

Corneal Endothelial Cell Changes Twenty Years After Penetrating Keratoplasty

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Purpose: To evaluate retrospectively the corneal endothelium in 15 eyes which showed clear cornea for 20 years or longer after penetrating keratoplasty.

Methods: The corneal endothelium was investigated in 15 eyes. The causative lesion had been keratoconus in 10 eyes and herpetic keratitis in 5 eyes. At the time of surgery, the patients were aged from 6 to 45 years, average 25.3 ± 10.4 years. The endothelial cell density was measured 10 and 20 years after surgery by specular microscope. The relation between the rate of endothelial cell density loss and postoperative graft rejection, final visual acuity, causative corneal lesion, age of the patient, and age of the donor was evaluated.

Results: The endothelial cell population per mm^2 averaged 998 ± 343 ten years after surgery and 852 ± 245 twenty years after surgery. The rate of endothelial cell density loss thus averaged $12.1\% \pm 16.3\%$ during the last 10 years. This rate was independent of postoperative graft rejection, final visual acuity, causative corneal lesion, age of the patient, or age of the donor.

Conclusions: The corneal endothelial cells become stabilized 10 years after surgery in cases where the grafts remain transparent 20 years after surgery. **Jpn J Ophthalmol 2002;46:189–192** © 2002 Japanese Ophthalmological Society

Key Words: Corneal endothelial cell, graft survival, penetrating keratoplasty, specular microscope.

Introduction

Penetrating keratoplasty (PK) is a very common form of corneal transplantation. Corneal clarity following PK depends on the maintenance of the endothelial cells in the transplanted cornea. In some cases, the endothelial cells did not decrease after PK;¹ in others, a decrease was reported.^{2–12} There are a few reports about endothelial cell loss during a long postoperative period.^{3–8} Endothelial cell loss

occurred for several years and rapidly in the first year postoperatively.^{8–12} The rate of endothelial cell loss was reported to be 10.4–17.0% at 2 weeks after PK, 16.0% at 1 month, 18.3–33.0% at 3 months, 39.4% at 6 months, and 33.6–48.2% at 12 months.^{8–12} During the long postoperative period, the rate of endothelial cell density loss per year was reported at 150% by 2 months after PK, 20% between 2 months and 2 years, 7.3% between 2 and 5 years, and 1.3% between 5 and 20 years.³ The rate of endothelial cell density loss per year was reported at 4.2% between 5 and 10 years after PK.⁸

We evaluated the corneal endothelial cell density only in cases showing clear cornea for 20 years or longer after PK.

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Materials and Methods

We made a retrospective study of the records of 15 PK surgery patients who showed clear cornea for 20 years or longer after PK. The surgery had been performed at the Tokyo University Hospital between July 1970 and February 1978. Endothelial cell density was measured at 10 and 20 years following PK. These 15 transplants were performed on 13 patients (9 male and 4 female patients) (Table 1). The causative lesion was keratoconus in 10 eyes and herpetic keratitis in 5 eyes. In Table 1, cases 2 and 5 were the same patient, and cases 3 and 6 were the same patient.

At the time of surgery, the patients were aged from 6 to 45 years (average = 25.3 ± 10.4 years). The mean age was 25.6 ± 5.7 years (range, 18–35 years) for keratoconus patients and 24.8 ± 17.5 years (range, 6–45 years) for herpetic keratitis patients.

Donor eyes, enucleated aseptically, were maintained in preservation media (EP®, Kaken, Tokyo) at 4°C. Transplantations were almost all done within 72 hours of enucleation. The age of donor was known in 10 eyes. The mean age of these donors was 65.3 ± 14.4 years (range, 41–82 years). PK was performed without any combined surgery in all cases. The diameter of the corneal graft was 7.0–7.5 mm. The diameter of the recipient cornea was 7.0 mm. The grafts were sutured to the recipient corneas with running 10-0 nylon sutures. Topical antibiotic and corticosteroid drugs were prescribed as postoperative treatment. Topical treatment was tapered off over

several months. The corneal sutures were usually removed 4 to 6 months after surgery. The mean postoperative follow-up period was 24.8 ± 3.1 years (range, 21–29 years).

No endothelial graft rejection was seen in 10 eyes; rejection occurred once in 4 eyes (3 eyes in keratoconus eyes and 1 eye in herpetic keratitis eyes), and twice in 1 eye in the herpetic keratitis eyes. Episodes of endothelial graft rejection in the keratoconus eyes were seen at 4, 5, and 7 years after PK. Endothelial graft rejection in the herpetic keratitis eyes was seen at 1 month after PK in one case, and at 3 years in 2 cases. A corneal graft was defined as rejected when it became edematous and showed such signs of immunological rejection as a rejection line, infiltrative keratic precipitates, or anterior segment inflammation. The clarity of the corneal graft was determined clinically using a slit-lamp biomicroscope. In case 11, final visual acuity was 0.2 due to cataract formation.

