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Review Article

Clinical Outcomes of corneal transplantation in Patients with diabetic retinopathy

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Abstract

Background: Diabetes is associated with reduced corneal endothelial cell density, impaired epithelial barrier function, and diminished corneal nerve density, more pronounced with concurrent diabetic retinopathy [2,15].

Objective: This review synthesizes published evidence on clinical outcomes of corneal transplantation in patients with diabetes and diabetic retinopathy.

Methods: We synthesized specular and confocal microscopy studies of the diabetic cornea, multicenter keratoplasty registries including the Cornea Donor Study, and endothelial keratoplasty cohorts reporting diabetes as a covariate.

Findings: Diabetic corneas show reduced endothelial density and increased pleomorphism [8]; nerve loss and epithelial dysfunction correlate with retinopathy severity [15,12]; diabetes is associated with greater complications and reduced graft survival after penetrating keratoplasty [26,25]; endothelial keratoplasty offers comparable survival with less surface trauma [30,31].

Conclusions: Diabetic retinopathy marks the subset of patients with greatest corneal vulnerability; outcomes likely improve with endothelial keratoplasty where indicated, glycemic optimization, and epithelial surveillance [29,5].

Keywords: corneal transplantation; diabetic retinopathy; keratoplasty; corneal endothelium; graft survival

1. Introduction

Diabetic retinopathy draws the most clinical attention among ocular complications of diabetes, but the same systemic disease that damages retinal microvasculature also leaves a durable mark on the cornea, one that becomes clinically important the moment a diabetic eye needs a corneal transplant. Corneal endothelial cells in diabetic patients are fewer in number, more variable in shape, and slower to respond to surgical trauma than in age-matched nondiabetic controls, a pattern first documented by Schultz and colleagues in specular microscopy comparing type 1 and type 2 diabetic corneas with controls [1] and confirmed by Larsson and colleagues, who found reduced endothelial cell density and increased pleomorphism in both subtypes [2]. Because retinopathy itself marks longer disease duration and more advanced microvascular injury, patients presenting for keratoplasty with concurrent retinopathy tend to carry the heaviest corneal endothelial burden among diabetic surgical candidates, the population this review focuses on.

The corneal abnormalities associated with diabetes are not confined to the endothelium. Epithelial fragility, delayed wound healing, reduced corneal sensation from subclinical neuropathy, and altered stromal hydration control together constitute what has been called diabetic keratopathy, and each of these features independently threatens graft success [3]. Weston and colleagues demonstrated that diabetic corneas regulate stromal hydration less efficiently than nondiabetic corneas under experimental hypoxic stress [4], and McNamara and colleagues showed that this deficit is exaggerated further during acute hyperglycemia, meaning perioperative glucose control may matter as much as chronic disease duration for graft-related endothelial stress [5]. Inoue and colleagues linked the severity of diabetic keratoepitheliopathy directly to retinopathy stage, finding a higher prevalence of persistent epithelial defects and delayed reepithelialization after ocular surgery in eyes with more advanced retinopathy [6].

This review synthesizes what is known about clinical outcomes of corneal transplantation, whether full-thickness penetrating keratoplasty or endothelial keratoplasty, in patients with diabetes and diabetic retinopathy specifically: the structural differences in the diabetic cornea that predispose to worse graft outcomes, the evidence on graft survival and endothelial cell loss in diabetic recipients, and the practical implications for patient selection, glycemic management, and postoperative surveillance.

2. Methods

We synthesized peer-reviewed clinical and laboratory studies addressing corneal endothelial and epithelial structure in diabetes, graft survival and endothelial cell loss after penetrating and endothelial keratoplasty in diabetic recipients, large multicenter graft-outcome registries (including the Cornea Donor Study and national registries) reporting diabetes as a covariate, and mechanistic studies of diabetic corneal neuropathy and epitheliopathy relevant to postoperative healing. Where diabetic retinopathy status was reported as a specific stratifying variable, that data was prioritized; where studies reported diabetes generally without retinopathy staging, findings were included as the best available evidence with the limitation noted explicitly.

