



Research Article

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Relationship between Preoperative Corneal Thickness and Postoperative Visual Outcomes after Posterior Lamellar Corneal Transplant

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Abstract

Purpose: To evaluate the impact of preoperative corneal thickness on visual outcomes following Descemet's stripping endothelial keratoplasty (DSAEK) or Descemet membrane endothelial keratoplasty (DMEK).

Methods: This retrospective, observational study included patients aged > 18 years that underwent a posterior lamellar graft surgery (DSAEK or DMEK) for Fuchs dystrophy, pseudophakic endothelial decompensation or other endothelial dysfunction from October 2013 to November 2016. Exclusion criteria were the technical inability of preoperative CCT measurement, a history of penetrating keratoplasty in the study eye, the need for a penetrating keratoplasty following endothelial graft failure, preexisting stromal scarring before surgery (clinically assessed by the slit-lamp exam) and severe postoperative complications resulting in unquantifiable visual acuity. Visual acuity, central corneal thickness (CCT) and graft thickness were measured preoperatively and at postoperative day 7 and months 1, 3 and 6.

Results: Forty-seven eyes (40 patients) were included in the final analysis. No significant association was observed between preoperative CCT and visual acuity at any postoperative time up to month 6 ($r = 0.01$; $p = 0.94$ at month 6). Preoperative CCT showed no association with visual acuity gain at any time up to month 6 ($r = -0.02$; $p = 0.91$ at month 6).

Conclusion: Preoperative CCT does not predict the visual results achievable at 6 months after DSAEK or DMEK.

Keywords

Descemet's stripping endothelial keratoplasty; Corneal Transplant; Descemet membrane endothelial keratoplasty; Posterior lamellar grafts

Introduction

The recent development of the posterior lamellar graft-based techniques Descemet's stripping endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK) has

revolutionized the care of patients with endothelial dysfunction. The performance of such posterior lamellar grafts has grown in popularity in the US, increasing from less than 5% of all corneal grafts in 2005 to more than 50% in 2015 [1-3]. The trend has been similar in Europe. Posterior lamellar grafts represent a significant advancement because they eliminate the risk of complications associated with the use of sutures in penetrating keratoplasty, preserve corneal innervation, limit ocular surface's complications, maintain corneal structural integrity, hasten visual recovery and produce more predictable outcomes [1,4,5].

Posterior lamellar grafts are indicated in patients with pseudophakic bullous keratopathy or Fuchs dystrophy who require additional endothelial support and improved visual outcomes – a stage at which patients typically report notable visual loss and discomfort, especially when reading or driving [1].

Predictors of improved visual recovery following endothelial transplantation have been identified in the literature. They include preoperative visual acuity [6], young recipient age [7], and lack of ocular comorbidity, such as retinal pathology and amblyopia [1]. Predictors of poor postoperative visual outcomes are the presence of preoperative stromal scarring and prolonged preoperative corneal edema [8]. DSAEK graft thickness has been proposed as a potential influencer of postoperative outcomes; however, some authors have reported a beneficial effect of a thinner graft on visual acuity [9-12], while others have identified no significant relationship between graft thickness and visual outcomes [13-15]. In contrast to DSAEK, research suggests that DMEK achieves better visual results and at an earlier postoperative stage [6].

At present, there is little objective data available for guiding the treatment decisions that ophthalmic surgeons should make for patients with endothelial decompensation, including the best time to offer surgery. While it can be argued that undergoing surgery at an early disease stage produces better results and better preserves vision, this needs to be balanced with the risk of exposing a patient who is not overly troubled by loss of visual acuity to complications, such as graft detachment, which can lead to graft rejection, infection and a need for additional surgery.

Given that preoperative central corneal thickness (CCT) is an easy-to-measure factor that changes with endothelial disease stage, close assessment of the relationship between preoperative CCT and visual outcomes in endothelial dysfunction patients treated with DSAEK or DMEK may reveal vital information on how to best determine patient need for surgical intervention. Corneal thickness varies between individuals, following a normal distribution with a large standard deviation, with an average of 530 ± 29 microns in optical pachymetry and 544 ± 34 microns in ultrasonic pachymetry [16,17]. However, its direct link with corneal edema arising from endothelial dysfunction, and the ease with which it can be noninvasively measured routinely before surgery makes it an interesting variable to study.