Endothelial cell density was measured 10 and 20 years after surgery. The central corneal endothelial cells were photographed by non-applanation contact specular microscopy (Konan Keeler, Konan Medical, Nishinomiya). Analysis of cell density was performed by cell analyzer (Konan). Three microphotographs of the central cornea were taken and a minimum of 50 cells was counted in each photograph to perform an analysis of cell density. The average of the cells counted in the three microphotographs was recorded.

The endothelial cell loss for the 10 years between 10 and 20 years after PK was calculated and ana-

Table 1. Data on Transplant Patients

Patient No.	Age	Sex	Causative Lesion	Age of Donor (years)	Rejection (times)	Final Visual Acuity	Follow-up (years)
1	19	Male	Keratoconus	Unknown	0	0.9	29
2*	18	Male	Keratoconus	Unknown	0	0.5	28
3†	30	Male	Keratoconus	Unknown	1	1.0	28
4	35	Female	Keratoconus	50	0	0.5	23
5*	19	Male	Keratoconus	82	1	1.2	27
6†	31	Male	Keratoconus	79	0	1.2	27
7	23	Male	Keratoconus	54	0	1.5	27
8	27	Male	Keratoconus	60	0	1.2	25
9	26	Male	Keratoconus	66	0	0.8	22
10	28	Male	Keratoconus	41	1	0.9	21
11	45	Female	Herpetic keratitis	Unknown	0	0.2	28
12	35	Male	Herpetic keratitis	82	0	0.8	24
13	31	Male	Herpetic keratitis	Unknown	2	0.7	21
14	7	Female	Herpetic keratitis	77	1	1.0	21
15	6	Female	Herpetic keratitis	62	0	0.8	21

* Cases 2 and 5 were the same patient.

† Cases 3 and 6 were the same patient.

lyzed in relation to the graft rejection episodes, final visual acuity, causative corneal lesion (keratoconus and herpetic keratitis), age of the patient, or age of the donor. The differences and correlations were analyzed by the independent *t*-test and Pearson's correlation coefficient.

Results

The overall endothelial cell density averaged 998 ± 343 cells/mm² (range, 645–1,980 cells/mm²) 10 years after PK, and 852 ± 245 cells/mm² (range, 622–1,569 cells/mm²) 20 years after PK (Table 2). The rate of endothelial cell density loss had averaged $12.1 \pm 16.3\%$ over the last 10 years.

The endothelial cell density 10 years after PK averaged 879 ± 162 cells/mm² (range, 645–1,124 cells/mm²) in keratoconus eyes and $1,235 \pm 497$ cells/mm² (range, 779–1,980 cells/mm²) in herpetic keratitis eyes. The endothelial cell density 20 years after PK averaged 774 ± 114 cells/mm² (range, 622–1,022 cells/mm²) in keratoconus eyes and $1,007 \pm 369$ cells/mm² (range, 634–1,569 cells/mm²) in herpetic keratitis eyes. The rate of endothelial cell density loss over the last 10 years averaged $10.2 \pm 16.0\%$ in keratoconus eyes and $15.9 \pm 18.3\%$ in herpetic keratitis eyes. There was no significant difference between the two groups ($P = .54$).

There was no significant difference between the rate of endothelial cell density loss and postoperative graft rejection episodes ($P = .24$). There were

no significant correlations between the rate of endothelial cell density loss and final visual acuity ($P = .48$), age of the patient ($P = .83$), or age of the donor ($P = .44$) (Table 3).

Discussion

Owing to recent developments in surgical techniques, materials, and postoperative management, indications for PK have been extended to high-risk patients with conditions such as regrafting, bullous keratopathy, or chemical burn. One of the most important factors that effects the clinical outcome of PK is still allograft rejection.¹³ As high-risk patients are more likely to suffer from allograft rejection than low-risk ones, their outcomes after PK have not been good.¹³

