• Clinical Research •

Late corneal ectasia after penetrating and deep anterior lamellar keratoplasty for keratoconus

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Abstract

● **AIM:** To investigate tomographic features of late corneal ectasia after keratoplasty for keratoconus and compare penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) in terms of incidence, time of onset and risk factors of corneal ectasia.

● **METHODS:** Sixty eyes with PK and 30 eyes with DALK operated between 1999 and 2021 were analyzed. Final Pentacam scans were evaluated together with vision and previous topographies. Main outcome measures were vision, K values, apparent thinning on graft-host cornea and the difference between opposing quadrants in the thinnest point measurements. Anterior segment optic coherence tomography was performed for further evaluation.

● **RESULTS:** Mean follow-up was 127.2mo (24–282mo) in PK, and 64.3mo (24–144mo) in DALK. K max was higher in DALK (60.6 *vs* 56.7 D, *P*=0.012). Inferior recipient was thinner (595.9 μm) in PK than DALK (662.2 μm, *P*=0.021), due to longer follow-up. Overall corneal ectasia rate was 20.0% within 24y. Ectasia rate was the same (6.7%) in DALK 2/30 and in PK 4/60 in 10y and 13.3% in 12y (4/30 and 8/60, respectively). It increased to 23.3% (14/60) in PK over 24y. While ectasia was not seen before 7y in PK, it could be seen in DALK starting from the 5th year. The intervals between keratoplasty and ectasia were 144.5mo in PK and 99mo in DALK. Inferior recipient was significantly thinner in 18 eyes with ectasia (502.7 μm) compared to 76 non-ectasia (649.1 μm, *P*=0.000). Inferior graft was thinner (561.0 *vs* 620.4 μm, *P*=0.006), K max (63.3 *vs* 56.5 D, *P*=0.000), and anterior elevation was higher in ectasia (89.1 *vs* 48.6 μm, *P*=0.002). Accelerated crosslinking was performed on 5 eyes.

● **CONCLUSION:** Inferior-superior recipient and inferior graft thinning on tomography, with high K max and anterior elevation emerge as the most reliable criteria for the diagnosis of late ectasia. The incidence of corneal ectasia increases with the time.

● **KEYWORDS:** keratoconus; penetrating keratoplasty; deep anterior lamellar keratoplasty; corneal ectasia

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INTRODUCTION

Keratoconus is a bilateral, progressive corneal ectatic disease that mostly affects young people[1-2]. It is characterized by paracentral corneal thinning and protrusion. Advanced cases that cannot be managed with spectacles or contact lenses may require corneal surgery[3-4]. In both penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK), the rate of clear graft over ten years is over 90%[5-6]. The median predicted graft survival was reported as 49.0y in DALK and 17.3y in PK[7]. However, late corneal ectasia can occur several years after keratoplasty since the entire cornea is not removed in both procedures. It has been described as developing as early as 7y and usually more than 10y following suture removal[8-9]. The latency period is, on average, 18–19y after PK[9-10]. It has been estimated to occur in 6%–11% of the patients at 20 to 25y after surgery[8]. Its prevalence is reported about 7% at 20y, increasing to 12% at 25y[10]. Late ectasia can also be seen after DALK, but data on this subject are scarce[11]. Keratometric studies after PK for keratoconus are mixed, some reporting progression of astigmatism and corneal steepening and others unable to detect a change[9].

Although recurrent keratoconus can occur in any part of the recipient cornea, it is mostly seen in the lower quadrant. The corneal graft is initially healthy. However, the progressive thinning of the recipient cornea invades the graft over time. Late ectasia may result from keratoconus recurrence in the donor button, progression of keratoconus in the host rim with consequent graft-host interface thinning and misalignment, or less likely; grafting a donor cornea with undiagnosed keratoconus. Corneal ectasia after PK is characterized by increased astigmatism, corneal aberrations and vision loss[8]. As there are few reportson recurrent ectasia, the details of recurrence, such as the frequency, risk factors and characteristics are not fully elucidated[8,12]. In recent years, with the development of tomographic imaging systems such as Scheimpflug corneal imaging and anterior segment optical coherence tomography (AS-OCT), the ectasia process can be visualized much better[13-14]. However, definitive tomographic diagnostic criteria for recurrent ectasia have not been fully established. An increase in maximum keratometry (K max) and increase in both steepest keratometry and astigmatism have been proposed as diagnostic criteria[10]. This study was conducted to investigate the topographic-tomographic features of late ectasia after keratoplasty for keratoconus and also to compare PK and DALK in terms of incidence, time of onset and the risk factors for ectasia.

SUBJECTS AND METHODS

Ethical Approval This study was conducted under the tenets of Helsinki Decleration and approved by the Ethics Committee of (Date: 31. 5. 2023, approval number: 2023/64), the University of Health Sciences, Izmir Bozyaka Education and Research Hospital. Informed consent was obtained from the patients.

