Original Article

Association between Endothelial Cell Density and Corneal Thickness in Transplanted versus Normal Corneas: A Retrospective Cohort Study

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Objective: To investigate the association between endothelial cell density (ECD) and corneal thickness (CT) in patients with clear corneal grafts after penetrating keratoplasty (PKP) and compare the results with normal corneas.

Materials and Methods: In the retrospective cohort study, the authors reviewed the medical charts of patients who underwent a PKP and whose grafts remained clear. Abnormal grafts such as those with irregular surfaces, central scarring, secondary guttae, and graft edema were excluded. The demographic data, ECDs, and CTs were recorded and compared with those of normal corneas. The ECDs were measured using corneal microscopy, and the CTs were measured by optical coherence tomography.

Results: Ninety-six eyes treated with PKP and 86 normal eyes were enrolled. One hundred four women and 78 men were included with a mean age of 64.0±16.7 and 68.6±14.3 years in the PKP group and normal group, respectively. The mean time after PKP was 3.7±3.1 years (range 0.3 to 12.6 years). The mean CTs did not differ between the two groups, but the mean ECD in the PKP group was significantly less than in the normal group (1,109.2 versus 1,905.4 cells/mm^2, $p<0.001$). The degree of polymegathism was significantly higher in the PKP group, while the degree of pleomorphism was significantly ($p<0.001$) lower compared to the normal group.

Conclusion: When comparing eyes with the same CTs, those treated with PKP had lower ECDs, more polymegathism, and less pleomorphism than normal corneas.

Trial registration: Thai Clinical Trials Registry, TCTR20170316001

Keywords: Corneal thickness, Endothelium, Endothelial cell density, Penetrating keratoplasty, Pleomorphism, Polymegathism

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The corneal endothelium is a key element in the maintenance of corneal transparency and clarity. The tissue acts both as an active pump to hydrate the stroma and as a special barrier to prevent fluid influx from the anterior chamber while allowing entrance of nutrients from the aqueous humor into the cornea, a process known as the pump-leak mechanism(1,2). The normal endothelial cell density (ECD) values range from 1,500 to 3,500 cells/mm^2(3) or approximately 2,400 cells/mm^2, a value that declines with age. When the ECD decreases to less than 1,000 cells/mm^2, the pumping function generally is insufficient and leads to stromal collagen derangement, increasing thickness, and decreasing transparency(4).

In penetrating keratoplasty (PKP), the ECD is essential for maintaining graft clarity and prolonging graft survival post-operatively(5). The initial ECD values of donor corneas from eye banks range from 2,300 to 3,300 cells/mm^2(2,5), and those values gradually decline every year to approximately 50%

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by three to six years post-operatively[2,6-8]. However, there is no cut-off value at which the corneal clarity can be maintained after PKP[4,6]. Several studies have reported clear grafts with very low ECDs[4,6,8,9].

The aim of the current study was to investigate the association between ECD and corneal thickness (CT) in patients who had normal corneal clarity after underwent PKP versus patients with normal corneas.

Materials and Methods

The present study was a retrospective cohort medical chart review of the patients who underwent PKP and whose grafts remained clear compared with other patients who had normal corneas and did not undergo any previous refractive or intraocular surgery. The present study was performed at the Department of Ophthalmology, Faculty of Medicine, Siriraj Hospital, Mahidol University between January 2008 and December 2011. The Committee for the Protection of Human Participants in Research at the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand (SiEC number, 715/2553(EC3)) approved the present study, and was conducted according to the tenets of the Declaration of Helsinki. The trial was registered with the Thai Clinical Trials Registry, identification number 20170316001.

The inclusion criteria for patients who underwent PKP (PKP group) were 18 years or older and clear grafts after PKP, a normal ocular surface, no central scarring, normal intraocular pressure (IOP), ability to cooperate during ECD and CT measurements, and no signs of active graft rejection or inflammation at the time of the examination. For the control group, every fifth patient was selected randomly from the data obtained using a corneal microscopy (Confoscan 4, Nidek Technologies SRL, Gamagori, Japan). The inclusion criteria for this group were 18 years or older, no history of refractive or intraocular surgery, a clear cornea without any corneal diseases, and the availability of complete data obtained using the Visante optical coherence tomography (OCT) (Carl Zeiss Meditec, Dublin, CA, USA) and medical chart history.

