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Incidence of Intraocular Pressure Elevation and Glaucoma after Lamellar versus Full-Thickness Penetrating Keratoplasty

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Purpose: To analyze the cumulated incidence of glaucoma after penetrating keratoplasty (PK), anterior lamellar keratoplasty (ALK), and endothelial keratoplasty (EK).

Design: Cohort study. Data were recorded prospectively and analyzed retrospectively.

Participants: A total of 1657 consecutive eyes of 1657 patients undergoing corneal transplantation between 1992 and 2013.

Methods: Penetrating keratoplasty (date range, 1992−2013), ALK (date range, 2002−2013), and Descemet's stripping automated EK (date range, 2006−2013).

Main Outcome Measures: Postoperative intraocular pressure (IOP), glaucoma treatments, and glaucoma-related loss of vision (loss of central visual function resulting in absence of light perception or light perception limited to the temporal visual field). Cox proportional hazard regression model was used to analyze risk factors for glaucoma after keratoplasty.

Results: The 10-year cumulated incidence of elevated IOP and elevated IOP requiring treatment was 46.5% and 38.7%, respectively. In multivariate analysis, 4 variables were significantly associated with a higher incidence of elevated IOP requiring treatment after keratoplasty: preoperative glaucoma or IOP >20 mmHg (adjusted hazard ratio [HR], 1.56; $P < 0.001$), penetrating keratoplasty (PK) (adjusted HR, 1.12 vs. ALK and 1.10 vs. EK; $P < 0.001$), postoperative lens status (adjusted HR vs. phakic eyes: 1.15 for posterior chamber intraocular lens, 1.43 for anterior chamber intraocular lens [IOL], 2.83 for aphakic eyes; $P < 0.001$), and IOL exchange or removal during surgery (adjusted HR, 1.48; $P < 0.001$). Recipient age, preoperative diagnosis, filtering surgery before keratoplasty, vitrectomy associated with keratoplasty, and filtering surgery associated with keratoplasty were significantly associated with a higher incidence of elevated IOP requiring treatment after keratoplasty in univariate analysis but not in multivariate analysis. The 10-year probability of loss of vision related to glaucoma was 1.0% after EK, 2.1% after ALK, and 3.6% after PK ($P = 0.036$).

Conclusions: The incidence of elevation of IOP after keratoplasty and development of glaucoma are significantly decreased with ALK and EK compared with PK. We believe this is due to diminished surgery-induced damage to the anterior chamber angle and trabecular meshwork, and reduced postoperative use of steroids. *Ophthalmology 2016;■:1−7 © 2016 by the American Academy of Ophthalmology.*

Glaucoma is a major complication after keratoplasty, and sustained intraocular pressure (IOP) elevation may result in endothelial cell decompensation with corneal graft failure and loss of vision.[1−3] The reported incidence of IOP elevation after keratoplasty ranges from 12% to 48%.[3,4] Potential mechanisms for such pressure elevation include retained viscoelastic material, hemorrhage, malignant glaucoma, uveitis, lens protein leakage, pupillary block, secondary angle-closure glaucoma, trabecular meshwork collapse, steroid-induced effects, and preexisting glaucoma.[4]

There is a current trend toward the substitution of penetrating keratoplasty (PK) by lamellar techniques if the corneal stroma or endothelium is healthy. This development is buoyed by reported decreased graft rejection, reduced loss of endothelial cells, and extension of graft survival after anterior lamellar keratoplasty (ALK).[5,6] Likewise, more rapid and predictable visual recovery, lower degrees of postoperative astigmatism, decreased need for topical corticosteroids, high midterm graft survival, and decreased incidences of rejection have been reported after endothelial keratoplasty (EK) vis-à-vis PK.[7,8] However, fewer studies are available comparing the incidence of glaucoma after lamellar keratoplasty compared with full-thickness keratoplasty.[9−12] We believed that glaucoma might be less likely to occur after lamellar keratoplasty because of decreased surgery-induced damage to the anterior chamber angle and trabecular meshwork, and the reduced postoperative need for steroids. The goal of this study is to determine the incidence of IOP elevation after keratoplasty and glaucoma after lamellar versus full-thickness (penetrating) keratoplasty.

Methods

Study Design

We studied 1905 consecutive penetrating, anterior lamellar, and endothelial keratoplasties performed in 1657 patients between

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December 1992 and December 2013. Data were prospectively recorded and retrospectively analyzed. In the 248 patients (13%) who received 2 grafts in the same or contralateral eye during the study period, only the first graft was included in the study, yielding a total of 1657 procedures in 1657 patients. From 1992 to 2001, all patients had undergone full-thickness PK. Between 2002 and 2013, patients with corneal diseases sparing, or only moderately affecting, the corneal endothelium underwent deep ALK whenever feasible. From 2006 to 2013, patients with endothelial diseases underwent Descemet's stripping automated EK when no stromal fibrosis was discernable on slit-lamp examination. Approval was obtained from the Ethics Committee of the French Society of Ophthalmology (Insitutional Review Board 00008855 Société Française d'Ophtalmologie IRB#1). No modifications to French standards of treatment and follow-up were made. Informed consent was obtained from all patients before surgery. The described research adhered to the tenets of the Declaration of Helsinki.