The current study comprised 73 eyes of 62 patients who had PK and 39 eyes of 36 patients who had DALK for advanced keratoconus between June 1999 and April 2021. All surgeries were performed by Yüksel B. The patient files were reviewed and the data were processed into the computer. In addition, patients were called by phone for a final examination and Scheimpflug imaging. Best spectacle corrected visual acuity, biomicroscopy, Goldmann applanation tonometry, fundus examination with a 90 D lens and non-contact specular microscopy with CEM-530™ (Nidek, Gamagori, Japan) were performed every 6mo for the first 3 postoperative years and yearly therafter. Corneal topographies started with shots taken aftersuture removal at the 1st postoperative year (I), and include second shots taken several years later with a placido disk topography (Keratograph III, Oculus, Wetzlar, Germany) (II) and the most recent Scheimpflug corneal tomography scans (Pentacam, Oculus, Wetzlar, Germany) (III). Inclusion criteria were: clear graft, minimum follow-up of two years and no ocular surgery or trauma after keratoplasty. Exclusion criteria were: patients with Down syndrome in whom topography or vision measurement could not be performed, cataract surgery or traumatic wound dehiscence requiring suture repair during follow-up and patients with missing visual acuity measurements or no topography analysis. Patients with pellucid marginal degeneration were also excluded from the study. One eye from the DALK group was excluded from the study since the patient has been grafted with a keratoconic cornea. He had also only 6mo of follow-up. Pentacam showed a central graft thickness of 400 μm with normal peripheral cornea thickness.

The latest Pentacam scans were evaluated together with vision and previous topographic images to diagnose late ectasia. First, four maps refractive display screen on Pentacam was evaluated in terms of axial curvature, corneal thickness map, anterior and posterior elevations. Steep, flat, mean and K max values and astigmatism were noted. Then, Scheimpflug tomographic images were reviewed one by one, and the quadrants of thinning and ectasia, if any, were determined. In addition, it was checked whether the thinning continued on the graft-host junction and the graft. By using the software on the device, manual thickness measurements were made at the thinnest place in the lower and upper quadrants of the graft and recipient cornea. It was concluded that there was no ectasia in eyes with almost uniform corneal thickness on both sides of the graft-host junction circumferentially. In patients with recurrent ectasia; there was thinning at the periphery of the graft or loosening at the wound site in the area of recipient thinning. AS-OCT was performed with Cirrus 5000 (Carl Zeiss Meditec, Germany) in patients with suspected late ectasia.

Main outcome measures were visual acuity, keratometry values, apparent thinning on recipient/graft and the difference between opposing quadrants in thinnest point measurements on tomography. After the diagnosis of ectasia established, the patient's visual acuity, age, degree of ectasia, status of the graft center, refraction, astigmatism and endothelial cell density were evaluated together and accelerated corneal cross linking with epi-off technique was applied in some of the cases with Peschke device (Huenenberg, Switzerland). Crosslinking was applied in a crescent shape to include the recipient and corneal graft in the ectasia region.

Statistical Analysis Statistical analysis was performed with the statistical program SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The data obtained by taking the average of all measurements were recorded as mean±standard deviation (range). Independent *t* test was used for comparisons between groups. The Chi-square test was used for analyzing categorical variables. Repeated measures ANOVA was used for multiple comparisons, and paired *t*-test was used for pairwise comparisons. A value of $P<0.05$ was considered statistically significant.

RESULTS

The rate of female patients was 41.9% (26/62) in PK and 66.7% (24/36) in DALK. None of the patients had diabetes mellitus. Mean follow-up was 94.7mo (approximately 8y) in whole study patients. Since DALK is a newer technique compare to PK, the number of patients in this group was low and the follow-up period was shorter. Patient characeristics of both groups were shown in Table 1. The only statistically significant difference was found in suture removal and steroid use. Sutures were removed significantly earlier in the DALK group and the duration of steroid use was also short.

The changes in keratometry and topographic astigmatism values in 3 topographies taken during the follow-up period were shown in Table 2. Mean interval between first and second topography was 71.0±31.6 (24–108)mo in PK and 45.0±29.5 (10–96)mo in DALK. First, second topographies and final Pentacam tomography were taken at 12, 83, and 127mo postoperatively on average in PK, 10, 55, and 64mo in DALK. K max was measured only with Pentacam.

In the first topography, both steep and mean keratometry values were statistically significantly higher in the DALK group (Figure 1).

Comparison of the two groups in terms of ectasia parameters in the III exam including Pentacam and specular microscopy analysis results were shown in Table 3.

Age at diagnosis of ectasia was younger in DALK but not statistically significant. During the last examination, PK cases were followed for a longer period of time. Inferior recipient thickness was statistically significantly thinner in the PK group compare to DALK. Again, this may be due to the fact that the postoperative period in PK eyes is above 10y on average and the ectasia progression at the inferior recipient during this time. Upper and lower graft thicknesses were not different between the 2 groups. Endothelial cell density was high in DALK since the recipient endothelium was left intact.

