Comparison of Deep Lamellar Keratoplasty and Penetrating Keratoplasty for Lattice and Macular Corneal Dystrophies

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• PURPOSE: **To compare the therapeutic outcomes after deep lamellar keratoplasty (DLKP) and penetrating keratoplasty (PKP) in patients with lattice corneal dystrophy (LCD) and macular corneal dystrophy (MCD).**
• DESIGN: **Age-matched control study.**
• METHODS: **We reviewed the clinical records of 84 eyes with LCD or MCD who had DLKP (41 eyes) or PKP (43 eyes). Primary pathology consisted of 60 eyes with LCD and 24 eyes with MCD. DLKP was performed by either removing stromal tissue gradually, or by viscodissection of Descemet's membrane. Graft clarity, best-corrected visual acuity (BCVA), endothelial density, and complications were compared between DLKP and PKP, as well as between LCD and MCD.**
• RESULTS: **All 84 eyes showed a postoperative improvement in visual acuity. The median final BCVA was not significantly different between PKP and DLKP groups. Endothelial cell loss rates were similar for DLKP and PKP. While the MCD-DLKP group showed progressive decrease in endothelial density, this was not observed in the LCD-DLKP group after surgery. In the DLKP group, most of the complications occurred intraoperatively or in the early phase, whereas late phase complications such as endothelial rejection and secondary glaucoma were the main complications in the PKP group.**
• CONCLUSIONS: **PKP is no longer an automatic choice for the surgical treatment for LCD and MCD; DLKP seems to be a safe alternative. While DLKP is a favorable method for LCD, MCD may not be a good candidate, as it might show progressive decrease in the corneal endothelium postoperatively. (Am J Ophthalmol 2006; 142:304–309. © 2006 by Elsevier Inc. All rights reserved.)**

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CORNEAL DYSTROPHIES ARE DEFINED AS PRIMARY, inherited, bilateral, heredofamilial disorders of the cornea affecting transparency or refraction, leading to varying degrees of visual disturbances.[1] These dystrophies have been traditionally classified according to the primary layer of involvement into anterior membrane dystrophies, stromal dystrophies, and endothelial membrane dystrophies.[1] Keratoplasty was performed to treat such corneal dystrophies, which accounted for 4% to 24% of all corneal transplants.[2–5] Among the variant of surgical procedure, penetrating keratoplasty (PKP) has been the definitive treatment for corneal dystrophies for many years;[6,7] deep lamellar keratoplasty (DLKP) was recently introduced as an alternative. In DLKP, a full-thickness corneal stroma with epithelium is placed on the host Descemet membrane containing little or no stroma.[8–19] There have been a number of reports indicating favorable visual outcome after DLKP for diseases without endothelial involvement such as keratoconus.[12,16,19] Therefore, corneal stromal dystrophy without endothelial abnormalities is also expected to be a good indication for DLKP, although no large-scale study has been conducted. Previous study suggested that postoperative endothelial loss was less in DLKP than PKP, but interface opacity or recurrence might be issues in DLKP.[15] The aim of this study was to compare the therapeutic outcomes after DLKP and PKP in patients with corneal stromal dystrophy. To our knowledge, this study is the largest case-controlled study of DLKP vs PKP in corneal stromal dystrophies, and the first study to apply both techniques to a single pathologic entity. We also compared the outcome between the subtypes of the corneal stromal dystrophies; lattice corneal dystrophy (LCD) and macular corneal dystrophy (MCD).