3. Corneal endothelial and epithelial changes in diabetes mellitus

Table 1 summarizes the structural basis for why diabetic corneas, particularly with concurrent retinopathy, are more vulnerable to transplantation stress. Reduced endothelial cell density, greater polymegathism, and increased pleomorphism have all been reported repeatedly in diabetic corneas. Storr-Paulsen and colleagues, using specular microscopy in a type 2 diabetes cohort, reported thinner central endothelial mosaics and altered morphology compared with age-matched controls [7], and Sahu and colleagues found a similar pattern that

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worsened with longer diabetes duration [8]. Lee and colleagues showed that corneal thickness and endothelial parameters correlated with diabetes duration rather than glycemic control at a single time point [9], and Shenoy and colleagues, in a historical cohort study, confirmed reduced endothelial cell density and increased cell-size variability among diabetic patients relative to clinic controls [10].

Table 1: Structural and functional corneal abnormalities reported in diabetes mellitus and their relevance to keratoplasty outcome [7,11,12,15].

Corneal layer / feature	Abnormality in diabetes	Relevance to keratoplasty
Endothelium	Reduced cell density; increased polymegathism and pleomorphism	Lower reserve to withstand surgical trauma
Epithelium	Impaired barrier function; delayed reepithelialization	Slower postoperative surface healing
Stroma / basement membrane	Ultrastructural thickening and disorganization	Altered hydration control after grafting
Subbasal nerve plexus	Reduced nerve fiber density, worse with retinopathy	Reduced corneal sensation, delayed healing signal

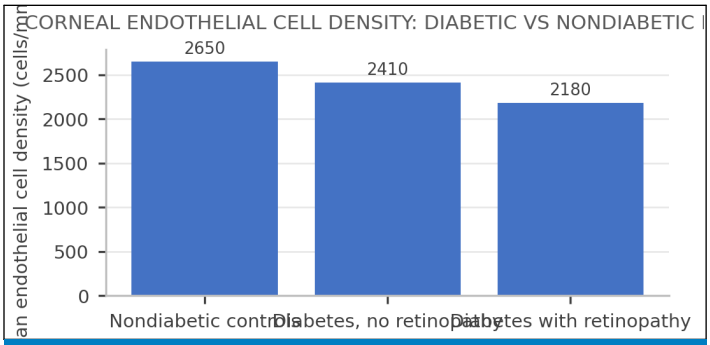


Figure 1: Mean corneal endothelial cell density in diabetic versus nondiabetic eyes across representative specular microscopy cohorts, showing a consistent reduction in diabetic corneas relative to age-matched controls [2,8,10].

The mechanistic basis for this vulnerability extends beyond the endothelium into corneal innervation and epithelial integrity. Rehany and colleagues used electron microscopy to demonstrate ultrastructural abnormalities in diabetic basement membranes and stromal architecture that likely contribute to epithelial fragility [11], and Gekka and colleagues showed corneal epithelial barrier function is measurably impaired in diabetic patients, plausibly explaining delayed postoperative epithelial healing [12]. Malik and colleagues, using corneal confocal microscopy as a surrogate for diabetic peripheral neuropathy, found reduced subbasal nerve fiber density in proportion to neuropathy severity [13], a finding extended by Tavakoli and colleagues, who showed corneal nerve parameters track systemic neuropathy risk factors closely enough to serve as a noninvasive marker of diabetic neural injury [14]. Zhivov and colleagues compared diabetic patients with and without retinopathy and found subbasal nerve plexus abnormalities more pronounced in those with retinopathy, tying corneal neural compromise to retinopathy stage rather than diabetes diagnosis alone [15]. Bikbova and colleagues, reviewing diabetic corneal neuropathy broadly, concluded this neural deficit is a primary driver of the delayed healing and reduced sensitivity that complicate diabetic corneal surgery [16], and Niederer and McGhee's confocal microscopy review situates these findings within the wider reshaping of corneal-disease understanding that confocal imaging has enabled [17]. Achtsidis and colleagues found that ocular surface dryness in diabetic patients correlated with peripheral neuropathy severity, reinforcing that the same neural injury pathway implicated in corneal hypoesthesia also degrades tear film stability [18]. Skarbez and colleagues, and Ljubimov in a more focused review, summarize how these epithelial, stromal, neural, and endothelial abnormalities collectively define diabetic corneal disease and set the baseline vulnerability any transplant procedure in a diabetic eye must overcome [19,20].