When all PK and DALK eyes were evaluated together, mean follow-up was 94.7mo (24–282mo) and the cumulative rate of ectasia was 18/90 (20.0%) during the study follow-up period, where the longest follow-up reached 24y. Mean time of occurrance was 122.9mo (little over 10y). During study period, late ectasia statistically significantly occurred more frequently in PK 14/60 (23.3%) compare to DALK 4/30 (13.3%, Chi-square test P=0.000). However, follow-up was statistically significantly shorter in DALK (P=0.000). While the mean follow-up time was 127.2mo (24–282mo) in PK, it was 64.3mo (24–144mo) in DALK. Therefore, rates were calculated over 10 and 12y periods. Ectasia development rate was the same within 10y. It was 2/30 (6.7%) in DALK and 4/60 (6.7%) in PK. That rate was 4/30 (13.3%) and 8/60 (13.3%) respectively within 12y. Since maximum follow-up was 12y in DALK, the incidence between 12y and 24y was calculated only for PK. It was 14/60 (23.3%) within 24y of follow-up. According to these results, the only proven risk factor for late ectasia for both type of surgeries seems to be the length of the postoperative period. While ectasia is not seen before 7y in PK, it can be seen in DALK starting from the 5th year.

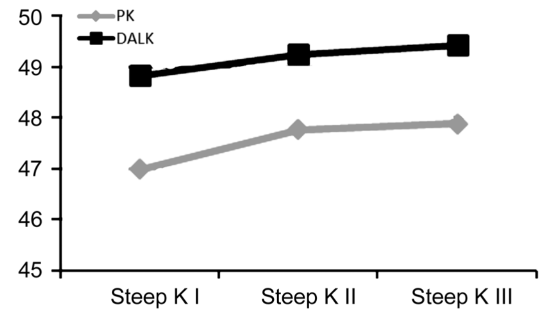

Figure 1 Changes in steep keratometry over years DALK corneas are steeper from the beginning. Steepening rate slows down over time. PK: Penetrating keratoplasty; DALK: Deep anterior lamellar keratoplasty.

Table 1 Patient characeristics of PK and DALK groups mean±SD (range)

Parameters	PK, *n*=73 eyes	DALK, *n*=39 eyes	P^a
Patient age at surgery	33.6±11.5 (9-63)	32.3±10.9 (15–54)	0.577
Donor corneal age	46.7±17.9 (12–79)	46.4±18.6 (11–76)	0.929
Preop. BCVA (logMAR)	1.6±1.5 (0.5–13)	1.4±0.5 (0.7–3.1)	0.382
Preop. IOP (mm Hg)	13.6±2.5 (5–20)	13.2±2.3 (4–16)	0.379
Recipient trephine (mm)	7.8±0.3 (7.5–8.0)	7.8±0.25 (7.5–8.0)	0.929
Donor trephine (mm)	8.0±0.3 (7.5–8.5)	8.0±0.3 (7.75–8.25)	0.850
Suture removal (mo)	12.3±1.9 (4–19)	9.1±3.0 (3–13)	0.000
Steroid use (mo)	38.0±36.3 (5–180)	22.8±21.5 (10–90)	0.022
IOP at last visit (mm)	15.1±2.6 (10–22)	15.3±(10–38)	0.763

PK: Penetrating keratoplasty; DALK: Deep anterior lamellar keratoplasty; BCVA: Best corrected visual acuity; IOP: Intraocular pressure. [a]Independent samples *t* test.

Table 2 Comparison of PK and DALK eyes in terms of changes in keratometry and astigmatism values in three topographies taken at different times mean±SD (range)

Diopters	PK, *n*=60 eyes	DALK, *n*=30 eyes	P^a
K flat I	42.2±2.8 (36.1–48.9)	43.4±3.5 (36.7–53.7)	0.105
K flat II	41.5±6.3 (30.0–48.5)	44.0±2.7 (38.1–47.9)	0.193
K flat III	42.9±2.6 (36.7–49.8)	44.5±3.4 (38.2–52.2)	0.032
K steep I	47.0±3.3 (41.6–61.7)	48.9±3.5 (42.3–56.1)	0.022
K steep II	47.8±3.9 (37.5–58.3)	49.2±3.6 (44.3–54.4)	0.294
K steep III	47.9±6.6 (26.4–55.3)	49.4±3.7 (43.3–58.9)	0.289
K mean I	44.6±2.6 (39–55.3)	46.2±3.1 (39.5–54.9)	0.018
K mean II	45.1±3.0 (34.5–50.3)	46.2±3.0 (39.7–51.0)	0.285
K mean III	45.5±2.1 (41.3–50.5)	46.7±3.2 (40.6–55.3)	0.055
K max	56.7±6.1 (47.1–72.1)	60.6±6.6 (52.8–80.8)	0.012
Topographic ast I	4.7±3.3 (0–14)	5.6±2.8 (0.5–10.6)	0.213
Topographic ast II	5.4±4.2 (0–20.6)	4.7±2.3 (1.6–7.7)	0.608
Topographic ast III	5.7±3.6 (0.5–17.2)	4.5±2.9 (0–10.5)	0.153

[a]Independent samples *t*-test. PK: Penetrating keratoplasty; DALK: Deep anterior lamellar keratoplasty; K: Topographic keratometry value; ast: Astigmatism.

The development times of ectasia were 89, 99, 101, 106, 111, 135, 135, 137, 150, 189, 193, 236, 260, and 282mo (mean 144.5mo; approximately 12.0y) in PK. These numbers were 57, 69, 128, and 142mo (mean 99.0mo, approximately 8.3y) in DALK.