The exclusion criteria included age younger than 18 years, abnormal corneas that precluded precise ECD and CT measurements, and the presence of intraocular diseases that could affect the ECD such as high IOP, uveitis, and iridocorneal endothelial syndrome.

Endothelial cell analysis

The corneas were examined using the Confoscan machine and the ECD was measured by fix frame technique. The coefficient of variation (CV) of the cellular area (polymegathism) and the percentage of hexagonal cells (pleomorphism) were evaluated. The measurements were performed from three photographs of the central cornea and then averaged and calculated.

CT measurement

The CT was measured using Visante anterior-segment OCT. Based on the mean CT of 530±31.5 µm from the study of Ueno et al(10), the normal CT range from 499 to 561 µm (mean ± standard deviation). The CTs were classified into three groups: less than 499 µm (below normal), 499 to 561 µm (normal), and over 561 µm (thicker than normal).

Statistical analysis

Statistical analyses were performed using PASW Statistics, version 18.0 (SPSS Inc., Chicago, Ill, USA). The categorical variables were expressed in numbers and percentages, whereas the continuous variables were expressed as the normal distribution, described as the mean, standard deviation, minimal and maximal values, and range, as appropriated. All statistical tests were two-sided, and significance was defined as p-value of less than 0.05. Continuous variables were analyzed between groups using the unpaired t-test (normal distribution) and 95% confidence interval of the mean difference; and Mann-Whitney (non-normal distribution) and categorical variables were analyzed using the Pearson chi-square test. The primary outcome of the present study was corneal ECD of both groups. Since there was no other similar study comparing ECD and CT between different groups, sample size could not be calculated. The authors then estimated the number of each group using 100 eyes to reassure normal distribution of the outcome.

Results

From 100 eyes of each groups, four eyes in the PKP groups and 14 eyes in the control were excluded due to measurement errors or incompletion of data. Therefore, 96 eyes of 95 patients (47 men, 49 women) underwent PKP and 86 eyes of 86 control patients (31 men, 55 women) were included in the present study. The patient demographic data is shown in Table 1.

The mean age of the patients with normal corneas was significantly higher than in the patients who had undergone PKP (68.6±14.3 versus 64.0±16.7 years, respectively). There was no difference in gender

Table 1. Patient demographic data

Characteristic	Group		p-value
	PKP (96 eyes)	Control (86 eyes)	
Age (years)			0.047
Mean±SD	64.0±16.7	68.6±14.3	
Min-max	23 to 96	18 to 90	
Sex (eyes); n (%)			0.099
Male	47 (49.0)	31 (36.0)	
Female	49 (51.0)	55 (64.0)	
Polymegathism (%)			<0.001
Mean±SD	56.3±15.2	46.7±9.9	
Min-max	28.3 to 96.4	33.5 to 75.5	
Pleomorphism (%)			<0.001
Mean±SD	32.4±9.0	42.5±7.8	
Min-max	17.2 to 58.9	22.1 to 56.3	
ECD (μm)			<0.001
Mean±SD	1,109.2±687.8	1,905.4±652.1	
Min-max	294.3 to 3,085.0	412.2 to 3,026.6	
Corneal thickness (μm)			0.086
Mean±SD	517.3±55.5	529.4±38.4	
Min-max	399 to 794	449 to 648	
UCVA (logMAR)			<0.001
Mean±SD	0.80±0.35	0.34±0.32	
Min-max	0.06 to 2	0 to 2	
BCVA (logMAR)			<0.001
Mean±SD	0.55±0.37	0.23±0.26	
Min-max	0 to 2	0 to 2	

SD=standard deviation; BCVA=best-corrected visual acuity; logMAR =logarithm of the minimum angle of resolution; ECD=endothelial cell density; PKP=penetrating keratoplasty; UCVA=uncorrected visual acuity

between the groups. The mean time after PKP was 3.7±3.1 years (range 0.3 to 12.6 years). There was no difference in the CTs between the patients underwent PKP and those with normal corneas (517.3 and 529.4 μm, p=0.086).

Notably, the mean ECD in the PKP group (1,109.2±687.8 cells/mm²) was significantly (p<0.001) less than in the normal group (1,905.4±652.1 cells/mm²). Moreover, the mean polymegathism value in the PKP group was significantly (p<0.001) higher (56.3±15.2 versus 46.7±9.9), while the mean pleomorphism was significantly (p<0.001) lower than in the normal group (32.4±9.0 versus 42.5±7.8) (Table 1).