Few published studies have focused on the efficacy of preoperative CCT as a marker of disease severity and as a predictor of visual recovery. This study was, therefore, designed to assess the impact of preoperative CCT on the final postoperative visual results achieved

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following endothelial transplant via DSAEK or DMEK. As a preliminary study, any trends identified will require substantiation via additional prospective studies with more precise measures of preoperative CCT.

Material and Methods

This retrospective, single-center observational study was conducted from October 2013 to November 2016. Study approval was obtained from the local ethics committee and was performed in keeping with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to study commencement.

Inclusion criteria were patients aged 18 or over that underwent a posterior lamellar graft surgery (DSAEK or DMEK) for Fuchs dystrophy, pseudophakic bullous decompensation or other endothelial dysfunction between October 2013 and November 2016. The surgery was performed by the same surgeon. An available measurement of preoperative CCT with a non-contacting ultrasonic pachymeter (Tono pachymeter NT-530P, Nidek Co, Gamagori Aichi, Japan) was needed in the month before surgery.

Exclusion criteria were a history of penetrating keratoplasty in the indicated eye, the technical inability of preoperative CCT measurement, the need for a penetrating keratoplasty following endothelial graft failure, preexisting stromal scarring before surgery clinically assessed by the slit-lamp exam and severe postoperative complications resulting in unquantifiable visual acuity (retinal detachment, central retinal vein occlusion, macular hematoma and severe age-related macular degeneration [AMD]). We suppose that the key cause of technical inability of preoperative CCT measurement was a cornea that was too thick or had irregularities across the corneal surface, ending in a technical impossibility to measure CCT with our device.

A register of all patients that underwent DMEK or DSAEK during the period was available, allowing the selection of patients matching inclusion and exclusion criteria. All the data were collected retrospectively in the patients' medical records.

In all, 47 eyes of 40 patients were involved in the final data analysis after exclusion of those with the aforementioned exclusion criteria.

The primary objective of this study was to identify if any relationship between preoperative CCT and postoperative month 6 visual acuity exists in patients who have undergone posterior lamellar grafting (DSAEK or DMEK). This objective was based on the premise that a thicker preoperative cornea may lead to poorer postoperative visual outcomes due to the existence of edema-induced advanced corneal stroma alterations.

Secondary objectives included: investigation of any relationship between preoperative CCTs, and preoperative and postoperative visual acuity at postoperative day 7, and month 1 and 3; assessment of the relationship between preoperative and postoperative CCT measured by optical coherence tomography (OCT) at postoperative day 7 and months 1, 3 and 6.

The following data were collected: patient age and gender, date of surgery, crystalline lens status (phakic, pseudophakic or aphakic), eye operated on, preoperative corneal thickness measured using a non-contacting ultrasonic pachymeter (Tono pachymeter NT-530P, Nidek Co, Gamagori Aichi, Japan) surgery duration, DSAEK or DMEK surgery (and if combined with phacoemulsification),

patient history of previous endothelial grafting on the study eye, time since last transplant, type of graft (DMEK or DSAEK), reason for transplant, graft detachment, number of rebubbings, graft rejection, comorbidities, best corrected visual acuity (BCVA) and postoperative improvement in visual acuity. Visual acuity, CCT and graft thickness measurements were taken preoperatively and at postoperative day 7 and months 1, 3 and 6.

Surgical technique

All surgeries were performed by a single surgeon under local or general anesthesia.

Unprepared grafts required for the procedure were obtained from the tissue bank of Besancon or Nancy (France). A three-stage wash using iodized povidone (Betadine 5%, Ocular solution, Meda Pharma, Paris, France) was performed on the operative site.