Table 3 Comparison of the two groups in terms of ectasia parameters in the last exam mean±SD (range)

Parameters	PK, *n*=60	DALK, *n=30*	*P*
Age at diagnosis of ectasia	43.3±11.5 (17–75)	38.8±11.0 (19–56)	0.093
Pentacam analysis time (mo)	127.2±58.0 (24–282)	64.3±46.1 (24–144)	0.000
BCVA (logMAR)	0.5±0.3 (0–1)	0.4±0.2 (0–1)	0.671
Total degree of ectasia	85.3±42.7 (40–190)	103.6±84.9 (50–290)	0.462
Superior recipient thickness (μm)	648.4±10.4.5 (290–850)	670.9±90.4 (440–800)	0.376
Inferior recipient thickness (μm)	595.9±106.5 (210–750)	662.2±122.6 (260–840)	0.021
Superior graft thickness (μm)	623.1±65.7 (470–780)	637.8±71.8 (560–860)	0.400
Inferior graft thickness (μm)	598.0±81.8 (350–740)	628.7±50.0 (550–730)	0.100
Anterior elevation (μm)	53.4±53.5 (-110 to 156)	69.1±26.0 (21–131)	0.194
Posterior elevation (μm)	68.2±64.6 (-137 to 220)	90.3±23.5 (32–134)	0.124
K max	57.5±6.7D (47.1–74.7)	60.5±6.2D (47.1–74.7)	0.044
ECD at last visit (cells/mm^2)	1102.5±426.5 (464–2149)	2017.3±404.9 (1049–2738)	0.000

Total degree of ectasia, thickness and elevation values were measured with Pentacam. PK: Penetrating keratoplasty; DALK: Deep anterior lamellar keratoplasty; BCVA: Best corrected visual acuity; K max: Maximum keratometry; ECD: Endothelial cell density.

Table 4 Pentacam data comparison of eyes with and without ectasia mean±SD (range)

Parameters	No ectasia, *n*=72	Ectasia, *n*=18	*P*[a]
Current age (y)	41.7±11.7	44.3±14.7	0.467
Superior recipient thickness (μm)	669.8±83.0 (460–850)	608.0±135.0 (290–790)	0.033
Inferior recipient thickness (μm)	649.1±83.0 (480–840)	502.7±149.1 (210–730)	0.000
Superior graft thickness (μm)	628.4±71.9 (470–860)	618.7±51.4 (540–710)	0.625
Inferior graft thickness (μm)	620.4±63.4 (490–740)	561.0±98.6 (350–690)	0.006
K flat (D)	43.4±3.0 (36.7–51.2)	43.2±2.9 (40.1–52.2)	0.755
K steep (D)	48.1±6.4 (36.4–57.6)	49.4±3.4 (44.7–58.9)	0.430
K mean (D)	45.9±2.6 (40.6–53.9)	46.1±2.8 (43.7–55.3)	0.819
K max (D)	56.5±5.9 (47.1–72.7)	63.3±7.0 (55.3–80.8)	0.000
Topographic astigmatism (D)	5.1±3.5 (0–17.2)	6.3±2.8 (0.8–11.4)	0.224
Anterior elevation (μm)	48.6±46.2 (-110 to 129)	89.1±34.2 (47–156)	0.002
Posterior elevation (μm)	68.5±58.3 (-137 to 220)	91.9±35.6 (45–168)	0.145
Endothelial cell density (cells/mm^2)	1420.3±628.0 (464–2738)	1274.6±55.6 (525–2245)	0.433

[a]Independent samples *t*-test. K: Keratometry.

When the eyes with (*n*=18) and without ectasia (*n*=72) were compared in terms of the parameters listed in Table 1, no statistically significant difference was found. Final visual acuity was 1.1±0.3 (1–2) logMAR in eyes with ectasia and 1.4±0.6 (1–3) in eyes without (*P*=0.070). Recipient trephine size was 7.7±0.3 (7.5–8.0) and 7.8±0.3 mm (7.5–8.0) respectively (*P*=0.178). Recipient trephine size was 8.0 mm in 3/4 (75%) of DALK eyes with ectasia and 4/14 (28.6%) of PK eyes with ectasia. Comparison of 2 groups in terms of topographic data shown in Table 2 revealed no statistically significant difference in any of keratometry values and astigmatism in consecutive topographies taken at three different times. Whereas, significant differences were found in comparison of Pentacam measurements (Table 4). The thickness data in the table are the thinnest point measurements in each location. Elevations were the highest values close to the ectasia region usually shown in the circle on the tomography device. Both inferior recipient and graft thicknesses were statistically significantly thinner, also K max and anterior elevations were significantly higher in eyes with ectasia. Mean central graft thickness was 530.0±44.5 μm (467–572 μm) in DALK ectasia eyes and 573.0±37.5 μm (486–649 μm) in PK ectasia eyes. Central graft thickness was under 500 μm in only one patient from each group. One of them was diagnosed 12y after DALK surgery (467 μm) and the other was diagnosed 16y after PK (486 μm). In other late ectasia cases, it was well above 500 μm.

