

A comparison of visual outcomes of deep anterior lamellar keratoplasty versus penetrating keratoplasty of keratoconus patients in two major corneal centres in Malaysia

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Abstract

Purpose: We conducted a retrospective study of keratoconus patients who underwent either penetrating keratoplasty (PKP) or deep anterior lamellar keratoplasty (DALK) in Malaysia from 2014 to 2018 to compare refractive and visual outcomes between PKP and DALK.

Study design: Retrospective case control study.

Methods: We studied 59 eyes of 53 keratoconus patients: 31 eyes underwent PKP and 28 underwent DALK. We obtained data that included demographic distribution, pre- and postoperative best-corrected visual acuity (BCVA in logMAR), postoperative refraction (spherical equivalent and astigmatism), postoperative topography (SimK1, SimK2, and Kcyl), type of correction (spectacles versus contact lens), incidence of rejection, and other complications.

Results: There were 22 female patients (42.0%) and 31 male patients (58.0%) with 55.0% Indians, 34.0% Malays, 7.0% Chinese, and 4.0% others. The mean age was 27.03 ± 8.68 years for the PKP group and 26.36 ± 7.26 years old for the DALK group ($p = 0.784$). There were no statistically significant differences in preoperative BCVA, postoperative refraction, and postoperative topography. However, there was a statistically significant difference in postoperative BCVA between PKP (0.16 ± 0.16)

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and DALK (0.33 ± 0.17) ($p = 0.001$). Graft rejection was a significant complication in the PKP group, with 5 eyes (16.0%) resulting in 2 graft failures (6.0%).

Conclusions: In this study, more men than women underwent corneal transplant for keratoconus within the second to third decades of life, most of whom were of Indian origin. PKP showed better visual outcome in terms of BCVA than DALK. Regarding refractive and keratometry parameters, there were no significant differences. However, DALK had a lower rate of graft rejection and graft failure compared to PKP.

Keywords: deep anterior lamellar keratoplasty, keratoconus, Malaysia, penetrating keratoplasty

Perbandingan hasil penglihatan pesakit keratokonus antara keratoplasti lapisan depan mendalam dengan keratoplasti ketebalan penuh di dua pusat kornea utama di Malaysia

Abstrak

Tujuan: Kita menjalankan kajian retrospektif tentang pesakit keratokonus yang telah melalui pembedahan keratoplasti ketebalan penuh dan keratoplasti lapisan depan mendalam di Malaysia dari tahun 2014 sehingga 2018 untuk membandingkan hasil penglihatan dan refraktif antara dua pembedahan tersebut.

Kaedah kajian: Kajian pemerhatian secara retrospektif

Langkah kajian: Kajian sebanyak 59 mata dari 53 pesakit keratokonus melibatkan 31 mata yang telah menjalani keratoplasti ketebalan penuh dan 28 mata yang dijalankan keratoplasti lapisan depan mendalam. Data yang diperolehi adalah taburan demografi, ketajaman penglihatan (logMAR) sebelum dan selepas prosedur, refraksi selepas prosedur (setara sfera dan astigmatisme), topografi selepas prosedur (SimK1, SimK2 dan Kcyl), jenis pembetulan (cermin mata atau kanta sentuh), kejadian penolakan organ kornea dan komplikasi lain-lain.

Keputusan: Seramai 22 pesakit perempuan (42%) dan 31 pesakit lelaki (58%) dengan 55.0% bangsa India, 34.0% bangsa Melayu, 7.0% bangsa Cina and 4.0% lain-lain. Umur minima adalah 27.03 ± 8.68 tahun untuk kumpulan keratoplasti ketebalan penuh dan 26.36 ± 7.26 tahun untuk kumpulan keratoplasti lapisan depan mendalam ($p = 0.784$). Ketajaman penglihatan yang terbaik sebelum dan selepas prosedur, refraksi selepas prosedur dan topografi selepas prosedur tidak menunjukkan perbezaan yang signifikan secara statistik. Tetapi, ketajaman

penglihatan yang terbaik selepas pembedahan adalah signifikan secara statistik antara keratoplasti ketebalan penuh (LogMAR 0.16 ± 0.16) and keratoplasti lamellar anterior dalam (LogMAR 0.33 ± 0.17) ($p = 0.001$). Penolakan graf kornea adalah satu komplikasi utama di dalam kumpulan keratoplasti ketebalan penuh, iaitu sebanyak 5 mata (16.0%) dengan akibatnya 2 kegagalan graf kornea (6.0%).