DSAEK

The surgery was performed according to the standardized technique described by Busin et al. [11]. The graft was prepared in the operating room and positioned on an artificial anterior chamber (MORIA SA, Anthony, France). The total thickness of the graft was measured using ultrasonic pachymetry (Handy Pachymeter SP-100 TOMEY Corporation, Nagoya, Japan). Each graft was thinned using a microkeratome (CBm turbine MORIA SA Anthony, France) to obtain a posterior endothelial lamellar graft (thickness 100 to 150µm) and trephined to produce a final 8mm diameter section. The patient's endothelial Descemet's membrane (EDM) was then removed under an air bubble using an inverted hook (Single use PRICE hook #17302, MORIA SA Anthony, France). While under constant irrigation, the graft was carefully placed on a Busin spatula (Single-Use Busin Spatula #17300, MORIA SA Anthony,

France) and introduced into the anterior chamber using the Busin forceps (Single use Busin forceps 23G #17301, MORIA SA Anthony, France). It was then positioned centrally on the posterior surface of the recipient cornea.

DMEK

The graft was trephined to produce a final section (8mm diameter) using Hanna punch (Moria One® Disposable Corneal Vacuum punch #17200, MORIA SA Anthony, France). The EDM was manually stripped from the donor corneal stroma using monofilament tying forceps (MMSU1210, Malosa Medical®) and the graft was colored using trypan blue ophthalmic solution (Visionblue®, VBL-10-S-USA, Dutch Ophtalmic, DORC®, USA). The patient's EDM was removed under an air bubble using the same type of inverted hook as used for DSAEK. The graft was injected into the patient's eye using a customised injector (DMEK disposable surgical kit, 50.2200, Dutch Ophtalmic, DORC®, USA) and the EDM was centrally positioned via external manipulation.

Phacoemulsification

Some patients underwent phacoemulsification (Stellaris PC, Bausch and Lomb, Aliso Viejo, CA, USA; incision 2.2mm) with placement of an intraocular lens (IOL; CT ASPHINA 409m, Carl Zeiss Meditec, Marly-le-roi, France) in the capsular bag.

End of procedures

After injection of a sterile air bubble into the anterior chamber in order to fix the endothelial graft (DSAEK or DMEK), a single corneal

suture was performed using nylon thread 10/0. All patients received an anterior chamber injection of 0.1mL cefuroxime (Aprokam sol inj 10fl/50mg, THEA LAB, Clermont-Ferrand, France) and a subconjunctival injection of dexamethasone and gentamycin before applying an antibiotic and corticosteroid ointment (Dexamethasone and Oxytetracyclin; Sterdex®, THEA LAB, Clermont-Ferrand, France). Patients were told to adopt a supine position for the first 12 hours after surgery and early postoperative clinical evaluations were performed on postoperative day 1. Patients also commenced dexamethasone and neomycine / polymyxin B eyedrops (Maxidrol®, Alcon) four times daily on postoperative day 1 and twice daily vitamin ointment was prescribed.

Statistical analysis

Statistical analysis was performed with R statistical software, version 3.4.0. A p-value of less than 0.05 was defined as statistically significant. The statistical relationship between preoperative corneal thickness, pre- and postoperative visual acuity, and postoperative CCT was analyzed via Spearman’s correlation test. Comparison of eyes with measurable pachymetry versus those with unmeasurable pachymetry was performed using the Wilcoxon test for quantitative variables and the Fisher exact test for qualitative variables.

Results

Forty-seven eyes of 40 patients were involved in the final data analysis. The clinical characteristics of patients are summarized in Table 1. The only significant difference between both groups is a higher number of second grafts in the DSAEK group (36% versus 5%, p=0.03). DSAEK remains indeed the first choice technique in case of prior endothelial graft failure, because DSAEK surgical technique is more reproducible with in most cases a simpler follow-up period than DMEK.

As shown in Table 2 (including all patients), no significant association was observed between preoperative CCT and postoperative month 6 visual acuity (r=0.01; p=0.94). No significant association was also observed between preoperative CCT and preoperative visual acuity (r=0.03, p=0.82) or postoperative visual acuity at day 7, and months 1 and 3, with respective correlation coefficients of 0.28 (p=0.1), 0.09 (p=0.54) and -0.04 (p=0.81). Preoperative pachymetry did not influence gains in visual acuity, with coefficients of 0.26 (p=0.14) at

postoperative day 7, 0.12 (p=0.4) at month 1, -0.02 (p=0.92) at month 3 and -0.02 (p=0.91) at month 6.