Ectasia involved an average of 99.5±66.0 degrees peripheral angle, that is, usually one quarter quadrant. Ectasia quadrants were inferior hemispheric, inferior, inferior nasal and infero temporal in DALK. Quadrants were inferior 5 eyes, inferonasal 5, inferotemporal 2, temporal 1, and superonasal 1 in PK. Overall, ectasia was observed at inferior hemispher in 16/18 (89.0%) of the eyes, 1/18 temporal (5.5%) and superonasal in 1/18 (5.5%). Twelve of 14 eyes showed steepening, thinning

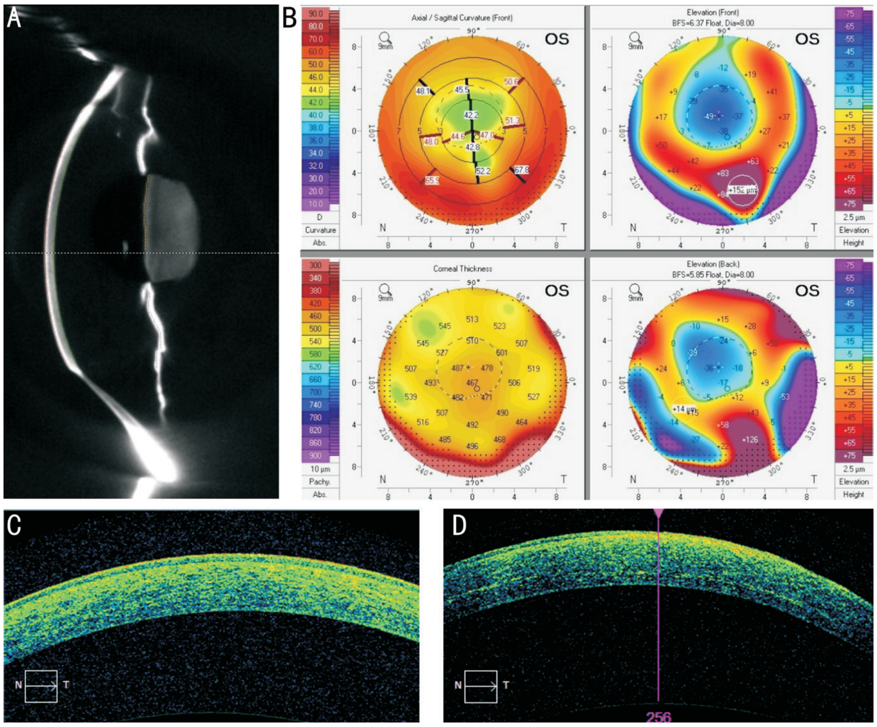

Figure 2 Late corneal ectasia after DALK Left eye of a 55 year-old woman who had big-bubble DALK for keratoconus 12 years ago. A: Generalized thinning and inferior protrusion including recipient and graft; B: Inferior steepening and graft thinning with high elevations are remarkable; C: Anterior segment optic coherence tomography scan of graft shows no residual stroma at descemet level; D: Inferior graft scan shows demarcation line separating the posterior stroma from cross-linked anterior stroma at fifth week. DALK: Deep anterior lamellar keratoplasty.

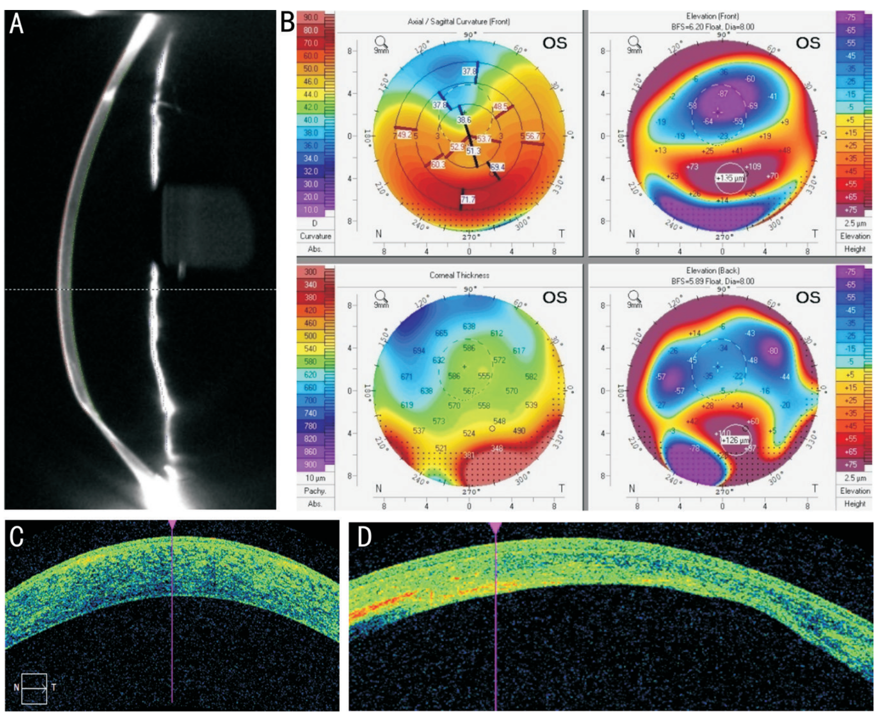

Figure 3 Late ectasia after PK Left eye of a 45 year-old man who had PK for keratoconus 24 years ago. A, B: Inferior steepening (71.7 D), thinning with high elevation. Note inferior thinning on Scheimpflug section. On the thickness map, a thinning area is seen entering from the lower temporal region and spreading towards the center. C: Central graft looks normal on anterior segment optic coherence tomography. D: Inferior section acquired 3mo after cross linking, demonstrates both recipient and graft thinning with increased stromal density due to keratocyte repopulation. PK: Penetrating keratoplasty.