Kesimpulan: Dalam kajian ini, insiden pembedahan pemindahan kornea untuk keratokonus didapati adalah lebih tinggi di kalangan lelaki berbanding perempuan, antara umur dua puluhan hingga tiga puluhan, dan majoriti dari kaum India. Hasil ketajaman penglihatan yang terbaik adalah lebih baik untuk kumpulan keratoplasti menembusi ketebalan penuh. Refraksi dan keratometri antara kedua-dua Kumpulan tidak mempunyai perbezaan yang signifikan secara statistik. Walau bagaimanapun, kumpulan keratoplasti lapisan depan mendalam mempunyai kadar yang lebih rendah untuk penolakan dan kegagalan graf kornea.

Kata kunci: keratokonus, keratoplasti lamellar anterior dalam, keratoplasti menembusi ketebalan penuh, kesihatan yang baik dan kesejahteraan

Introduction

Keratoconus is a non-infectious and non-inflammatory disease where the paracentral or central cornea experiences continuous progression of corneal thinning and ectasia causing an irregular astigmatism and often coupled with myopic shift, which may severely impair vision.¹ The reported keratoconus incidence ranges from 1.3 to 25 per 100,000 per year across different populations and has been reported to have higher prevalence with earlier onset and advanced progression in Asian descendants such as Arabs, Indians, Pakistanis, and Polynesians compared to Caucasians.² A study conducted in a specialised corneal centre in Malaysia reported a prevalence of 1.2%, approximately 1 per 100, with higher percentage in Malays and Indians.³

The nature of the disease progression is variable, and the severity can range from very mild to moderate irregular astigmatism that can be corrected with glasses, contact lenses, intracorneal ring segments, and corneal cross-linking⁴ to extreme thinning, ectasia, and acute hydrops leading to scarring warranting keratoplasty.⁵ Corneal transplant has been stipulated when visual rehabilitation is insufficient with spectacle correction, unsupportable contact lens wear, and very poor, unacceptable vision⁶ in approximately 12% to 20% of affected keratoconus patients.⁷⁻⁹

Penetrating keratoplasty (PKP) has been the mainstream surgical treatment for advanced keratoconus for more than 7 decades^{10,11} as it is well established with good reported safety profile and visual acuity outcomes, usually past 18 to 24 months.^{11,12} Nevertheless, full thickness corneal transplant poses risks

of immune-mediated endothelial rejection, attrition of endothelial cells, and intraoperative complications such as expulsive haemorrhage, expulsion of eye content, and endophthalmitis.^{13,14} Deep anterior lamellar keratoplasty (DALK) has gained attention in the past 2 decades for the management of keratoconus with the notion of preserving the host's own endothelial cells, reducing the risk of endothelial graft rejection.^{15,16} Moreover, early tapering of steroids is feasible in DALK, with decreased risk of secondary glaucoma and cataract as well as increased wound strength.¹⁵ However, DALK is taxing on the surgical skills, posing a steeper learning curve for surgeons. Additionally, unlike PKP, which has established a good visual acuity outcomes profile, DALK outcomes wage heavily on the regularity and clarity of host-donor interface. DALK cases have drastically increased parallel to advancement in techniques and surgical instruments, with the most pertinent techniques being reported by Melles¹⁷ and Anwar.¹⁸

Methods

A retrospective case-control study was conducted whereby the clinical data of keratoconus patients having received corneal transplant in Hospital Sungai Buloh or Hospital Kuala Lumpur from June 2014 to June 2018 were traced and reviewed. Ethical approval for this study was obtained from by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH), and adhered to the tenets of Declaration of Helsinki.