Donor Corneas

Donor corneas were stored according to methods described previously.[5] The average donor age was 69.3±13.8 years (mean ± standard deviation), and the average preoperative endothelial cell density was 2233±349 cells/mm.[2]

Surgical and Medical Treatment

All transplants were performed at the same institution by 6 surgeons. One surgeon performed 76% of the procedures. The average graft diameter was 8.21±0.24 mm. All EK procedures were Descemet's stripping automated endothelial keratoplasties. Surgical techniques and patient postoperative treatments were uniformly performed and administered according to previously reported methods.[5] After ALK and PK, sutures were removed between 12 and 36 months, according to corneal vascularization, with no differences between both surgical techniques. To prevent graft rejection, we used topical dexamethasone (1 mg/ml) in all eyes. This treatment was tapered for several months without standardization of postoperative steroid management. However, steroid tapering was more rapid in eyes with ALK or EK than in eyes with PK. The initial regimen was 1 drop hourly in patients with vascularized corneas and 1 drop every 6 hours in the other patients. After PK and ALK, corticosteroid use was never stopped in the former patients, and it was discontinued when all the sutures were removed in the latter. After EK, corticosteroids were discontinued after 3 years. The initial dexamethasone regimen (i.e., 4 drops/day for low-risk patients and 16 drops/day for high-risk patients) typically was progressively decreased to 1 drop per day over a 9-, 6-, or 4-month period in PK, ALK, and EK cases, respectively. Patients who received PK and had no IOP elevation were further kept under dexamethasone 1 drop per day up to steroid discontinuation. In patients who received PK and had IOP elevation, who received ALK, and who received EK, dexamethasone was further replaced by fluorometholone 1 drop per day up to steroid discontinuation.

Recipients and Transplant Outcome

The mean age of the patients was 59.2±21.4 years. Recipient rejection risk was determined according to corneal vascularization and recipient history. High-risk recipients were defined as those having a vascularized cornea (≥2 quadrants of corneal vascularization) or a history of irreversible corneal allograft rejection in the operated eye. Only grafts performed for optical indications were included in the study. Patient characteristics are shown in Table 1.

Patients were examined 1 and 2 weeks; 1, 3, 6, 9, 12, 18, 24, and 36 months; and 4, 5, 6, 8, 10, and 15 years after surgery. Slit-lamp findings, central corneal thickness (ultrasound pachymetry), and IOP (Goldmann applanation tonometry performed in both the steepest and the flattest corneal meridians) were recorded at each examination. The IOP was considered elevated when >24 mmHg. The number of glaucoma treatments and surgical interventions to reduce IOP was recorded. Elevated IOP was considered to require treatment whenever the addition of medications or surgical procedures was performed to reduce the IOP. Management of postoperative elevated IOP was similar in all cases, with no differences according to preoperative diagnosis or keratoplasty technique. The criteria for glaucoma-related loss of vision were loss of central visual function resulting in the absence of light perception or light perception limited to the temporal visual field in a glaucomatous eye.

Statistical Analysis

Qualitative variables were analyzed using the chi-square test. To assess the incidence of glaucoma after keratoplasty, we used a survival method. Elevated IOP-free graft survival and elevated IOP requiring treatment-free graft survival were analyzed using the Cox proportional hazard regression model. Patients with graft failure were excluded from analysis at the postoperative time point of graft failure. Association of covariates with survival was tested by the log-rank test. Ten-year survival was computed using the Kaplan–Meier method. A multivariable Cox proportional hazard regression was then carried out, including survival time and covariates that were significant at a univariate level ($P < 0.05$). The following covariates were studied: recipient age, preoperative diagnosis, recipient rejection status, trephination size, preoperative IOP, filtering surgery before keratoplasty, type of keratoplasty, lens status, and combined procedures that included intraocular lens (IOL) removal/exchange, vitrectomy, trabeculectomy, and cataract surgery. Analysis of variance with appropriate post hoc tests was used to analyze quantitative variables.

Results

Overall Results

The average follow-up time was 90.7±75.2 months (mean ± standard deviation; range, 1–275 months). Elevated IOP and elevated IOP requiring treatment were observed during follow-up in 715 and 597 of 1657 eyes, respectively. The 10-year cumulated incidence of elevated IOP and elevated IOP requiring treatment was 46.5% and 38.7%, respectively (Fig 1). The average IOP was 14.2 mmHg preoperatively (n = 1657), 16.0 mmHg at 1 year postoperatively (n = 1547), 14.6 mmHg at 3 years (n = 1193), 14.6 mmHg at 5 years (n = 890), and 14.4 mmHg at 10 years (n = 487). The average maximum postoperative IOP was 24.1±9.0 mmHg (range, 8–66 mmHg). The number of glaucoma treatments was on average 0.8±1.1 (range, 0–4). It was 0 in 981 eyes (59.2%), 1 in 339 eyes (20.5%), 2 in 196 eyes (11.8%), 3 in 107 eyes (6.5%), and 4 in 34 eyes (2.1%). In 137 eyes (8.3%), medical treatment alone was considered insufficient and filtering surgery was necessary to control glaucoma during the follow-up after keratoplasty.

Factors Influencing the Incidence of Elevated Intraocular Pressure after Keratoplasty

Table 2 shows analysis of the cumulated incidence of postoperative elevated IOP. In multivariate analysis, 4 variables were significantly