and elevation at the area of ectasia (Figures 2 and 3). Whereas, 1 eye from DALK group and 1 from PK group showed flattening at the area of ectasia. In this type of ectasia; there was thinning, elevation but flattening instead of steeepening

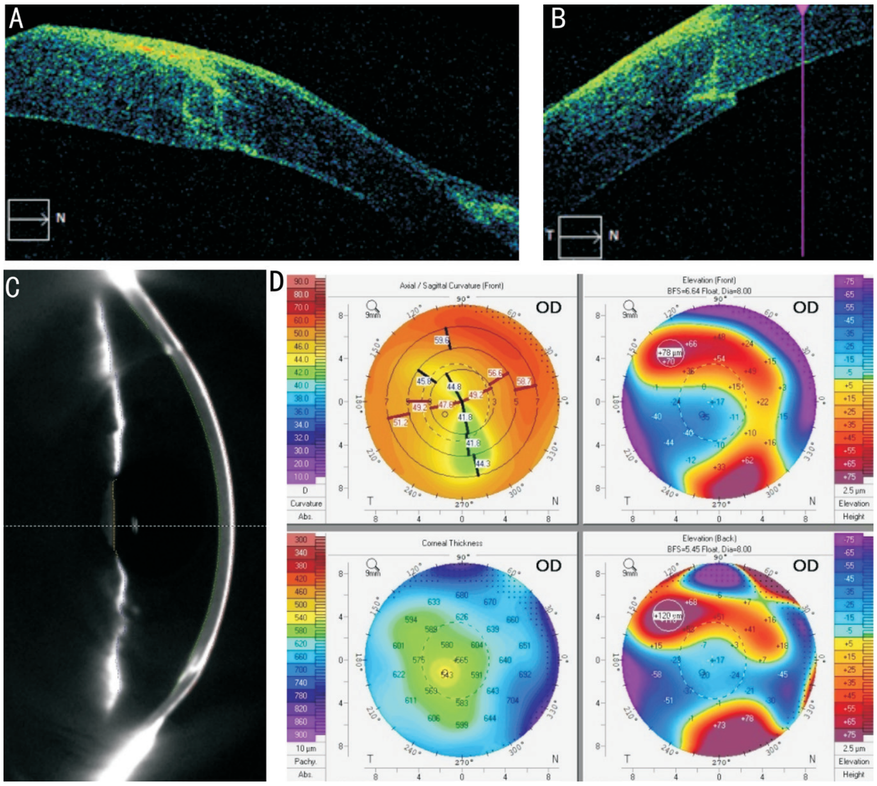

Figure 4 Ectasia with inferior wound loosening A: Inferior hourglass shaped recipient thinning on anterior segment optic coherence tomography; B: Scan was acquired 4d after inferior cross linking. Recipient cornea and keratoplasty wound look healthier at superior quadrant; C: Scheimpflug section shows thinning at inferior recipient cornea; D: Maps show inferior graft flattening due to wound slippage and high anterior elevation.

because of loosening of the graft-host junction due to ectasia spreading from recipient cornea (Figure 4). Notch-shaped dimpling was observed at the graft-host junction in three patients. This finding may be interpreted as a cone residue or thinning as a precursor to ectasia (Figure 5).

Increases during 3 measurements of flat, steep, mean keratometry values and topographic astigmatism in each eye were evaluated with the repeated measures ANOVA test. However, changes during three time points were not found statistically significant. This analysis was also performed in the form of PK-DALK comparison and ectasia present-absent comparison, but no significant difference was found. Only, Wilk's lambda value was 0.058 for steep keratometry in the ectasia group. That means almost statistically significant steepening occurs in ectasia group compare to non-ectasia group.

Of 18 eyes with ectasia, 12 eyes were taken under follow-up, 1 eye was managed with scleral contact lens, and peripheral crosslinking applied to the ectasia area in 4 eyes with PK and 1 eye with DALK. Mean age was 41.4y (17–57y). Mean age at keratoplasty surgery was 29.2y (9–45y). Mean endothelial cell density before crosslinking was 1268.4 (792–1964) cells/mm^2 and after crosslinking was 1152.5 (767–2176) cells/mm^2. Vision increased in one eye, remained unchanged in two and decreased in two eyes. Minimum recipient thickness at ectasia area did not change after crosslinking in 3 eyes (260, 430, 670 μm), decreased in 2 eyes (from 630 to 620, and 680 to 550 μm). Since the follow-up period was 5mo in 3 patients and 3mo in 2 patients, no statistical analysis was performed. No serious ocular complication occurred except mild endothelial loss. Therefore, it is wise to be careful when making the crosslinking decision in PK eyes with critically low endothelial cell density.