In this study, we evaluated the corneal endothelium in 15 eyes that had shown a clear cornea for 20 years or longer after PK and in which we could measure endothelial cell density at 10 and 20 years after PK. The causative lesion was keratoconus in 10 eyes and herpetic keratitis in 5 eyes. The graft survival rate of PKs performed in our institution between 1987 and 1997 was 98.8% in keratoconus eyes and 87.0% in herpetic keratitis eyes, and was better than that in other diseases (mean follow-up period = 3.9 years).¹⁴ The graft survival rate of PKs in keratoconus eyes was reported as 96.7% (mean follow-up period = 6.3 years),¹⁵ 90.5% (follow-up period 10 years),⁷ and 90% (mean follow-up period = 11.3 years).¹⁶ The graft survival rate of PKs in herpetic keratitis eyes was reported as 80% (follow-up period 1–12 years).¹⁷ The rate of endothelial cell density loss was different from the loss after causative corneal lesion. The least endothelial cell density loss reported for 1 year after PK was in keratoconus (33.4%), followed by corneal leukoma including herpetic keratitis (42.5%).¹¹ In this study, the subjects were limited to patients maintaining clear cornea for 20 years or longer after PK. The causative corneal lesions were only keratoconus and herpetic keratitis,

Table 2. Postoperative Endothelial Cell Density in Transplant Patients

Patient No.	10 Years (cells/mm ²)	20 Years (cells/mm ²)	Rate of Loss (%)
1	976	714	26.8
2	932	762	18.2
3	938	794	15.4
4	682	766	-12.3
5	645	626	2.9
6	679	798	-17.5
7	857	622	27.4
8	1124	852	24.2
9	922	783	15.1
10	1037	1022	1.4
11	1076	634	41.1
12	779	771	1.0
13	1479	1159	21.6
14	859	900	-4.8
15	1980	1569	20.8
Average	998	851	12.1
SD	343	245	16.3

SD: standard deviation.

Table 3. The Relation Between the Rate of Endothelial Cell Density Loss and Various Factors

Factors	<i>p</i>	Statistical Analysis
Herpetic keratitis or keratoconus	.54	<i>t</i> -test
Rejection	.24	<i>t</i> -test
Age of recipient	.83	Pearson's correlation coefficient
Age of donor	.44	Pearson's correlation coefficient
Final visual acuity	.48	Pearson's correlation coefficient

which showed low age at the time of surgery, and showed high graft survival rate, and slow endothelial cell density loss. The eyes in which graft rejection was so severe that clarity of graft was lost were excluded from this study. The graft rejection occurring in 5 of our cases was not so severe that it greatly affected endothelial cell density.

The endothelial cell density at about 10 years after PK has been reported at 960 ± 470 cells/mm² (10 years),⁸ 957 cells/mm² (2–13 years),⁶ 856 cells/mm² (10 years),⁷ 642 ± 166 cells/mm² (9.5–12.5 years),⁵ and at about 20 years after PK, 855 cells/mm² (13–24 years),⁶ 613 cells/mm² (15–30 years),⁴ 666 ± 284 cells/mm² (17.6–22.5 years).⁵ Kimura reported measuring 9 eyes for endothelial cell density 10 and 20 years after PK.³ The endothelial cell density was 840 ± 150 cells/mm² 10 years after PK and 710 ± 70 cells/mm² 20 years after PK. The endothelial cell density was lower than in our study. The rate of endothelial cell density loss was 15.5%, which was similar to that reported here.

In this study, the endothelial cell density 10 and 20 years after PK in herpetic keratitis eyes was slightly higher than in keratoconus eyes. This result was due to a difference in graft conditions at surgery. The rate of endothelial cell density loss over the last 10 years showed no significant differences between the two groups, but that in keratoconus eyes was slightly lower than that in herpetic keratitis eyes. This result was one of the reasons that PK in keratoconus eyes showed a good prognosis.

Sato,² Ing et al,⁸ and Bourne¹² reported no significant correlation between the endothelial cell area or density after PK and graft rejection episodes. There was no significant correlation between the endothelial cell density and recipient age.⁶ Many previous reports showed no significant correlation between the endothelial cell density and donor age.^{2,5,6,10,18} Linn et al reported in 92% of cases after PK (follow-up period, 2.5–35 years) that visual acuity was better than 20/50.⁶ The endothelial cell density, however, was not related to visual acuity. These previous reports were found to be in agreement with this study. The central corneal thickness showed no significant correlation to endothelial cell density loss.^{2,5,6} In this study, we did not measure central corneal thickness and could not evaluate the relation between endothelial cell density loss and central corneal thickness.

In cases that showed clear cornea for 20 years or longer after PK, regardless of conditions at surgery or progress after surgery, the endothelial cell damage was suppressed to a minimum after the first 10 years after PK. However, as there is one of our cases that showed more than a 20% decrease in endothe-

lial cell density in the 10 years between 10 and 20 years after PK, we should carefully observe the progress of all PK patients in the future.

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