The study included a total of 59 eyes (53 patients): 31 eyes underwent PKP and 28 underwent DALK. These data were retrieved from the clinical examination records including diagnosis, pre- and postoperative best-corrected visual acuity (BCVA in logMAR), postoperative refractive and keratometry parameters, and clinical events including any postoperative complications such as graft rejection, graft failure, glaucoma, and cataract. All the patients were clinically diagnosed as keratoconus from the history, slit-lamp examination, refraction, and topography. The patients included in the study had either BCVA of 0.6 logMAR or worse with contact lenses, could not tolerate contact lenses, or had corneal scarring. All patients with scarring involving Descemet's membrane underwent PKP. The severity of keratoconus was matched for both groups, with a mean pre-operative BCVA of 1.36 ± 0.53 for the PKP group and 1.41 ± 0.52 for the DALK group ($p = 0.316$). Patients who had previous ocular surgeries, incomplete or missing data, and defaulted follow-up were excluded. Selective suture removals were applied for all patients for visual rehabilitation.

DALK was performed according to surgeon preference with the Melles technique¹⁷ or big bubble technique,¹⁸ while PKP was performed using manual corneal trephine for both recipient and donor tissues. Full thickness graft tissue, preserved in Optisol (Bausch and Lomb, Rochester, NY, USA) was used for both

groups and trypan blue (Vision Blue, D.O.R.C. International, The Netherlands) was used for removal of endothelium-Descemet's membrane complex from donor tissue for DALK cases. Sixteen interrupted sutures were placed for both techniques.

Statistical analysis

Descriptive analysis was performed by calculating mean \pm standard deviation for quantitative data. For qualitative data, frequencies were represented by a number and percentage. A between-group comparison was performed using Fisher's exact test for categorical variables and with rank-sum test for non-parametric continuous variables. A *P* value less than 0.05 was considered statistically significant.

Results

Patient data

A total of 53 patients (59 eyes) were studied, with bilateral eyes in 6 patients and unilateral eye in 47 patients. There were 22 female patients (42.0%) and 31 male patients (58.0%). The racial distribution was 55.0% Indians, 34.0% Malays, 7.0% Chinese, and 4.0% other (Iban) (Fig. 1). The analysis was on the total number of eyes that underwent corneal transplant rather on the total number of patients in view that patients with bilateral eyes had similar or different corneal transplant procedure performed. Thus, a total of 59 eyes were analysed: 31 eyes underwent PKP and 28 underwent DALK. Thirteen right eyes and 18 left eyes underwent PKP, while 9 right eyes and 19 left eyes underwent DALK (Fisher's exact test, $p = 0.591$). There were no significant differences in age and gender between the PKP and DALK

Racial Distribution

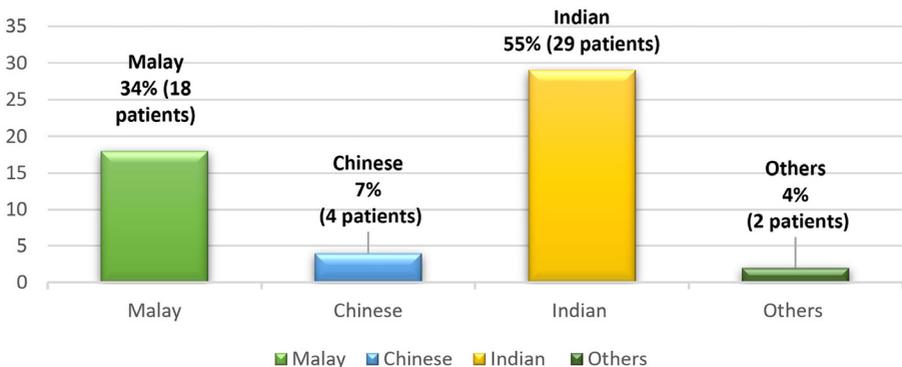


Fig. 1. Racial distribution pattern.

Table 1. Characteristics and surgical data

| Variable | PKP (n = 31) | DALK (n = 28) | P value |
|---|------------------|------------------|---------|
| Male: Female | 17:14 | 16: 12 | |
| Right: Left | 13:18 | 9: 19 | |
| Age (mean \pm standard deviation) years | 27.03 \pm 8.68 | 26.36 \pm 7.26 | 0.749 |

groups. The mean age was 27.03 \pm 8.68 years for the PKP group and 26.36 \pm 7.26 years for the DALK group (Mann-Whitney test, $p = 0.784$) (Table 1).