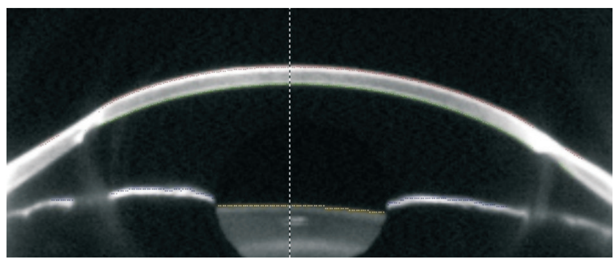

Figure 5 Notch-shaped dimpling at graft-host junction on Pentacam section.

DISCUSSION

In our study, it was observed that corneal grafts in eyes with DALK were steeper than those with PK. In the first topography taken after suture removal at 1y, the mean keratometry value was 1.6 D steeper in the DALK. Likewise, K max was 3.9 D steeper in the DALK group in the last Pentacam tomography (P=0.012). This may be due to earlier removal of sutures in DALK, causing loss of flattening effect earlier. In addition, DALK patients were operated at an older age (39.5), compare to PK (32.5), in other words, more advanced stage of keratoconus. This can lead to reduced support of the graft and to a fast steepening of the cornea. However, inferior recipient thickness on last Pentacam analysis was significantly thinner in PK compare to DALK. Ectasia, albeit slowly progressing in PK, may have caused this finding in a significantly longer follow-up of 127.2mo on average. Besides, due to the low endothelial density in PK, the increase in the water content of the cornea may also facilitate ectasia. The faster progression of keratoconus during pregnancy can be an example of this[12]. Overall rate of the late ectasia after keratoplasty for keratoconus was 20.0% during the follow-up period reaching 24y. Mean time of occurrance was 122.9mo. Ectasia rate was the same in both PK and DALK within 10y (6.7%) and 12y (13.3%). Raecker *et al*[9] reported that rate 6% for PK. Lim *et al*[15] reported the average age at surgery as 28.4 and at the diagnosis of ectasia as 41.2y. These ages were 36.0 and 41.7 in our study. The mean latency to diagnosis was reported as 13.5–18y for PK[9,15]. It was 12.0y in PK and 8.4y in DALK in our study. Earlier ectasia in our study may be related to the fact that our country is in a different climate zone and that our patients can reach keratoplasty later. Our results suggested that ectasia may occur earlier in DALK. It starts as early as at 5y in DALK but not earlier than 7y in PK. Ziaei *et al*[16] reported the latency period as mean 2–3y in DALK and 19y in PK. Ectasia develops faster especially in manual DALK[11,16]. Leaving Descemet's layer, carrying the diseased collagen, in place may play a role in this.

Although late ectasia can be seen in all quadrants, it is usually located inferiorly and rarely at the superior quadrant[8]. It was seen in the lower quadrant in almost 9/10 of our patients too. The reason may be that this region is exposed to external factors such as ultraviolet, dryness, eye rubbing, interleukins in the tear meniscus and absence of lid protection[14]. Ongoing allergy is another factor in young patients[8,17]. Scheimpflug tomography has the sensitivity to detect ectatic disease before any visual loss or significant slit-lamp finding[14]. It provides precise corneal thickness and elevation with good repeatability[10]. AS-OCT is also helpful for closer visualization of the graft-host junction[8,18]. Pentacam thickness maps usually cover an area of 8–9 mm where the corneal graft is located, and the condition of the peripheral recipient cornea cannot be observed. Therefore, it is necessary to look at Scheimpflug tomography cross sections. Our main criterion for the diagnosis of ectasia was the thickness measurements on tomography scans. If ectasia invades the graft, thinning can also be seen in the thickness map. We detected two types of recurrent ectasia. In the first type, which is more common and reported earlier, there is steepening, thinning and elevation at the area of ectasia[8] (Figure 3). In the second type, which is less common, flattening is observed in the curvature map at the ectasia area, as there is loosening at the keratoplasty wound. This type is also accompanied by thinning and elevation (Figure 4).