Regarding the three CT subgroups, the ECD in each subgroup was significantly (p<0.001 for all comparisons) lower in the PKP group than in the normal group (Table 2). The mean CVs in the patients underwent PKP also were abnormal in every CT subgroup (normal CV <0.4). In the patients underwent PKP with a CT of 561 μm or less (thin or normal CT), the mean polymegathism value was significantly (p=0.006, 0.002) higher than in the control group with the same CT (Table 3) and the mean pleomorphism value was significantly (p<0.001) lower than in the control group (Table 4). However, in the subgroup

Table 2. Association between CT and ECD in patients who underwent PKP and normal corneas

CT (μm)	Group	Eyes	ECD Mean±SD	p-value	Mean difference (95% CI)
<499	PKP	39	984.3±542.8	<0.001	877.1 (514.6 to 1,239.6)
	Control	15	1,861.4±716.6		
499 to 561	PKP	39	1,311.7±818.6	<0.001	630.6 (324.5 to 936.8)
	Control	56	1,942.4±594.8		
>561	PKP	18	941.1±571.9	0.001	870.2 (377.2 to 1,363.1)
	Control	15	1,811.2±813.2		

SD=standard deviation; CI=confidence interval; CT=corneal thickness; ECD=endothelial cell density; PKP=penetrating keratoplasty

Table 3. Association between CT and polymegathism in patients who underwent PKP and normal corneas

CT (μm)	Group	n	Polymegathism Mean±SD	p-value	Mean difference (95% CI)
<499	PKP	39	59.1±16.3	0.006	–10.4 (–17.7 to –3.2)
	Control	15	48.7±9.6		
499 to 561	PKP	39	53.6±14.6	0.002	–8.2 (–13.4 to –3.0)
	Control	56	45.4±8.2		
>561	PKP	18	56.0±14.0	0.220	–6.3 (–16.5 to 4.0)
	Control	15	49.7±14.9		

SD=standard deviation; CI=confidence interval; CT=corneal thickness; PKP=penetrating keratoplasty

Table 4. Association between CT and pleomorphism in patients who underwent PKP and normal corneas

CT (μm)	Group	n	Pleomorphism Mean±SD	p-value (t-test)	Mean difference (95% CI)
<499	PKP	39	30.5±8.5	<0.001	9.8 (4.7 to 15.0)
	Control	15	40.4±8.2		
499 to 561	PKP	39	34.1±8.8	<0.001	9.8 (6.4 to 13.2)
	Control	56	43.9±7.0		
>561	PKP	18	32.8±10.2	0.063	6.7 (–0.4 to 13.7)
	Control	15	39.5±9.5		

SD=standard deviation; CI=confidence interval; CT=corneal thickness; PKP=penetrating keratoplasty

Table 5. Characteristics of corneal grafts over time

Parameter	Time after PKP			
	<3 years	3 to <5 years	5 to <10 years	>10 years
Eyes; n (%)	44 (45.8)	23 (24.0)	24 (25.0)	5 (5.2)
ECD (cells/mm^2)				
Mean±SD	1,462.6±722.8	1,024.7±596.0	650.7±346.3	586.4±215.8
Min-max	337.9 to 3,085.0	294.3 to 2,333.0	308.8 to 1,544.2	348.8 to 908.4
Polymegathism (%)				
Mean±SD	50.6±13.5	56.5± 17.3	65.1±12.8	65.5±10.1
Min-max	31.5 to 85.2	28.3 to 96.4	43.6 to 88.9	52.9 to 79.6
Pleomorphism (%)				
Mean±SD	34.7±8.6	33.5±12.2	28.5±5.4	26.7±0.9
Min-max	17.2 to 48.6	20.6 to 58.9	21.5 to 44.5	25.3 to 27.5
Corneal thickness (µm)				
Mean±SD	511.0±63.6	508.7±49.0	529.0±42.8	553.0±57.9
Min-max	399 to 794	435 to 608	471to 640	451 to 592
UCVA (logMAR)				
Mean±SD	0.84±0.34	0.78±0.44	0.74±0.29	0.70±0.34
Min-max	0.06 to 1.60	0.30 to 2.0	0.20 to 1.5	0.18 to 1.00
BCVA (logMAR)				
Mean±SD	0.61±0.37	0.51±0.46	0.49±0.28	0.51±0.29
Min-max	0.00 to 1.60	0.06 to 2.00	0.10 to 0.90	0.06 to 0.80

SD=standard deviation; BCVA=best-corrected visual acuity; ECD=endothelial cell density; PKP=penetrating keratoplasty; UCVA=uncorrected visual acuity; logMAR=logarithm of the minimum angle of resolution

with a thicker cornea (CT >561 µm) after PKP, the mean polymegathism and pleomorphism values did not differ from those in the control group with the same CT.