METHODS

AN AGE-MATCHED CASE CONTROLLED STUDY WAS UNDERtaken whereby clinical data were retrieved from computerized databases of patients with corneal stromal dystrophy

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TABLE 1. Demographic Data of the Patients Undergoing Deep Lamellar Keratoplasty and Penetrating Keratoplasty

	DLKP			PKP			
	LCD	MCD	Subtotal	LCD	MCD	Subtotal	Total
Number of eyes (n)	31	10	41	29	14	43	84
Male:Female	23:8	6:4	29:12	19:10	9:5	28:15	57:27
Age (mean ± SD) (yrs)	59 ± 15	42 ± 10	55 ± 15	59 ± 12	46 ± 11	55 ± 13	55 ± 14
Follow-up [mean (interquatile range)] (mos)	21.3 (6–90)	55.4 (6–111)	29.6 (6–111)	50.2 (6–149)	29.5 (6–64)	42.3 (6–149)	36.1 (6–149)
Preoperative BCVA (logMAR)	−1.069	−0.811	−1.000	−0.763	−1.16	−0.892	−0.948
Preoperative endotheliad density (mean ± SD /mm^2)	2446 ± 619	2433 ± 85		2414 ± 384	N/C		

DLKP = deep lamellar keratoplasty; PKP = penetrating keratoplasty; LCD = lattice corneal dystrophy; MCD = macular corneal dystrophy; BCVA = best-corrected visual acuity; SD = standard deviation.

having received DLKP (41 eyes) or PKP (43 eyes) at the Department of Ophthalmology, Tokyo Dental College, Chiba, Japan, between 1994 and 2004. These data were updated from examination of clinical records to obtain pathologic results, surgical details, and postoperative clinical course including best-corrected visual acuity (BCVA), endothelial density, and postoperative complications. Corneal stromal dystrophy was diagnosed clinically from the history, familial history, slit-lamp examination, and pathologic examination in both groups. Patients with less than six months follow-up were excluded. Each patient signed a written informed consent as a part of institutional review board-approved study.

• **PATIENT DATA:** The 41 patients with LCD and MCD who underwent DLKP had a mean age of 55 ± 15 (standard deviation) years and a median follow-up of 29.6 months (range, six to 111 months). Forty-three patients who underwent PKP had a mean age of 55 ± 13 years. This group was followed up for a median time of 36.1 months (range, six to 149 months). The indication for grafting was to improve vision in all patients. All patients had full explanation regarding advantages and disadvantages of both PKP and DLKP. Table 1 summarizes the characteristics and operative data of the patients in the study. There were no differences between baseline characteristics such as age, gender, and preoperative BCVA. Postoperative period was longer in the PKP group than DLKP group ($P = .02$).

Primary pathology consisted of 60 eyes with LCD and 24 eyes with MCD. In the MCD group, we limited the indication of DLKP to the cornea in which the opacity was limited to the anterior to middle stromal layer by slit-lamp examination. This attributed to the difference in preoperative endothelial density; MCD-DLKP group was 2433/mm^2, whereas that of MCD-PKP was uncountable. Preoperative endothelial density of DLKP-LCD had very large standard deviation.

Two of the LCD patients had cataract surgery previously in the DLKP group. In the PKP group, one MCD patient had buckling surgery. None of the eyes had a history of glaucoma.

• **SURGICAL TECHNIQUE:** All donor corneas were transported from eye banks in the United States and met the criteria of the Eye Bank Association of America for donor quality. In DLKP, recipient corneal stroma was trephinated 1/2 to 2/3 in depth using the Hessbarg-Barron trephine (JedMed Instrument, Co, St Louis, Missouri, USA or Katena Products, Inc, Denville, New Jersey, USA) and additional stroma was excised by lamellar surgical knives (Ultrasharp microsurgical knives, No. 681.01 and 681.25, Grieshaber, Switzerland). Intrastromal injection of air, balanced saline, or ophthalmic viscosurgical device (HealonV) was performed to facilitate stromal dissection.[16] As dissection of deep stromal tissue proceeded, aqueous humor was aspirated through a small limbal incision to lower the intraocular pressure and filled with air to check the specular light-reflex at the air-to-endothelium interface.[11,13,16] Typically, the central Descemet membrane of 7.5 mm in diameter was exposed. Donor corneas were trephined using Barron donor punch (Katena) with a diameter 0.25 mm larger than the recipient bed. The donor endothelium and Descemet membrane were dissected using toothed forceps (Ultrafine notched forceps F240W, Inami, Tokyo, Japan).

