnosed with a posttraumatic RD, and all underwent operative management with PPV. The median time between diagnosis and treatment of RD was 47 days (IQR = 13, 130). In those with a RD, operative treatment of RD within 1 month was associated with a significantly higher rate of subsequent graft success, OR = 6.00 (P = 0.008). RD repair was concurrent with (14 eyes) or after PKP (5 eyes).

The frequency of graft failure was evaluated in relation to silicone oil status after PKP. Of the 19 eyes that underwent RD repair, 11 of 19 (57.9%) had silicone oil placement and 9 of these eyes (81.8%) had a failed graft at the last follow-up. Among these eyes, 7 (63.6%) had retained silicone oil posttransplant and 4 (36.4%) had oil removed, with tamponade durations of 2.7, 3.7, 5.3, and 7.7 months. A retention suture was placed in 1 eye that eventually had the silicone oil removed and 1 eye in which oil was retained.

For the 42 eyes that did not undergo enucleation, 15 of 42 (35.7%) regained ambulatory vision (20/200 or better) and 7 of 42 (16.7%) regained vision 20/40 or better. The median final logMAR VA was 1.82, essentially count fingers vision (IQR = 0.70, 2.86). This final best-corrected VA was attained with glasses in 14 of 42 (33.3%), contacts in 10 of 42 (23.8%), and without correction in 18 of 42 eyes (42.9%). When comparing pretransplant VA with posttransplant acuity, 22 of 42 eyes (52.4%) had improvement in vision, P = 0.003.

Factors Associated With Graft Failure Over Time

Risk factors for graft failure were determined using Cox proportional hazards models run on all baseline characteristics and surgical factors. Pretransplant VA, graft rejection, RD, vitreous hemorrhage at the time of wound closure, keratoconus, and TKP at the time of PKP were found to statistically increase the risk of graft failure in the univariate Cox regression analysis (Table 1). A multivariable Cox model was selected adjusting for graft rejection, RD, and endophthalmitis. Hazard ratio estimates and their 95% CIs for these variables from the univariate and final multivariable models are shown in Table 1.

Factors Associated With Blindness

To investigate risk factors for poor VA after transplantation, a univariate regression analysis was performed on all baseline characteristics and surgical factors. Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/ICO/B316 reports the association between each preoperative and operative parameter examined and the odds of blindness or vision worse than 20/200 at the last follow-up. Univariate logistic regression analysis found 8 variables that had a statistically significant association with blindness. Strong predictors of blindness were non–workplace-related injury (vs. workplace injury), P = 0.02; wound length >10 mm (vs. ≤ 10 mm), P = 0.01; RD, P = 0.002; vitreous hemorrhage at the time of wound closure, P = 0.01; uveal prolapse, P = 0.005; pretransplant VA, P = 0.004; TKP at the time of grafting, P = 0.02; and graft rejection, P = 0.03 (Table 2). Risk factors that approached significance were silicone oil use, P = 0.086; injury mechanism (penetrating vs. rupture), P = 0.069; and transplant indication (corneal edema vs. corneal scar), P = 0.064 (see Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/ICO/B316). After the results of univariate analysis, multivariable regression modeling was used to investigate the joint effects of variables. The variables retained in the final model were RD, OR = 43.88 (P = 0.003); graft rejection, OR = 12.42 (P = 0.024); and injury outside the workplace, OR = 25.05 (P = 0.014, Table 2).

Postoperative Complications

Postoperative complications included glaucoma in 15 of 46 eyes (32.6%), hypotony in 16 of 46 eyes (34.8%), and corneal neovascularization (NV) in 21 of 46 eyes (45.7%). In the 21 recipient corneas with NV, 12 of 21 (57.1%) had 1 to 2 quadrants of vascularization and 9 of 21 (42.9%) had 3+ quadrants of vascularization. Among the 15 eyes that developed glaucoma postoperatively, 8 of 15 (53.3%) were managed with medical therapy alone and 7 of 15 refractory cases (46.7%) required glaucoma surgery. Four of the 15 eyes (26.7%) that received glaucoma surgery went on to become hypotonus.