In the current study, 55% (53/96) of eyes had corneas that remained clear and a ECD of 1,000 cells/mm² or less after PKP as did 15% (13/86) of controls, a difference that reached significance ($p<0.001$). Among corneas with ECDs between 500 and 1,000 cells/mm², 34% (33/96 eyes) and 13% (11/86 eyes) were in the PKP group and control group, respectively ($p<0.001$). The CTs of eyes with ECDs between 500 and 1,000 cells/mm² also were significantly ($p<0.05$) thinner in the PKP group than in the control group (510.6 µm versus 557.6 µm). Moreover, 21% (20/96 eyes) of eyes in the PKP group and 2% (2/86 eyes) of the control eyes had clear corneas and very low ECDs (<500 cells/mm²). However, the numbers of patients with this low ECD and a clear cornea in both groups (20 and 2 eyes, respectively) were too small to demonstrate statistical significance.

Table 5 shows the patient characteristics after PKP patients over time. The mean ECD declined over time, from 1,462.6 cells/mm² during the first three years to 586.4 cells/mm² 10 years post-operatively. Furthermore, the mean polymegathism value increased from about 51 during the first three years to over 65 after 10 years, while the mean pleomorphism decreased from about 35 to about 27 after 10 years.

Discussion

The corneal endothelium is crucial for maintaining corneal transparency via its fluid barrier property and metabolic pumping functions[1]. At birth, normal corneas have an ECD of 6,000 cells/mm², which declines over time to 1,500 to 3,500 cells/mm² in individuals 40 to 90 years of age. This number is sufficient to maintain corneal clarity and an average normal thickness of 530±31.5 µm[2-4,7,10-13]. When the ECD decreases below 1,000 cells/mm², the endothelial functions begin to be compromised, and decompensation usually occurs when the ECD drops to 300 to 500 cells/mm²[3].

In patients who have undergone PKP, the corneal endothelium also functions as an active pump and a barrier to maintain stromal hydration and graft clarity.

The ECD and CT are associated strongly with graft survival[5]. After transplantation, donor endothelial cells decrease more rapidly than during the normal aging process. This rate of endothelial loss varies among studies[14]. Borderie et al[6] reported that the ECD declined from 2,270 cells/mm² to 1,058 cells/mm² and 865 cells/mm², at 5- and 10-year after PKP, respectively. However, the Cornea Donor Study reported that the median ECD was 778 cells/mm² in clear grafts at 5-year[8], and Bourne[15] reported a mean ECD of 766 cells/mm² at 20-year. Moreover, Kus et al[4] reported a mean ECD of 808±194 cells/mm² (range 575 to 1,243). However, despite the low ECD, many studies have reported that these grafts remained clear[4,8,15,16].

The aforementioned studies have indicated that corneal grafts can remain clear and compact despite a low ECD. The current study supported this finding with the result that the mean ECD of the grafts that were clear and compact after PKP was significantly lower compared with the control group. In the current study, the minimal ECDs that maintained corneal clarity and compact were 294.3 cells/mm² in the PKP group and 412.2 cells/mm² in the control group. The ability of very low ECDs to maintain graft clarity after PKP had been reported previously[4,6,8,15].

Eyes with clear corneas and ECDs of 1,000 cells/mm² or less in the current study included more patients who had undergone PKP than controls. The same result also was seen in clear corneas with ECDs below 500 cells/mm², most of which had undergone PKP. These findings emphasized that an ECD that can maintain corneal clarity is lower in eyes that underwent PKP compared with those that did not. Moreover, among corneas with ECDs from ranging from 1,000 to 500 cells/mm², the current results showed that eyes underwent PKP had significantly thinner corneas than in the control group. Nevertheless, corneal grafts with ECDs below 500 cells/mm² usually were at increased risk of graft failure[5,15].