Penetrating keratoplasty was performed with a standard technique using a Hessburg-Barron trephine. Seven different surgeons operated on the DLKP group, and nine surgeons operated on the PKP group. Fresh, full-thickness graft material, preserved in Optisol GS (Bausch & Lomb, Rochester, New York, USA) for up to five to seven days, was used for penetrating and for deep lamellar grafts. In both techniques, same trephine size of donor/recipient was applied, and four interrupted cardinal sutures and a single continuous 24-bite 10-0 nylon suture were placed. The cardinal sutures were removed, and the continuous suture was adjusted with the aid of circle LED lights attached on a surgical microscope (Nevious light, Varitronix Ltd, Los Angeles, California, USA) or Keratech astigmatic ruler

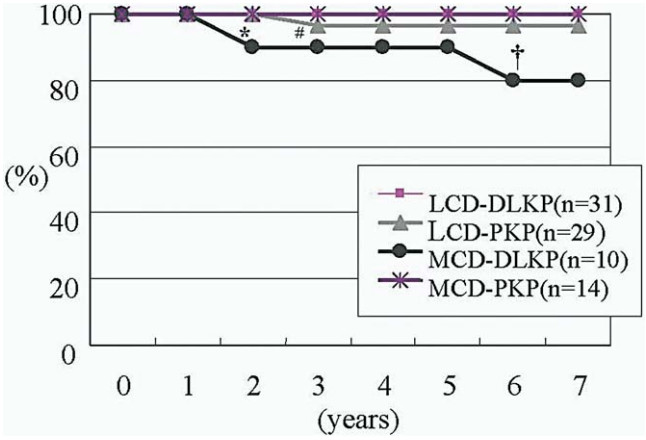

FIGURE 1. Graft survival curve after deep lamellar keratoplasty (DLKP)/penetrating keratoplasty (PKP) for lattice corneal dystrophy (LCD)/macular corneal dystrophy (MCD). At the most recent visit, 39 grafts (95.1%) were clear in the DLKP group and 42 grafts (97.7%) were clear in the PKP group. In the DLKP group, two eyes with MCD developed endothelial decompensation; one had failed at 1.5 years without complications (asterisk), the other had failed at six years with intraoperative microperforation treated by air injection (dagger). In the PKP group, one eye with LCD developed graft failure due to irreversible rejection (number sign).

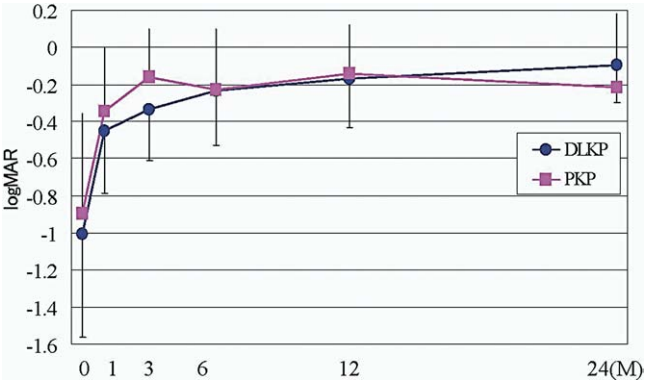

FIGURE 2. Change of best-corrected visual acuity (BCVA) after deep lamellar keratoplasty (DLKP) and penetrating keratoplasty (PKP). Mean BCVA preoperatively (0) and up to 24 months (M) after DLKP (circles) and PKP (squares) was provided. There are no statistical differences in BCVA between DLKP and PKP groups throughout the observation period.