Corneal scar was present after PKP in 31 of 46 eyes (67.4%). Scars were found centrally in 13 of 46 (28.3%),

TABLE 2. OR of Being Blind (Visual Acuity Worse Than 20/200) at the Last Follow-up in Eyes Undergoing Penetrating Keratoplasty After Ocular Trauma

Variable N included in Analysis		OR	P*
Location of injury N = 46	Nonworkplace vs. workplace	13.00	0.020
Wound length N = 43	>10 vs. ≤ 10 mm	7.00	0.011
Uveal prolapse N = 31	Yes vs. no	8.63	0.004
Vitreous hemorrhage N = 15	Yes vs. no	11.20	0.039
Retinal detachment N = 19	Yes vs. no	17.50	0.001
Pretransplant visual acuity N = 46	Continuous	4.22	0.004
TKP at the time of PKP N = 19	Yes vs. no	7.00	0.022
Rejection episode N = 19	Yes vs. no	6.09	0.032

Variable		OR	P†
Rejection episode	Yes vs. no	12.42	0.024
Retinal detachment	Yes vs. no	43.88	0.003
Location of injury	Nonworkplace vs. workplace	25.05	0.014

Only variables significant at a univariate and multivariable level are shown.
*Univariate logistic regression analysis.
†Multivariable logistic regression analysis.

diffusely in 2 of 46 (4.3%), and peripherally in 1 of 46 eyes (2.2%). The scar location was not recorded for the other 15 eyes with corneal scarring. Of the 44 eyes with documented topography, 22 of 44 (50%) had irregular astigmatism and 3 of 44 (6.8%) had regular astigmatism. Eighteen eyes with corneal scarring received correction of vision with rigid gas permeable contact lenses either before or after transplant. Four patients eventually required enucleation of affected eye (Table 3).

DISCUSSION

Corneal transplantation can play an important role in the process of visual rehabilitation of patients with OGI. This study presents the anatomic and visual outcomes in a series of patients who underwent PKP after OGI and is the largest study of its kind to date. This series suggests a high graft survival rate despite significant ocular trauma. Visual outcomes were, however, poor and limited by noncorneal pathology. RD due to ocular trauma was a significant predictor for both graft failure and poor VA.

Graft survival was high initially, with 80.4% of grafts surviving at the 1-year follow-up. Survival declined sharply by 5-year follow-up to 41.7%. At the last follow-up, those eyes that had repeat grafts after trauma only had a 40.0% survival rate. The short-term graft survival rate in this study was comparable with other series of PKP after ocular trauma, which have reported 1-year graft survival rates of 42% to 84%.[6,7,15,16] Surprisingly, the 1-year graft survival in this current OGI series was also comparable with PKP performed for nontraumatic indications, which report 1-year survival rates of 80% to 95%.[17–20] However, beyond the 2-year mark, the graft survival rate in this OGI series was considerably lower compared with long-term survival rates of grafts for nontraumatic indications, 41.7% compared with 73% to 95%, respectively.[17,18,20–22] Collectively, these results suggest that PKP after OGI has favorable short-term graft survival rates, but not long-term success compared with grafts for nontraumatic indications. All patients with successful grafts at the last follow-up used topical steroids beyond 18 months after surgery, whereas 3 patients with failed grafts discontinued steroids because of noncompliance. Therefore, the long-term graft survival in this series could be correlated with discontinuation of topical steroids, increased frequency of NV, or concurrent pathology in trauma eyes.

The cornea is an immunologically privileged site. The Collaborative Corneal Transplantation Study defined "high risk" as a cornea in which a graft had been previously rejected or with 2 or more quadrants of NV.[23] Several studies, including this current one, have conducted multivariable analysis demonstrating the negative impact of a rejection event on the long-term viability of corneal grafts.[21,24] In this