Based on the current results, the authors hypothesized that, compared with normal corneas, corneal grafts required fewer endothelial cells to maintain its function. The results reported by Bourne[17] and Bourne and Bruebaker[18] might be explained by increasing endothelial barrier function and decreasing endothelial permeability of the transplanted cornea despite the larger endothelium and the decreased endothelial pump rate. Furthermore, the transplanted endothelial cells were only responsible for the areas of the grafts that were smaller than the entire cornea[9]. Thus, fewer endothelial cells were required to maintain the corneal function.

Normal corneal endothelial cells have a mosaic-like hexagonal configuration and more than 60% of the cells have the same shape and size. With endothelial loss, the adjacent endothelial tissue migrates to restore the defect through cellular enlargement and sliding. This mechanism increases the CV of the cellular area, i.e., polymegathism, and also decreases the percentage of hexagonal cells, i.e., pleomorphism[2,12]. Thus, the corneal endothelium is considered abnormal in the presence of polymegathism over 40% or pleomorphism under 40%[12].

For eyes with thin or normal CTs (561 µm or less), polymegathism and pleomorphism differed significantly between the PKP and control groups (Table 3, 4). However, this difference was not detected in eyes with CTs exceeded 561 µm likely because of abnormal functioning of the endothelial cells in both groups.

As shown in Table 5, and in previous studies[2,7,8], the ECD gradually declined with time after PKP. Interestingly, the mean ECD of grafts that were followed for more than 10 years post-operatively did not differ significantly from the ECDs during 5 to 10 years post-operatively. Patel et al reported that 10 to 15 years after PKP, the rate of graft endothelial cell loss was the same as in normal corneas[7]. Several reasons explain the decreases in endothelial cells in grafts, i.e., inflammation, graft rejection, and sliding of the donor ECs to replace recipient cells[2]. The ages of the donor and recipient and the ECD of the donor also affect endothelial loss after PKP[2,19].

The CT has a linear relationship with corneal hydration and graft survival time and was considered predictive of graft survival by some[5,16]. When the graft thickness increased over 600 µm, the chance of graft failure increased to 20%[13,20]. The average normal graft thicknesses after PKP are 530 to 560 µm (range 430 to 751 µm)[6,14,16]. However, the graft thickness usually increases over time. This finding was also consistent with the current results (Table 5).

The current control group was not selected from a normal population, i.e., they were patients with eye diseases such as cataract and retinal degeneration without corneal involvement. Eyes from various diseases were included intentionally to simulate a real population. However, the visual acuity in the present study did not reflect the corneal clarity or graft quality since several associated factors affected the vision such as cataracts, refractive errors, and retinal status. The details of the associated findings were beyond the scope of the current study.

The current study had some limitations that might have affected the outcomes. First, because the study was retrospective, some data might have been missing or incomplete. Second, the sample size might not have been sufficiently large to encompass all varieties of normal corneas; thus, the current lowest ECD that maintained the corneal clarity reported might not have represented completely an actual normal population. Nevertheless, this number of sample size is sufficient to demonstrate significant difference between the two groups. Third, other confounding factors such as the length of time after PKP, donor and recipient diseases, and diseases in the control group could have interfered with the study results. However, the aim of the present study is to investigate the association between ECD and CT in patients who had normal corneal clarity after undergoing PKP versus patients with normal corneas regardless of the underlying diseases or the length of follow up. Fourth, all of the current patients were recruited from one center, which might not represent the vast majority of patients. Another multicenter study with a larger sample size and various types of keratoplasties is required to confirm the current findings.

In conclusion, the authors found that regarding the same CT, patients who underwent PKP had a lower ECD than patients with normal corneas. Moreover, eyes that underwent PKP also had higher polymegathism and lower pleomorphism values than those who did not undergo PKP. These findings imply that to maintain clarity, corneal grafts might need fewer endothelial cells than normal corneas. Surgeons should be aware of and carefully evaluate the ECDs and CTs before performing intraocular surgeries in patients who underwent PKP, despite the presence of a clear corneal graft. Surgeons should perform the surgeries cautiously to avoid endothelial injury, and both ECDs and CTs should be monitored periodically during the follow-up period.

What is already known on this topic?