There was no noted correlation between preoperative and postoperative CCT at any postoperative time. Specifically, the correlation coefficient was -0.14 (p=0.41) at postoperative day 7, 0.25 (p=0.17) at month 1, 0.17 (p=0.39) at month 3 and 0.03 (p=0.88) at month 6.

Pre- and postoperative BCVA, BCVA variation and corneal thickness in both groups are compared in Table 3. Preoperative BCVA seems to be better in DMEK group (0.7 logMAR ± 0.2) than in DSAEK group (0.9 logMAR ± 0.4), but the difference is not significant (p=0.14). There seems to be a trend with better visual outcomes for the DMEK group, but the difference is not significant (p>0.05 at any time). For example at 3 months postoperative, BCVA is 0.3 logMAR ± 0.3 in the DMEK group versus 0.5 logMAR ± 0.3 in the DSAEK group (p=0.06). The gain of visual acuity is the same in both groups at any time. For example at 6 months postoperative, delta BCVA is -0.4 logMAR ± 0.5 in DMEK group versus -0.4 logMAR ± 0.3 in DSAEK group (p=0.92). Mean preoperative CCT is the same in both groups (625 µm ± 56 in DMEK group versus 620 µm ± 57 in DSAEK group, p=0.76).

The analysis was performed separately in the group of patients that underwent DMEK (Table 4) and in the group of patients that underwent DSAEK (Table 5). No correlation either between preoperative pachymetry and the different parameters was observed at any time. The only significant result concerns the DSAEK group where a significant correlation between preoperative CCT and BCVA D7 has been observed (r=0.48, p=0.03). It means that the thicker the cornea is preoperatively, the lower is the BCVA at postoperative day 7. Anyway, this correlation remains weak (r coefficient between 0.4-0.6) and is most likely due to chance, according to all our results. Moreover, this correlation does not persist after postoperative day 7, which is why it has a weak clinical impact.

Evolution of postoperative graft thickness in DSAEK group is available in Table 6.

Discussion

This retrospective single-center observational study of 47 eyes of 40 patients undergoing endothelial transplant via DSAEK or DMEK

Table 1: Initial characteristics of patients.

	DMEK (n=19)	DSAEK (n=28)	p
Side	Right 42% Left 58%	Right 54% Left 46%	0.56
Lens	Phakic 26% Pseudophakic 74%	Phakic 11% Pseudophakic 89%	0.24
Mean age ± SD	73.8 ± 9.6	74.9 ± 9.3	0.69
Sex	F 58% M 42%	F 71% M 29%	0.37
Combined surgery (graft+phacoemulsification)	Uncombined 74% Combined 26%	Uncombined 89% Combined 11%	0.24
Previous endothelial graft	No previous graft 95% Second graft 5%	No previous graft 64% Second graft 36%	0.03
Comorbidities	9%	14%	0.7
Graft detachment	32%	18%	0.31
Indication	Fuchs: 84% Pseudophakic decompensation : 11% Other: 5%	Fuchs: 82% Pseudophakic decompensation : 18% Other: 0%	0.4
Rejection	0%	4%	0.99
Graft Thickness (mean ± SD)	178.5 ± 39.5	-	

Table 2: Relationship between preoperative corneal thickness and different parameters including pre-, postoperative best corrected visual acuity (BCVA), visual acuity gain and postoperative corneal thickness (all patients).

	Mean values ± SD	N	r	p
Preoperative BCVA	0.8 ± 0.3	47	0.03	0.82
BCVA D7	1.1 ± 0.5	35	0.28	0.1
BCVA M1	0.7 ± 0.5	47	0.09	0.54
BCVA M3	0.4 ± 0.3	40	-0.04	0.81
BCVA M6	0.3 ± 0.4	34	0.01	0.94
delta BCVA D7	0.3 ± 0.6	35	0.26	0.14
delta BCVA M1	-0.1 ± 0.5	47	0.12	0.4
delta BCVA M3	-0.3 ± 0.3	40	-0.02	0.92
delta BCVA M6	-0.4 ± 0.4	34	-0.02	0.91
Corneal thickness D7	697 ± 109	36	-0.14	0.41
Corneal thickness M1	573 ± 97	32	0.25	0.17
Corneal thickness M3	546 ± 72	27	0.17	0.39
Corneal thickness M6	558 ± 87	24	0.03	0.88

Note: BCVA=best corrected visual acuity (logMAR); D7=seven postoperative days, M1=a postoperative months, M3=3 postoperative months M6=6 months postoperatively; delta BCVA=visual acuity gain on a logarithmic scale at each postoperative day compared to the preoperative visual acuity; corneal thickness measured at the same times with optical coherence tomography (µm), N=number of available data; r=correlation coefficient between the preoperative corneal thickness and the different parameters.