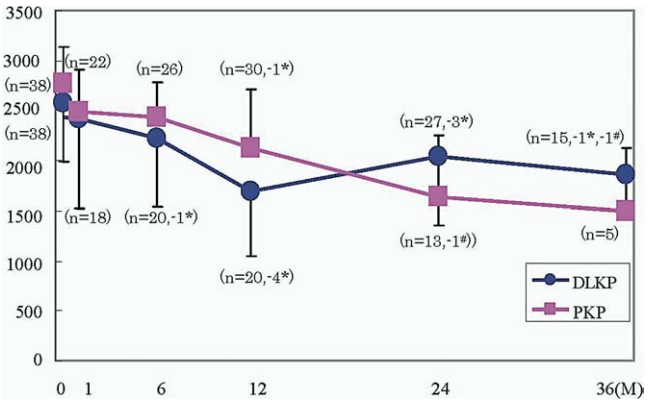

FIGURE 3. Change of endothelial cell density after deep lamellar keratoplasty (DLKP) and penetrating keratoplasty (PKP). Endothelial cell density was similar for DLKP (circles) and PKP (squares) throughout the observation period, and there are no statistical differences between DLKP and PKP groups throughout the observation period. (asterisk) Data of eyes that had cataract surgery were excluded from analysis after the development of events.

(Altomed Ltd, Tyne and Wear, United Kingdom)[13] For DLKP, the bites were placed into the undercut pocket of the host cornea with less thickness. Extended wear soft contact lenses were placed at the end of the surgery and continued until the epithelialization was completed. Eyes in both groups received topical antibiotics (ofloxacin, Tarivid, or levofloxacin, Cravit, Santen Pharmaceutical, Co, Osaka, Japan) and betamethasone 0.1% (Sanbetason, Santen Pharmaceutical, Co, Osaka, Japan) five times a day postoperatively. These eye drops were tapered in the following several months with earlier tapering in the DLKP group. The number of the PKP group was included in that conversion from DLKP to PKP.

• **VISUAL FUNCTIONS:** Visual acuity was measured by using the standard Snellen chart and BCVA with spectacle correction was recorded. The examination was performed preoperatively and six, 12, and 24 months after surgery. The results were converted into logMAR units.

• **SPECULAR MICROSCOPY:** Endothelium was photographed at one, three, six, 12, and 24 months after surgery using a noncontact specular microscope (Noncon Robo SP-8000, Konan, Hyogo, Japan). Approximately 50 cells were analyzed for mean cell density. Data of eyes that had cataract surgery were excluded from analysis in specular microscopy after the development of events.

• **STATISTICAL ANALYSIS:** Our analysis was conducted on 41 DLKP eyes and 43 PKP eyes. Baseline characteristics and outcome variables were compared between the DLKP and PKP groups with the Mann-Whitney *U* test. *P*-value of less than .05 was considered significant.

RESULTS

• **GRAFT CLARITY:** The results of graft survival are summarized in Figure 1. At the most recent visit, 39 grafts (95.1%) were clear in the DLKP group, and 42 grafts (97.7%) were clear in the PKP group. In the DLKP group, all corneal grafts with LCD were clear until last follow-up, whereas two of 10 with MCD developed endothelial decompensation; one failed at 1.5 years without intra-/

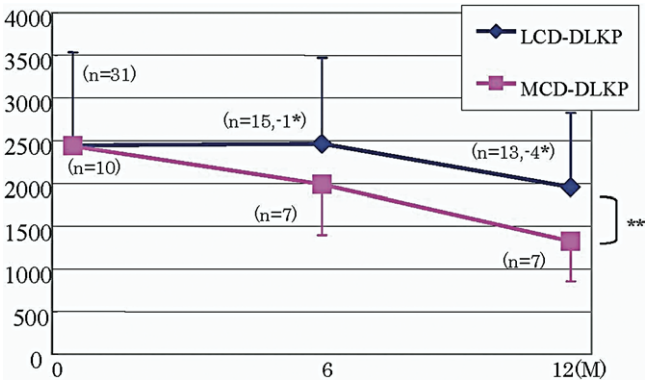

FIGURE 4. Change of endothelial cell density in lattice corneal dystrophy (LCD) and macular corneal dystrophy (MCD) group after deep lamellar keratoplasty (DLKP). Endothelial cell density of LCD was similar for DLKP and penetrating keratoplasty throughout the observation period. The MCD-DLKP group (squares) showed progressive decrease in endothelial density, which was not observed in the LCD-DLKP group (circles) after surgery. There was a significant statistical difference in endothelial density at 12 months. (double asterisk) $P = .03$) (asterisk) Data of eyes that had cataract surgery were excluded from this analysis after the development of events.