Diagnostic criteria for recurrent ectasia have not been clearly defined to date[8]. In our study, inferior recipient, superior recipient and inferior graft thicknesses alongside with high K max and anterior elevation values on Pentacam, emerge as the most reliable criteria for the diagnosis of late ectasia. Significant inferior graft thinning found in our ectasia group showed that ectasia started at the recipient, over time passeed the wound site and included the corneal graft. The presence of thinning at the graft periphery almost certainly makes the diagnosis of recurrent ectasia. Likewise, Yoshida *et al*[3] reported that the smaller ratio of inferior recipient and graft thicknesses to the central graft thickness on AS-OCT can be used indicators of recurrent ectasia after PK. Postoperative ectasia occurs in the peripheral cornea and the graft center is not affected for a long time. As a result of this, vision loss in eyes with ectasia was not found statistically significant in our study. Although there are reports on progressive increase in corneal curvature and astigmatism years after PK[9,15], central keratometry and topographic astigmatism values have little value in the diagnosis of late ectasia[3]. Yoshida *et al*[3] reported central graft thickness on AS-OCT as 570 μm in PK for keratoconus at 25y. In our study, it was 530 μm in DALK ectasia eyes and 573 μm PK ectasia eyes. These values indicate normal central graft thickness even decades after surgery, except for very advanced recurrent ectasia cases. Whereas, in our study, K max was significantly higher in eyes with ectasia (63.3 *vs* 56.0 D) indicating localized steepening at ectasia area. Likewise, Pedrotti *et al*[10] reported K max as 64.5 D in recurrent ectasia. An early 3.0 D of steepening in K max was detected on tomography in the third year after PK[19]. Weller *et al*[18] reported more significant thinning at the interface, compared to the limbus and center, forming hourglass-like appearance on AS-OCT.

The exact mechanism of ectasia is still under discussion. It may result from the incomplete removal of peripheral ectasia during surgery or due to new onset from the diseased peripheral stroma[8-9]. Changes in stromal collagen and keratocyte morphology lead to lamellar slippage and biomechanically weakened corneal region bulges outward under the influence of intraocular pressure[8,16]. Ectasia eventually involves the corneal graft by infiltration of low density of abnormal host keratocytes into donor tissue with abnormal collagen production. This has been histologically demonstrated in patients undergoing repeat PK[10,16]. Another study revealed breaks and gaps in Bowman's layer[20]. No evidence of ectasia in the center was found in the histology of any of the buttons obtained from eyes regrafted 10-28y after primary PK[21]. Electron microscopy images revealed a disruption of collagens in all layers in the inferior periphery, but not in the center[18]. Ectasia progresses more quickly in young since the collagen turnover is faster. Therefore, it is recommended that ectasia be stopped before surgery in children[22]. The fact that none of our 98 patients had diabetes, supports the information that keratoconus is not seen in diabetics due to collagen crosslinking called Maillard reaction[23].

Corneal crosslinking has been proposed for both the prevention and treatment of late ectasia[24]. Ziaei *et al*[16] reported successful results of prophylactic peripheral crosslinking (6.5–9.5 mm), 3mo before keratoplasty with repopulation of the peripheral keratocytes and no significant endothelial cell loss. Reduced host keratocyte density can also decrease the immunological rejection. Pedrotti *et al*[10] performed accelerated crosslinking with epithelium-off technique in 18 eyes with recurrent ectasia with a mean age of 48.5 (34–61)y. Improved vision and decreased astigmatism suggest crosslinking's potential as first-line therapy for late ectasia[12]. Richoz *et al*[25] reported that crosslinking halted the progression of ectasia up to one year. In our patients with ectasia, mean inferior recipient thickness was 502.7 μm allowing safe peripheral crosslinking. Mean age was 41.4 (17–57)y. Four PK and 1 DALK eyes with ectasia had accelerated crosslinking with epithelium-off technique. No serious complications occurred. However, if the patient's age is over 40–50y, it may be more appropriate to monitor the patient as the progression of keratoconus slows down after this age, due to natural crosslinking with the help of lysyl oxidase[23]. If the graft center is not affected and vision is good, the patient can also be monitored. Scleral contact lenses may be useful[26-27]. Another important issue is endothelial density. After 20y, endothelial cell density decreases significantly in PK, so crosslinking may cause permanent endothelial failure.

Ectasia recurrence after keratoplasty in keratoconus has been known for many years. But the information is scattered. Publications about post-DALK ectasia are scarce. Due to the more recent introduction of DALK[28] in the treatment of keratoconus, long-term data regarding the frequency of post-DALK ectasia are still lacking[8]. The diagnosis may be missed in retrospective studies with a follow-up period of under 10y and looking only at central keratometry values[29-30]. There is a need for large studies spanning 15–20y and primarily aimed at detecting ectasia findings on corneal tomography scans[3]. Our study has considerable number of patients and follow-up period, also includes detailed presentation of 14 eyes of post-PK and 4 eyes of post-DALK ectasia. Therefore, it may be considered as a contribution to the literature. However, the current study has also limitations. First two topographies were acquired with a placido-disc system (Keratograph) and some of the patients could not be reached for final Pentacam examination.

In conclusion, Scheimpflug imaging system is indispensable tool for the diagnosis of late ectasia after keratoplasty for keratoconus. Direct visualization of recipient and graft thinning in cross sections of the entire cornea, numerical thickness measurements, K max and anterior elevation are reliable diagnostic criteria. AS-OCT has a supportive value. DALK has no protection against recurrent ectasia, on the contrary, ectasia develops faster because more pathological collagen tissue remains. However, 10 and 12y ectasia rates are the same as PK. Two types of ectasia patterns are identified on corneal tomography. Our study did not show any risk factors for ectasia, such as patient-donor age and graft size. The only proven risk factor is the length of the postoperative period. Peripheral crosslinking may be useful in both prevention and management of late ectasia. Larger series with longer follow-up are needed to determine the effectiveness of this method.

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