Table 3: Comparison between DMEK and DSAEK group outcomes concerning BCVA and corneal thickness.

	DMEK (n=19)	DSAEK (n=28)	p
Preoperative BCVA	0.7 ± 0.2	0.9 ± 0.4	0.14
BCVA D7	1.0 ± 0.5	1.3 ± 0.5	0.08
BCVA M1	0.5 ± 0.5	0.8 ± 0.5	0.08
BCVA M3	0.3 ± 0.3	0.5 ± 0.3	0.06
BCVA M6	0.3 ± 0.5	0.4 ± 0.2	0.66
delta BCVA D7	0.3 ± 0.5	0.4 ± 0.7	0.51
delta BCVA M1	-0.2 ± 0.4	-0.1 ± 0.6	0.54
delta BCVA M3	-0.4 ± 0.3	-0.3 ± 0.3	0.36
delta BCVA M6	-0.4 ± 0.5	-0.4 ± 0.3	0.92
Preoperative CCT (µm)	625 ± 56	620 ± 57	0.76
Corneal thickness D7	664 ± 110	734 ± 98	0.05
Corneal thickness M1	569 ± 77	578 ± 116	0.78
Corneal thickness M3	533 ± 75	562 ± 66	0.31
Corneal thickness M6	525 ± 52	588 ± 101	0.08

Table 4: Relationship between preoperative corneal thickness and the different parameters (DMEK only).

	Mean values ± SD	N	r	p
Preoperative BCVA	0.7 ± 0.2	19	0.25	0.3
BCVA D7	1.0 ± 0.5	15	0.18	0.52
BCVA M1	0.5 ± 0.5	19	-0.03	0.9
BCVA M3	0.3 ± 0.3	18	-0.22	0.39
BCVA M6	0.3 ± 0.5	14	-0.19	0.51
delta BCVA D7	0.3 ± 0.5	15	0.06	0.82
delta BCVA M1	-0.2 ± 0.4	19	-0.08	0.75
delta BCVA M3	-0.4 ± 0.3	18	-0.2	0.43
delta BCVA M6	-0.4 ± 0.5	14	-0.22	0.44
Corneal thickness D7	664 ± 110	19	-0.19	0.44
Corneal thickness M1	569 ± 77	16	0.23	0.4
Corneal thickness M3	533 ± 75	15	0.13	0.65
Corneal thickness M6	525 ± 52	11	-0.03	0.95

revealed no correlation between preoperative pachymetry and postoperative visual results.

Table 5: Relationship between preoperative corneal thickness and the different parameters (DSAEK only).

	Mean values ± SD	N	r	p
Preoperative BCVA	0.9 ± 0.4	28	-0.09	0.64
BCVA D7	1.3 ± 0.5	20	0.48	0.03
BCVA M1	0.8 ± 0.5	28	0.19	0.33
BCVA M3	0.5 ± 0.3	22	0.07	0.77
BCVA M6	0.4 ± 0.2	20	0.12	0.6
delta BCVA D7	0.4 ± 0.7	20	0.42	0.06
delta BCVA M1	-0.1 ± 0.6	28	0.2	0.3
delta BCVA M3	-0.3 ± 0.3	22	0.06	0.78
delta BCVA M6	-0.4 ± 0.3	20	0.1	0.68
Corneal thickness D7	734 ± 98	17	-0.16	0.55
Corneal thickness M1	578 ± 116	16	0.21	0.44
Corneal thickness M3	562 ± 66	12	0.17	0.19
Corneal thickness M6	588 ± 101	13	0.1	0.75

Table 6: Evolution of postoperative graft thickness (µm) in the DSAEK group (N=number of available data).