postoperative complications, the other failed at six years with microperforation treated by air injection in the anterior chamber. Both had subsequent penetrating keratoplasty, and the grafts remained clear thereafter. In the PKP group, one eye with LCD developed graft failure because of irreversible rejection.

• **VISUAL OUTCOME:** Figure 2 shows the changes in BCVA in the DLKP and PKP groups. BCVA level in the DLKP and PKP groups stabilized at approximately six and three months after surgery, respectively. There were no notable relationships between speed of recovery and age or original disease. No difference was observed in BCVA between DLKP and PKP groups throughout the observation period (Figure 2).

• **CORNEAL ENDOTHELIAL CELL DENSITY:** Cell loss rates were similar for DLKP and PKP throughout the observation period (Figure 3). Mean endothelial cell density after six, 12, 24, and 36 months was 2246, 1701, 2058, and 1870/mm^2 in the DLKP group and 2451, 2136, 1649, and 1517/mm^2 in the PKP group. Endothelial cell density of LCD was also similar for DLKP and PKP throughout the observation period, and there was no significant difference between MCD-PKP and LCD-PKP. The MCD-DLKP group showed progressive decrease in endothelial density after surgery, which was not observed in the LCD-DLKP group. Those difference in endothelial density at 12 months reached statistical significance ($P = .03$, Figure 4). Mean endothelial cell density after 12 months was 1952 ± 608/mm^2 in DLKP patients with LCD and 1325 ± 470/mm^2 in DLKP patients with MCD.

TABLE 2. Complications in the Deep Lamellar Keratoplasty and Penetrating Keratoplasty Groups

	DLKP(LCD:MCD) n = 41(31:10)	PKP(LCD:MCD) n = 43(29:14)
Intraoperative		
Descemet microperforation	7(5:2)	0
Conversion to PKP		
(macroperforation)	6	–
Postoperative, early phase		
Double anterior chambers	10(6:4)	0
Transient ocular hypertension	3(2:1)	0
Postoperative, late phase		
Endothelial rejection	0	6(6:0)
Graft failure	2(0:2)	1(1:0)
Secondary glaucoma	1(0:1)	5(5:0)
PED	2(1:1)	4(4:0)

PED = persistent epithelial defect; DLKP = deep lamellar keratoplasty; PKP = penetrating keratoplasty; LCD = lattice corneal dystrophy; MCD = macular corneal dystrophy.

• **COMPLICATIONS:** Complication rates were similar in both DLKP and PKP; however, the nature of the complications varied (Table 2). In the PKP group, there were no notable intraoperative complications. Microperforation in the Descemet membrane occurred in seven eyes during DLKP, and six eyes required conversion to PKP. There were 10 eyes complicated by double chamber formation postoperatively.

In the DLKP group, two eyes with LCD and one eye with MCD had increased intraocular pressure, which was transient. One year after surgery, one eye in the DLKP and five eyes in the PKP group used antiglaucoma medication. Six (LCD;6, MCD;0) other eyes in the DLKP and seven (LCD;6, MCD;1) eyes in the PKP groups had cataract surgery three to 48 months after keratoplasty. Endothelial rejection was a complication in the PKP group only, occurring in six eyes and one graft was lost as a result of rejection at 18 months.