TABLE 3. Postoperative Complications and Risk of Graft Failure

Variable	N = 46, (%)	Hazard Ratio (95% CI)	*P**
Rejection episode	17 (37.0%)	3.47 (1.56, 7.73)	0.002
Glaucoma	15 (32.6%)	0.39 (0.15, 0.99)	0.047
Medical management only	8/15 (53.3%)		
Surgical management	7/15 (46.7%)		
Hypotony	16 (34.8%)	3.75 (1.69, 8.29)	0.001
Neovascularization	21 (45.7%)	1.55 (0.71, 3.37)	0.273
1–2 quadrants	12/21 (57.1%)		
3+ quadrants	9/21 (42.9%)		
Corneal scar	31 (67.4%)	0.95 (0.42, 2.14)	0.905
Centrally	13/31 (41.9%)		
Peripherally	1/31 (3.2%)		
Diffusely	2/31 (6.5%)		
Not recorded	15/31 (48.4%)		
Rigid gas permeable contact lens	18 (39.1%)	0.52 (0.23, 1.21)	0.130
Astigmatism	25/44 (56.8%)	0.80 (0.10, 6.25)	0.830
Irregular	22/25 (88%)		
Regular	3/25 (12%)		
Under 2 diopters	1/25 (4%)		
2 to under 4 diopters	4/25 (16%)		
4 to under 6 diopters	4/25 (16%)		
6 diopters or greater	14/25 (56%)		
Too high to measure	2/25 (8%)		
Median diopters of astigmatism (IQR, range)	8.6 (4.13–10.20, 0.5 min- 47.90 max)		
Endophthalmitis	1 (2.2%)	N/A	N/A
Enucleation	4(8.7%)	2.75 (0.82, 9.23)	0.102

NA, Not Applicable

series, 37.0% of eyes experienced at least 1 rejection episode during follow-up after primary PKP. This rate of rejection is considerably higher compared with rates in non-OGI series, which varies from 12% to 27% in large multicenter studies.[21,24,25] As rejection frequently goes on to graft failure, the more frequent rejection episodes after trauma likely contribute to the higher overall rate of graft failure in this series. Accordingly, Kaplan–Meier curves showed that those with a rejection episode had a significantly higher chance of graft failure than those without, $P = 0.001$, demonstrating rejection as a postoperative complication that can predict graft failures. Another well-documented risk factor for graft failure is corneal NV. A large meta-analysis, combining studies with univariate or multivariate analysis, revealed that NV of corneas increased rejection and failure rates of transplanted corneas.[26] In this OGI series, 8.7% of eyes had preoperative corneal NV and 45.7% of eyes developed postoperative NV, consistent with the 8.3% preoperative and 41% postoperative rates reported in eyes undergoing PKP for nontraumatic indications.[26–28] These results have implications for patient selection with careful attention to the presence of NV and appropriate tapering of steroids postoperatively because these eyes tend to be at greater risk for rejection than eyes undergoing KP for nontraumatic indications.

Although keratoconus and endophthalmitis at the time of presentation are stated to be predictive factors of graft failure, the results of univariate and multivariate analysis should be interpreted with caution because of small sample size. The significance of keratoconus in univariate analysis could be due to the copresence of cofounding factors such as previous grafting before OGI. In addition, the significance of keratoconus could be caused by its small counts because its effect no longer seems significant once accounting for other factors in multivariable analysis. Although endophthalmitis was a significant risk factor for graft failure in our multivariable Cox regression model, these results need to be verified in the future studies because of a sample size of 3. Endophthalmitis did not reach significance in univariate analysis ($P = 0.056$).

Although factors that affect anatomic success of PKP are critical to understand, the ultimate goal is to provide patients with improvement in their VA so that they may better be able to perform their activities of daily living. In this current series, just over half of the eyes experienced at least 1 line of improvement after PKP. The large variation in preoperative diseased state, difference in nature of ocular trauma, and retrospective nature of this study limit the comparability with other OGI studies. With this in mind, the visual outcomes in this series are worse than outcomes reported by Dana et al,[7] in which VA was better after PKP in 15 of 18 children (83%). However, the children in this series had fewer comorbidities compared with subjects in the present series. Only 27% of children in the study by Dana et al had posterior segment pathology after trauma, compared with the 33% and 41% of the patients in the current series that had vitreous hemorrhage and RD, respectively. Similarly, Doren et al found that VA was better than 20/200 in 74% of eyes receiving PKP after trauma, with patients referred from the Retina Service having worse final VA. The relatively favorable outcomes in the study by Doren et al[6] could be attributed to the lower rates of RD, astigmatic errors, glaucoma, and endophthalmitis compared with our study. Ultimately, these results demonstrate that despite high graft survival rates, visual outcomes are limited by noncorneal pathology related to trauma. These findings suggest that in cases of OGI, ocular salvage, not VA, may be the most realistic goal.