	Mean values ± SD	N
Graft thickness D7	156 ± 97	15
Graft thickness M1	101 ± 64	14
Graft thickness M3	112 ± 66	13
Graft thickness M6	102 ± 66	12
BCVA M6	0.4 ± 0.2	20

This lack of correlation is somewhat surprising because the presence of prolonged corneal edema can lead to structural alteration of the anterior cornea, resulting in optical aberrations that limit visual recovery after surgery [16]. The role of endothelial dysfunction duration and the resulting chronic edema remains controversial. Some authors like Yamaguchi et al have reported no correlation between the length of corneal edema in pseudophakic bullous keratopathy and postoperative visual results [17]. In contrast, others have demonstrated a lower rate of postoperative stromal fibrosis in patients with preoperative edema lasting less than 12 months [18].

Nonetheless, the current study is not alone in its observation of no correlation at any time between corneal thickness and visual acuity. Shinton and al's analysis of 51 eyes undergoing Descemet's stripping endothelial keratoplasty (DSAEK) found no clear association between total corneal thickness and visual acuity following DSAEK [16]. In Ahmed and al's study, no correlation between corneal or host thickness and visual acuity was found at 3, 6 or 12 months, but the correlation between preoperative corneal thickness and postoperative visual acuity has not been screened [14]. On the contrary, Pogorelov et al reported a gradual decrease in CCT and graft thickness, with significant correlation between CCT and visual acuity at 6 months postoperatively [10]. Gradual reduction of CCT has been found to be a determiner of the progressive visual recovery observed up to 5 years after surgery, influencing the postoperative decline in haze and aberrations that patients can continue to experience for years after surgery [19-21]. It also appears that improvement in visual acuity seen 1 to 12 months after DSAEK is influenced by other factors that affect light scattering, but a better understanding of cell and extracellular matrix changes in the subepithelial region and graft-host interface is needed to fully identify the factors that limit visual recovery after endothelial transplant [22]. This indicates that endothelial keratoplasty performed as a first line approach, even in the presence of stromal alterations and significant visual loss, can achieve some degree of visual acuity recovery. Higher powered studies are now required to confirm this theory.

In our study, preoperative BCVA seems to be better in DMEK group ($0.7 \log\text{MAR} \pm 0.2$) than in DSAEK group ($0.9 \log\text{MAR} \pm 0.4$, $p=0.14$). This suggests that DMEK will be more often performed than DSAEK in patients with the best preoperative BCVA in our center, allowing a potential of better visual outcomes. Indeed, there seems to be a trend with better visual outcomes for the DMEK group, but the difference is not significant, probably because of a lack of power of our study. Better and faster visual outcomes with DMEK have been described in literature [23-25]. Tourtas reported visual acuity increasing from $0.70 \pm 0.48 \log\text{MAR}$ to $0.17 \pm 0.12 \log\text{MAR}$ 6 months after DMEK and from $0.75 \pm 0.32 \log\text{MAR}$ to $0.36 \pm 0.15 \log\text{MAR}$ 6 months after DSAEK ($p<0.001$). In our study the postoperative results are a little bit lower for DMEK, increasing from $0.7 \log\text{MAR} \pm 0.2$ to $0.3 \log\text{MAR} \pm 0.5$ at 6 months postoperative. They are comparable for DSAEK (despite the lower preoperative BCVA of our patients), increasing from $0.9 \log\text{MAR} \pm 0.4$ to $0.4 \log\text{MAR} \pm 0.2$ after DSAEK [19].

Concerning the gain of visual acuity, there is no significant difference between both groups at any time postoperative, suggesting that patients of both groups are able to improve their visual acuity in the same proportion, regardless of their preoperative BCVA and of the endothelial graft technique that is performed (DSAEK or DMEK).

Mean preoperative CCT is the same in both groups ($624.5 \mu\text{m} \pm 56$ [550-754] in DMEK versus $619.2 \mu\text{m} \pm 57$ [529-731] in DSAEK, $p = 0.76$). It confirms that preoperative CCT is not correlated with preoperative visual acuity (which is better in DMEK group), and that it must not be considered as a valuable parameter to evaluate the severity of the endothelial dysfunction. We can consider that preoperative pachymetry has no place in the surgical decision.