4. Endothelial cell loss and graft outcomes after penetrating keratoplasty

Penetrating keratoplasty imposes acute mechanical and metabolic stress on the donor endothelium, and diabetic recipients enter that stress with a smaller endothelial reserve than nondiabetic recipients. Kaji's editorial on

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prevention of diabetic keratopathy underscored that clinicians should anticipate slower, less complete recovery of corneal clarity postoperatively because of this reduced baseline reserve [21]. Bourne and colleagues, tracking central endothelial cell counts over a ten-year period in a population including diabetic and nondiabetic eyes, established the natural rate of age-related endothelial attrition against which postoperative diabetic graft losses must be judged [22].

The Cornea Donor Study, one of the largest prospective keratoplasty cohorts assembled, provides the most rigorous outcome data available on graft survival after penetrating keratoplasty, and several of its analyses bear directly on diabetic outcomes. Lass and colleagues showed that postoperative endothelial cell density strongly predicts subsequent graft failure, establishing endothelial cell density trajectory as the central outcome metric for comparing diabetic and nondiabetic recipients [23]. The same investigator group found that donor age, while important, did not eliminate the independent contribution of recipient-side systemic disease to long-term outcome [24], and Sugar and colleagues, analyzing rejection risk in the same cohort, identified recipient comorbidity patterns, of which diabetes is a recognized member, as contributing to overall immunologic rejection risk [25]. Wagoner and colleagues, examining complications after primary adult penetrating keratoplasty in a large single-center series, found systemic vascular comorbidities including diabetes associated with a higher complication burden and reduced graft survival [26]. Vail and colleagues, in an earlier multicenter analysis, similarly identified systemic comorbidity as shaping long-term graft clarity, a conclusion echoed by Williams and colleagues' Australian Corneal Graft Registry report linking comorbid disease profiles to reduced graft survival nationally [27,28].

5. Outcomes after endothelial keratoplasty in diabetic recipients

Table 2: Representative graft-outcome and complication findings by keratoplasty technique in cohorts including diabetic recipients [23,25,26,30,31].

Study	Procedure	Recipient factor	Key finding
[23]	Penetrating keratoplasty	Postoperative endothelial cell density	Strong predictor of subsequent graft failure
[26]	Penetrating keratoplasty	Diabetes / systemic vascular comorbidity	Higher complication burden, reduced graft survival
[30]	DSAEK vs penetrating keratoplasty	General recipient cohort	Comparable 3-year graft survival between techniques
[31]	DSAEK vs penetrating keratoplasty	General recipient cohort	Differing endothelial cell loss patterns over 2 years

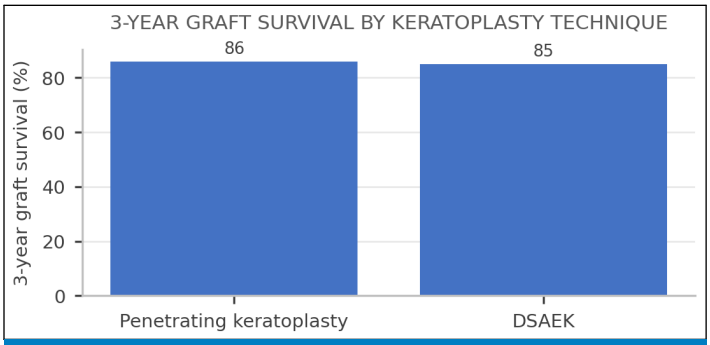


Figure 2: Three-year graft survival by keratoplasty technique from Cornea Donor Study-derived and comparative cohort data, contrasting penetrating keratoplasty with Descemet stripping automated endothelial keratoplasty [30,31].