DISCUSSION

IN THIS COMPARATIVE STUDY OF DLKP VS PKP IN CORneal stromal dystrophy, both procedures provided similar visual outcomes and graft survival, which suggested that postoperative outcomes were successful in both procedures. However, there were several differences in the nature of the complications. In the DLKP group, most of the complications occurred intraoperatively or in the early phase, but did not influence final graft clarity because of adequate recovery. Although microperforation of De-

scemet membrane was the main complication in the DLKP group (13 of 47, 27.7%), which could be recovered. Successful DLKP was performed in most of the cases (41 of 47, 87.2%). We noted that no graft rejection was observed following the DLKP group in this study. Recently, the techniques for stromal excision in DLKP have been improved, including the use of viscoadaptive material,[16] injection of air into the stroma (big bubble technique), and guidance of excision depth by observing reflection from air in the anterior chamber (Melles technique).[11,15] In the results, DLKP has been performed safely and successfully. In contrast, the main complications of the PKP group occurred in the late phase, which means graft rejection was observed only in the PKP group (six of 43, 14%), and secondary glaucoma was observed mainly in the PKP group (five of 43, 11.6%). Previous reports suggested that immunologic rejection remains a major cause of graft failure after PKP, which developed in approximately 20% of patients.[6,17,19] Shimazaki and associates demonstrated that the intraocular pressure 12 months after PKP was significantly higher than preoperative values,[15] but there was no difference in DLKP. This is probably attributable to the prolonged use of topical corticosteroid after PKP. In DLKP, we used corticosteroid eye drops for approximately six months, after which all medications other than lubricants were discontinued. These results indicated that DLKP has clear advantages over PKP in low risk of endothelial rejection and intraocular complications including increasing intraocular pressure.

In addition, continuous loss of corneal endothelium is a major concern after PKP. Previous studies showed that endothelial density continued to decrease up to 10 years after PKP with the rate several times higher than the normal population,[8] but the recipient corneal endothelial density after DLKP had a small initial drop with the physiologic rate.[18] There was, however, no significant difference throughout the observation period in the present study. It may be because of the preoperative high endothelial cell density in the both groups (2414 to 2446/mm^2), or the relatively low rate of endothelial rejection in the PKP group compared with previous reports. The endothelial density might decrease more after PKP than after DLKP which will cause a longer follow-up period. In addition, continuous loss of endothelium in the MCD-DLKP group might obscure the difference as we describe later.

We also compared the outcome between the subtype of the corneal stromal dystrophies; LCD and MCD. The MCD group was preselected for DLKP on the basis of the degree of severity of the disease. While corneal endothelial density stabilized after 12 months in LCD-DLKP, continuous loss was noted in the MCD-DLKP group (Figure 4). We found a significant difference in endothelial density between the MCD and LCD groups at 12 months, and the difference tends to be greater with time. Although data were not shown, endothelial cell loss of the MCD-DLKP group has continued for over 24 months. Furthermore, two of 10 eyes with MCD developed endothelial decompensation.

MCD, a recessively inherited disorder, is the most severe, but the least common of stromal dystrophies among the three classic stromal dystrophies. In Japan, MCD accounts for 13% of all corneal dystrophies undergoing transplantation, and which is much less than 61% in Saudi Arabia.[3] The treatment of MCD, LKP, or PKP was selected by the patient's severity as we did in this study.[3] Histopathologically, MCD is characterized by an accumulation of glycoaminoglycans between the stromal lamellae, within and underneath the epithelium, and within keratocytes and endothelial cells, which may explain continuous endothelial cell loss after MCD-DLKP.[1–6]

Although in this study, DLKP was performed for MCD without deep stromal and endothelial opacity or both by slit-lamp examination, postoperative endothelial density was lower than LCD-DLKP. It might be because the MCD group had subclinical endothelial cell damage.[20]

In summary, DLKP is more technically challenging but allows the risk of endothelial rejection to be avoided, and may reduce the risk of increase in intraocular pressure or late endothelial cell loss. In particular, DLKP is a favorable method for LCD, but not for MCD, which showed progressive decrease in the corneal endothelium postoperatively. Collectively, we concluded that DLKP is a safe alternative for treatment of LCD independent from its subtype, but not for MCD, even in eyes with normal endothelial density.

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