Visual acuity and refractive results

There were no statistically significant differences in mean preoperative BCVA, postoperative unaided visual acuity, postoperative refraction (spherical equivalent and astigmatism), and postoperative topography (SimK1, SimK2, and Kcyl) (Table 2). However, there was a statistically significant difference in mean postoperative BCVA between PKP (0.16 \pm 0.16) and DALK (0.33 \pm 0.17) (Fisher's exact test, $p = 0.001$).

Most of the patients were satisfied with unaided vision. Three patients from the PKP group (10.0%) and 4 patients from the DALK group (14.0%) preferred spectacles. Three patients from the PKP group (10.0%) and 5 patients from the DALK group (18.0%) required contact lenses to achieve BCVA (Table 3).

Complications

Graft rejection was a significant complication in the PKP group, with 5 eyes (16.0%) resulting in 2 graft failures (6.0%). There were no graft rejections nor graft failures reported in the DALK group. Three patients (1 in the PKP group [3.0%] and 2 in the DALK group [7.0%]) developed cataract postoperatively; 1 patient from the DALK group underwent cataract surgery. One patient from the PKP group (3.0%) and 2 from the DALK group (7.0%) developed glaucoma. Both groups had 1 patient that underwent glaucoma surgery (Table 4).

Discussion

The mean age of the patients in this study was comparable to a study¹⁸ conducted in Singapore, which found that the onset was earlier with progression to severe keratoconus requiring corneal transplant in the second to third decades of life in the Asian community. There were more male patients (58.0%) than female patients

Table 2. Preoperative and postoperative comparison of vision and postoperative refractive parameters of eyes that underwent PKP and DALK for keratoconus (Fisher's exact test)

| Parameters | PKP Mean \pm SD (Min to max) | DALK Mean \pm SD (Min to max) | Sig | P value | 95% CI |
|-----------------------------------|--------------------------------------|---------------------------------------|-------|---------|----------------|
| Preoperative BCVA (logMar) | 1.36 \pm 0.53 0.6 to 3.0 | 1.41 \pm 0.52 0.6 to 2.0 | 0.316 | > 0.05 | 1.25 to 1.52 |
| Postoperative unaided VA (logMar) | 0.51 \pm 0.33 0.0 to 1.6 | 0.65 \pm 0.32 0.2 to 1.6 | 0.298 | > 0.05 | 0.49 to 0.67 |
| Postoperative BCVA (logMar) | 0.16 \pm 0.16 0.0 to 0.5 | 0.33 \pm 0.17 0.0 to 0.6 | 0.001 | < 0.05 | 0.19 to 0.29 |
| Postoperative SE (SD) | -2.33 \pm 2.79 -8.50 to +4.75 | -2.5 \pm 3.31 -11.50 to 4.00 | 0.154 | > 0.05 | -3.20 to -1.63 |
| Postoperative astigmatism (DC) | -4.22 \pm 2.20 -0.50 to -11.00 | -4.39 \pm 1.83 -8.00 to -1.00 | 0.163 | > 0.05 | -4.83 to -3.77 |
| Postoperative Sim K1 (D) | 42.32 \pm 5.4 25.90 to 52.70 | 44.60 \pm 3.10 38.80 to 50.60 | 0.308 | > 0.05 | 42.21 to 44.59 |
| Postoperative Sim K2 (D) | 45.17 \pm 5.14 28.90 to 55.60 | 47.50 \pm 3.9 40.40 to 55.20 | 0.773 | > 0.05 | 45.05 to 47.50 |
| Postoperative Kcyl (D) | 4.99 \pm 3.52 1.00 to 13.80 | 5.18 \pm 2.42 1.40 to 13.80 | 0.722 | > 0.05 | 4.29 to 5.87 |