Previous studies demonstrated that cornea with ECD below 1,000 cells/mm² tended to have functional compromise and higher risk of corneal decompensation after intraocular surgery while one with ECD of 500 cells/mm² or below usually developed corneal decompensation. It was also known that transplanted grafts remained clear despite a low ECD.

What this study adds?

The present study supported the aforementioned finding and demonstrated that transplanted cornea could remain clear and compact with ECD as low as 294 cells/mm². The authors also demonstrated that among cornea with the same thickness, transplanted cornea had significantly lower ECD than normal cornea to maintain clarity. Corneal pleomorphism, polymegathism and CV of clear transplanted graft were statistically different from normal cornea with the same thickness.

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Availability of data and materials

The datasets used and analyzed during the current study are available from corresponding author on reasonable request.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Maurice DM. The cornea and sclera. In: Davson H, ed. The Eye. 3rd ed. Orlando: Academic Press; 1984. p.85.
2. Bourne WM. Biology of the corneal endothelium in health and disease. Eye (Lond) 2003;17:912-8.
3. American Academy of Ophthalmology. Corneal endothelial photography. Three-year revision. Ophthalmology 1997;104:1360-5.
4. Kus MM, Seitz B, Langenbucher A, Naumann GO. Endothelium and pachymetry of clear corneal grafts 15 to 33 years after penetrating keratoplasty. Am J Ophthalmol 1999;127:600-2.
5. Sugar A, Gal RL, Kollman C, Raghinaru D, Dontchev M, Croasdale CR, et al. Factors associated with corneal graft survival in the cornea donor study. JAMA Ophthalmol 2015;133:246-54.
6. Borderie VM, Boelle PY, Touzeau O, Allouch C, Boutboul S, Laroche L. Predicted long-term outcome of corneal transplantation. Ophthalmology 2009;116: 2354-60.
7. Patel SV, Hodge DO, Bourne WM. Corneal endothelium and postoperative outcomes 15 years after penetrating keratoplasty. Am J Ophthalmol 2005;139:311-9.
8. Lass JH, Gal RL, Dontchev M, Beck RW, Kollman C, Dunn SP, et al. Donor age and corneal endothelial cell loss 5 years after successful corneal transplantation. Specular microscopy ancillary study results. Ophthalmology 2008;115:627-32.e8.
9. Joyce NC. Proliferative capacity of the corneal endothelium. Prog Retin Eye Res 2003;22:359-89.

10. Ueno Y, Hiraoka T, Miyazaki M, Ito M, Oshika T. Corneal thickness profile and posterior corneal astigmatism in normal corneas. Ophthalmology 2015; 122:1072-8.
11. Doughty MJ, Muller A, Zaman ML. Assessment of the reliability of human corneal endothelial cell-density estimates using a noncontact specular microscope. Cornea 2000;19:148-58.
12. Thomas C. Use specular microscopy to diagnose corneal disease: specular microscopy is a noninvasive photographic technique that facilitates rapid and accurate diagnosis of corneal endotheliopathies. Rev Optom 2009;146:69-74.
13. Ing JJ, Ing HH, Nelson LR, Hodge DO, Bourne WM. Ten-year postoperative results of penetrating keratoplasty. Ophthalmology 1998;105:1855-65.
14. Kettesy B, Nemeth G, Kemeny-Beke A, Berta A, Modis L. Assessment of endothelial cell density and corneal thickness in corneal grafts an average of 5 years after penetrating keratoplasty. Wien Klin Wochenschr 2014;126:286-90.
15. Bourne WM. Cellular changes in transplanted human corneas. Cornea 2001;20:560-9.
16. Borderie VM, Touzeau O, Bourcier T, Allouch C, Zito E, Laroche L. Outcome of graft central thickness after penetrating keratoplasty. Ophthalmology 2005; 112:626-33.
17. Bourne WM. Clinical estimation of corneal endothelial pump function. Trans Am Ophthalmol Soc 1998;96: 229-39.
18. Bourne WM, Brubaker RF. Decreased endothelial permeability in transplanted corneas. Am J Ophthalmol 1983;96:362-7.
19. Musch DC, Meyer RF, Sugar A. Predictive factors for endothelial cell loss after penetrating keratoplasty. Arch Ophthalmol 1993;111:80-3.
20. Verdier DD, Sugar A, Baratz K, Beck R, Dontchev M, Dunn S, et al. Corneal thickness as a predictor of corneal transplant outcome. Cornea 2013;32:729-36.