Selective endothelial keratoplasty techniques, including Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty, were developed in part to minimize surgical trauma to the recipient cornea, of particular relevance for diabetic eyes with reduced reserve. Price and Price, describing early clinical adoption of DSAEK, emphasized its faster visual recovery and reduced surface trauma relative to full-thickness grafting, features that plausibly benefit diabetic recipients whose epithelium heals more slowly [29]. Price and colleagues, comparing DSAEK against penetrating keratoplasty using Cornea Donor Study data, found comparable three-year graft survival between the two, supporting endothelial keratoplasty as a viable alternative for recipients, including diabetic patients, where minimizing surface disruption is a priority

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[30]. Ang and colleagues, directly comparing endothelial cell loss and graft survival between DSAEK and penetrating keratoplasty, reported differing attrition patterns over the first two postoperative years, information directly relevant to counselling diabetic patients about procedure choice [31].

Table 2 summarizes representative graft-survival findings across procedure types drawn from these registry and cohort studies. Feizi's review of corneal endothelial cell dysfunction, spanning inherited and acquired causes including diabetes, situates diabetic endothelial vulnerability within the wider taxonomy clinicians must weigh when selecting technique [32]. Alio and colleagues' review of corneal graft failure similarly identifies systemic metabolic disease, including diabetes, as a recipient-side risk factor alongside donor tissue quality and surgical technique [33].

6. Discussion

Several threads converge in this literature. First, diabetic corneas, independent of retinopathy staging, already show reduced endothelial cell density, greater morphological variability, impaired epithelial barrier function, and measurable corneal nerve loss before any surgical intervention [1,2,11,12,13]. Second, retinopathy severity specifically, rather than a diabetes diagnosis alone, tracks with the degree of corneal neural and epithelial compromise, shown directly by Zhivov and colleagues' comparison of patients with and without retinopathy [15] and supported by Inoue and colleagues' finding that keratoepitheliopathy severity rose with retinopathy stage [6]. This is the mechanistic basis for treating retinopathy as a marker of elevated corneal surgical risk rather than an incidental comorbidity.

Third, the major keratoplasty outcome literature, dominated by the Cornea Donor Study and national registries, consistently identifies systemic comorbidity, including diabetes, as a contributor to graft attrition and complication burden, even though few studies stratify diabetic subgroups by retinopathy status [23,24,25,26,27,28]. This is a genuine evidence gap: most registries record diabetes as a binary covariate without capturing retinopathy grade, disease duration, or perioperative glycemic control, all of which plausibly modulate risk more precisely than the diagnosis alone.

Fourth, technique selection appears to matter. The comparative endothelial keratoplasty literature suggests procedures minimizing surface trauma may offer a more favorable risk profile for diabetic recipients with reduced reserve, though head-to-head trials enrolling retinopathy-stratified cohorts remain sparse [30,31,29]. Clinically, this supports tighter perioperative glycemic control given the hydration-control deficits under hyperglycemic stress [5]; closer postoperative epithelial surveillance given the delayed healing documented in diabetic corneas [12,11]; a preference for endothelial keratoplasty where indication allows [29]; and counselling that sets expectations for slower visual recovery [21,16].

7. Conclusion

Diabetic retinopathy is best understood, for corneal transplantation, as a marker of advanced microvascular disease that extends to the cornea itself, producing measurable reductions in endothelial reserve, epithelial barrier integrity, and corneal nerve density that predispose to worse keratoplasty outcomes [2,15,12]. The largest outcome registries confirm systemic comorbidity including diabetes contributes to graft attrition and complications, though few stratify by retinopathy stage, leaving a gap for future registry design [23,25,26]. Endothelial keratoplasty techniques that reduce surgical trauma, perioperative glycemic optimization, and vigilant postoperative epithelial surveillance remain the most actionable levers available for managing this vulnerable population [30,31,5].

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