There is abundant literature documenting poor prognosis attributable to vitreous hemorrhage after OGI.[29,30] In this series, vitreous hemorrhage showed statistical significance in increased risks for graft failure in the Cox proportional hazards regression analysis and poor vision in univariate logistic regression analysis. The relationship with vitreous hemorrhage and poor vision is likely due to the fact that trauma significant enough to cause vitreous hemorrhage damages vital structures of the eye including the intraocular lens, retina, and optic nerve. Indeed, the transplant surgeon should consider that in eyes with vitreous hemorrhage at the time of injury, noncorneal pathology may lead to an unfavorable prognosis for PKP.

RD often occurs during OGI and is often not diagnosed until days after initial injury. In our univariate analysis, RD was a predictor of both graft failure and poor vision. Because all patients with RD repair also received TKP at the time of PKP, posterior segment comorbidities requiring TKP are likely the cause of increased cases of graft failure and blindness in these patients. Therefore, the need for TKP during surgery may be a prognostic factor for graft failure and blindness, not TKP itself. The χ^2 test demonstrated that RD repair within 1 month of detachment was associated with a higher rate of graft success, $P = 0.008$. In addition, the timing of keratoplasty after ocular trauma has not been shown to significantly affect graft survival.[15] These findings suggest that in cases with comorbid RD, intervention with early PPV, TKP, and PKP may yield better outcomes for graft survival.

Directly related to RD repair in eyes undergoing PKP and RD repair is the fact that these are often complicated RDs that require silicone oil placement. Silicone oil is a known risk factor for endothelial decompensation in both native corneas and transplanted corneas.[31,32] This is consistent with the results of this current series, where 9 of the 11 eyes receiving silicone oil ultimately had graft failure during the study period. In eyes with long-term silicone oil tamponade, silicone oil may enter the anterior chamber and directly contact the corneal endothelium causing decompensation.[33] Possible considerations include placement of retention sutures or consultation with the vitreoretinal surgeon for earlier removal of the silicone oil in cases of OGI that require PKP.

An important consideration in cases of PKP after OGI is the need for contact lens correction even in cases with graft clarity or anatomic success. Corneal scarring was present in two thirds of patients after PKP; in one third of these patients, the scar was noted to be central. Postoperatively, 50% of eyes had irregular astigmatism with a median degree of astigmatism greater than 8 diopters. Again, patients should be counseled preoperatively that even when graft clarity is achieved, achievement of useful vison requires further work, which often involves adjunctive corrective contact lenses.

A major limitation of this study is its retrospective nature, which lends itself to inherent differences in follow-up duration, management protocol, and documentation of clinical findings. Despite these limitations, this study has unique strengths. Perhaps the biggest strength of this study is that the relatively large patient numbers, allowing for identification of factors that influence corneal transplant success or failure. In addition, the sample size in this series is amenable to multivariable analysis that looks beyond the independent statistical significance of individual variables and reveals possible interactions among risk factors. Other strengths of this series include its application of survival analysis techniques, which compensate for those lost to follow-up and provide an accurate assessment of time to graft failure and factors related to graft failure.

In conclusion, OGI commonly induces both anterior and posterior segment trauma that requires close collaboration between corneal and vitreoretinal surgeons to achieve the best outcomes for these patients. Despite a high graft success rate at the 1-year follow-up, graft success at the 5-year follow-up was less than 50%. Furthermore, PKP only provided ambulatory vision in one third of cases. Factors that significantly increased the risk of graft failure included rejection episode, history of RD, and history of endophthalmitis. The most powerful predictors of loss of ambulatory acuity were comorbid RD, injury outside the workplace, and episodes of graft rejection. Candidates for PKP after OGI should be carefully selected and reasonable expectations need to be set before electing transplantation and the frequent postoperative visits that accompany this procedure.

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