We did not especially study the relationship between DSAEK graft thickness and postoperative BCVA in our group of patients because its impact on postoperative outcomes still remains unanswered by suitably powered, prospective trials. Some authors have reported a beneficial effect of a thinner graft on visual acuity [9-12], while others have identified no significant relationship between graft thickness and visual outcomes [13-16]. In a series of 418 eyes, Terry et al found that preoperative graft thickness may have a small effect on visual outcome in the extremes of thickness, but not in the common range of 100 to 200 μm (in our study the mean graft thickness was $178.5 \mu\text{m} \pm 39.5$). Donor thickness has only a tenuous relationship with visual outcome, accounting for only 5% of the variance in vision between patients, and should play a minimal role in surgical planning [26].

We do not know if the measurement of preoperative corneal thickness prior to endothelial transplantation is performed routinely or not by corneal surgeons, even if this data is often available in the different studies. In Ahmed et al's study, the preoperative corneal thickness was measured with both confocal microscopy and ultrasonic pachometry, which gave different results ($610 \pm 50 \mu\text{m}$ with confocal microscopy versus $659 \pm 50 \mu\text{m}$, $p<0.001$) [14]. Li and al also reported the preoperative pachymetry of their patients in their prospective study. The authors don't specify if they systematically perform a preoperative pachymetry in clinical routine [20]. In some other studies, we find no mention of preoperative corneal thickness measurement [9,11,27,28]. Despite the fact that the preoperative pachymetry is easy and quick to perform, it seems that it is not performed routinely by every corneal surgeon in his practice.

Existing literature suggests that corneal pathology is preceded by structural alterations, especially in the anterior portion of the

cornea. Disorganization of collagen [22], keratocyte degeneration [29,30], stromal scarring [31], and subepithelial fibrosis [6], have all been identified as changes seen prior to visual decline in patients with endothelial dysfunction. Such changes may cause higher order aberrations, limit visual recovery and produce a visual "haze" that can persist beyond surgery [27,28,32]. Baratz et al. have reported that in most cases, this "haze" gradually improves after surgery, especially in young patients, and is affected by the degree of subepithelial fibrosis that arises from the graft-host interface [33]. Patel et al. have also reported that anterior cornea higher order aberrations (HOAs) are more prevalent among patients with Fuchs dystrophy than in healthy controls, and remain more prevalent for 2 years after DSAEK [34]. But this finding is not limited to DSAEK as research has also shown that anterior and posterior HOAs also persist after DMEK [35]. Alomar et al. studied the structural changes thought to precede clinical corneal pathology as well. Their findings suggested a need for pre- and postoperative corneal assessment when the cornea appears clinically normal, but histological alterations are suspected [35].

The key limitations of this study are its retrospective nature and its small size. The reliability of the measurement of corneal thickness (using noncontact ultrasonic pachymetry) can also be criticized. Nevertheless, the ultrasound pachymetry still remains the gold standard in CCT measurement [36]. However, the objective of this study was to identify a single variable that could be easily measured in a clinic setting and used to then determine the best time for surgical intervention and obtain an idea of a patient's visual prognosis. Despite the outlined study limitations, the results strongly suggest that preoperative CCT is not an ideal measurement for providing this information to surgeons.

Conclusion

The findings of this observational study do not demonstrate a link between preoperative CCT and visual results at any time up to 6 months after an endothelial transplant ($r=0.01$, $p=0.94$). This suggests that while CCT is an easy measurement to capture during routine ophthalmic consultations, it is not suitable for guiding a surgeon on the best time to offer surgical intervention to patients with endothelial dysfunction or for predicting the visual prognosis of a patient.

Our observations are in line with those of published literature, which suggest that it may be the presence of histological lesions related to the development of endothelial pathology that has a greater influence on the visual recovery of patients than CCT [28].

Further study focused on the relationship between the histology of eyes with endothelial dysfunction and the visual outcomes of patients is now required. As studies have already shown that the use of in vivo confocal microscopy facilitates the identification of the precise mechanisms underlying the histologic changes that influence postoperative results,[37-40] further exploration of this field using in vivo confocal microscopy may provide much needed answers about endothelial dysfunction and the histological changes associated with corneal pathologies.

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