VA: Visual acuity

DC: Diopter count

SE: Spherical equivalent

Kcyl: Keratometric cylinder

Sig: Statistical significance

Table 3. Preferred correction used to achieve best-corrected visual acuity

| Preferred correction | PKP (n = 31) | DALK (n = 28) | Total (n = 59) |
|----------------------|-----------------|------------------|-------------------|
| Unaided | 25 (81.0%) | 19 (68.0%) | 44 (75.0%) |
| Spectacles | 3 (10.0%) | 4 (14.0%) | 7 (12.0%) |
| Contact lenses | 3 (10.0%) | 5 (18.0%) | 8 (13.0%) |

Table 4. Complications of PKP and DALK

| Complications | PKP (n = 31) | DALK (n = 28) | Total (n = 59) |
|-------------------------|-----------------|------------------|-------------------|
| Graft rejection | 5 (16.0%) | 0 (0.0%) | 5 (8.0%) |
| Graft failure | 2 (6.0%) | 0 (0.0%) | 2 (3.0%) |
| Cataract | 1 (3.0%) | 2 (7.0%) | 3 (5.0%) |
| Glaucoma | 1 (3.0%) | 2 (7.0%) | 3 (5.0%) |
| Faint scar at interface | - | 1 (4.0%) | 1 (2.0%) |
| Microbial keratitis | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Cataract surgery | 0 (0.0%) | 1 (4.0%) | 1 (2.0%) |
| Glaucoma surgery | 1 (3.0%) | 1 (4.0%) | 2 (3.0%) |

(42.0%) in this study. The racial distribution was 55.0% Indians, 34.0% Malays, 7.0% Chinese, and 4.0% others (Iban). This distribution was consistent with a study by Bariah and associates³ that observed a higher percentage of keratoconus in Malays and Indians origin than other races.

DALK has gained popularity considering the advantages over PKP over the years. The advantages of DALK encompass less postoperative immune reaction, conserving the patient's own endothelium, thus minimising the risk of graft rejection, shorter duration of steroid usage, and elimination of complications entailing open-sky system such as expulsive haemorrhage, anterior synechiae, angle narrowing and cataract. The visual acuity outcomes were reported to be inconsistent in many studies comparing DALK and PKP,²⁰⁻²² as the inclusion criteria, follow-up criteria, and outcome measurements varied. However, in our study, PKP yielded a better postoperative visual outcome compared to DALK, which is similar to many reported studies.²³⁻³¹

Watson *et al.*²³ and Han *et al.*¹⁹ reported no significant difference in spherical equivalent and astigmatism between the 2 groups, which is consistent with our study. We found that the keratometry parameters outcomes of Sim K1, Sim K2, and K cylinder were equivalent in both groups. Similar to a previous study by Watson and colleagues, our study included several techniques under DALK; thus, DALK subgroups could not be compared to the PKP group.

Overall, most of our patients were satisfied with unaided vision, with 25% of patients requiring spectacles (3 patients in the PKP group, 4 in the DALK group) and contact lenses (3 patients in the PKP group, 5 in the DALK group) for vision optimisation.

The incidence of graft rejection and graft failure was higher in the PKP group compared to the DALK group, consistent with many reported studies. However, other complications, such as cataract and glaucoma, were not significantly different between the 2 groups. No microbial keratitis cases were reported in our study. While DALK has lower immunological response and risk of graft rejection, PKP generally yields better visual acuity and refraction as the surgical interface of DALK contributes to higher-order aberrations and astigmatism.

To the best of our knowledge, this is the first comparative corneal transplantation study for keratoconus patients in Malaysia. However, our study has some limitations. A large, randomised series of patients with detailed surgical techniques, assessment of visual function using contrast and glare sensitivity, quality of life post-keratoplasty, and longer follow-up are required.

Conclusion

Both PKP and DALK are effective treatment options for keratoconus patients. The PKP group had better postoperative BCVA outcomes. Even though PKP showed a better postoperative visual outcome compared to DALK, its disadvantages of higher graft rejection and graft failure cannot be overlooked, consistent with several reported studies. Despite DALK having a steeper learning curve for beginners and being technically more challenging, it has a distinct and higher safety profile.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH).

Competing interests

None to declare.

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