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## Review article

# Systematic review comparing penetrating keratoplasty and deep anterior lamellar keratoplasty for management of keratoconus

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### ABSTRACT

**Aim:** Perception of reduced incidence of graft rejection after deep anterior lamellar keratoplasty (DALK) has attracted many surgeons towards this technique in keratoconus. This review aims to compare the visual, refractive and graft outcomes after penetrating keratoplasty (PK) and DALK for keratoconus.

**Methods:** Electronic searches of PubMed, MEDLINE, EMBASE, Latin American and Caribbean Health Sciences Literature database (LILACS), metaRegister of Controlled Trials (mRCT), ClinicalTrial.gov and the WHO International Clinical Trials Registry Platform (ICTRP) were performed. We included randomized control trials (RCTs) and comparative studies to assess primary and secondary outcomes after PK and DALK in eyes with keratoconus. Primary outcome was best-corrected visual acuity (BCVA) LogMAR at  $\geq 6$  months. Secondary outcomes included number of patients with BCVA  $\geq 0$  LogMAR, uncorrected visual acuity (UCVA) LogMAR, spherical equivalent (SE), refractive and keratometric astigmatism, endothelial cell density (ECD) cell/mm<sup>2</sup>, graft rejection and graft survival.

**Results:** Eighteen studies (including 2 RCTs) compared DALK (965 eyes) and PK (2402 eyes) for keratoconus. There was strong evidence through RCTs suggesting better LogMAR BCVA at  $\geq 6$  months and better LogMAR UCVA with PK; reduced refractive astigmatism and rejection with DALK and no difference in SE and keratometric astigmatism. Moreover, there was weak evidence to suggest better BCVA  $\geq 0$  LogMAR after PK and no difference in ECD between the two techniques.

**Conclusions:** Despite the popularity of DALK amongst corneal surgeons for keratoconus, there is a paucity of high quality RCTs. The existing limited evidence confirms reduced rejection and refractive astigmatism with DALK but better visual outcomes with PK. Internationally agreed data sets and follow-up protocol are warranted.

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**1. Introduction**

In keratoconus, visual rehabilitation can be achieved with spectacles and contact lens correction, whereas, progression can be arrested by corneal crosslinking and advanced cases need a conventional penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK).

PK has been performed for management of keratoconus for over 7 decades [1,2]. Literature shows that keratoconus is one of the most common indications for PK and the recipients have higher graft survival in keratoconus irrespective of whether the graft was same size or over sized [3,4]. DALK has gained popularity in past one and half decades [5–11]. Although DALK is generally a longer procedure it has attracted a lot of interest from surgeons due to its claims of fewer allogeneic endothelium rejection episodes so much so that it has been reported to have good outcomes even after hydrops [12]. In the literature DALK has been broadly classified as pre Descemet where a small amount of posterior stroma is left intact along with Descemet’s membrane and Descemet DALK achieving dissection to bare Descemet’s membrane. Several techniques have been employed to achieved these dissections including big bubble technique [13] using hydrodissection [14], viscodissection [15], manual dissection [16] and Femtosecond laser [17–19].

There is some evidence that surgeon’s learning curve may affect the outcomes of DALK procedure [20]. Coster et al. in an Australian registry study observed a decrease in PK procedures and a rise in DALK procedures for keratoconus from 1996 to 2012 and that graft survival and visual outcomes were significantly better with PK<sup>2</sup>. Advocates of DALK procedure believe that DALK has better outcomes overall in comparison of PK. Studies comparing the outcomes of PK versus DALK have varying inclusion and follow-up criteria. Moreover, the number of randomized studies is sparse and underpowered to detect any meaningful difference [21]. We designed this review to compare the outcomes of PK and DALK for management of keratoconus with set inclusion, exclusion and follow-up criteria.

**2. Methods**

*2.1. Eligibility criteria for contributing studies for the review*

*2.1.1. Inclusion criteria*

For the purposes of this review, DALK was defined as the replacement of anterior cornea down to Descemet’s membrane regardless of the surgical method used including pre Descemet and Descemet DALK techniques.

Patients of any age or gender diagnosed with keratoconus of any grade were included. Studies with sample size of at least 22 eyes in each intervention were included for meta-analysis for the primary outcome, post-operative best-corrected visual acuity (BCVA). Based on the BCVA data published in previous studies [6,22] a

sample size of 22 in each arm was needed to detect a minimum difference of 0.05 BCVA LogMAR with a statistical power of 80% and significance of 5%. We included randomized controlled trials (RCTs) and non-randomized comparative studies (nRCS) directly comparing PK with DALK for keratoconus. Studies reporting at least one of the primary or the secondary outcomes described below were eligible for inclusion.

*2.1.2. Exclusion criteria*

Exclusion criteria of hydrops, corneal scarring and history of confounding disorders were applied. Studies were excluded if they were non-comparative studies, case reports or if they lacked data on any primary or secondary outcomes for this meta-analysis.

*2.2. Primary and secondary outcomes*

Characteristics extracted from each study included the surname of the first author, the year of publication, journal of publication, the country of participants, number of participants, gender, mean age, type of keratoplasty, size of graft and bed, average length of follow up and time to suture removal.

Primary outcome:

1. Postoperative best-corrected visual acuity (BCVA) LogMAR at 6 months or more. Latest LogMAR BCVA was considered when the follow-up was longer than 6 months.

Secondary outcomes:

1. Number of patients with BCVA  $\geq$  0 LogMAR at 12 months follow-up
2. Postoperative uncorrected visual acuity (UCVA) LogMAR at 12 months
3. Spherical equivalent (SE) dioptres at the latest follow up examination
4. Refractive astigmatism (dioptres)
5. Keratometric astigmatism (dioptres)
6. Endothelial cell density (ECD) cell/mm<sup>2</sup> at 12 months follow up
7. Graft rejection episodes
8. Graft survival

*2.3. Search methods for identifying studies*

Electronic searches of PubMed, MEDLINE, EMBASE, Latin American and Caribbean Health Sciences Literature database (LILACS), metaRegister of Controlled trials (mRCT), ClinicalTrial.gov and the WHO International Clinical Trials Registry Platform (ICTRP) were performed up to January 2015. English language restrictions were applied to the searches. See Appendices for details of search strategies for PubMed (Appendix 1), MEDLINE (Appendix 2), LILACS (Appendix 3), mRCT (Appendix 4), [ClinicalTrials.gov](http://ClinicalTrials.gov) (Appendix 5) and ICTRP (Appendix 6). Reference lists of relevant studies were searched to identify additional studies. The search

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