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Main issues in deep anterior lamellar keratoplasty: A systematic narrative review

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Abstract:

Deep anterior lamellar keratoplasty (DALK) has emerged as a transformative approach in managing corneal pathologies, notably keratoconus (KC), providing a viable alternative to penetrating keratoplasty (PK). This systematic review explores the intricacies of DALK, comparing its preoperative, intraoperative, and postoperative considerations with PK. Extensive literature searches revealed a wealth of data regarding DALK's advantages and challenges, with an emphasis on graft survival, visual outcomes, and complications. In the preoperative phase, DALK showcases its versatility, catering to a wide spectrum of patients, including those with KC and ocular surface disorders. Intraoperatively, it offers innovative techniques to address emphysema, bubble formation, and Descemet's membrane perforation, all while maintaining a strong focus on patient-centered outcomes. Postoperatively, DALK's lower rejection rates and decreased complications underscore its potential superiority over PK, although unique challenges such as graft failure from nonimmunologic factors demand vigilant management. This comprehensive review not only serves as a valuable resource for ophthalmic surgeons but also sheds light on the evolving landscape of corneal transplantation, highlighting DALK's role as a transformative force in the field.

Keywords:

Cornea, femtosecond, keratoconus, keratoplasty, lamellar

Introduction

Keratoconus (KC), a bilateral corneal disorder characterized by progressive thinning and asymmetry, presents a formidable challenge in the realm of ophthalmology. This condition leads to corneal protrusion, severe myopia, and irregular astigmatism.[1] While early stages are typically managed with corrective lenses, advanced cases often necessitate corneal transplantation, making KC a leading indication for such procedures in 10%–20% of cases.[2] Conventionally, penetrating keratoplasty (PK) served as the gold standard for addressing various corneal pathologies, including KC, demonstrating commendable graft survival rates.[3] However, PK was marred by complications, including the risk of endothelial rejection, endothelial cell loss, and various postoperative issues.[4]

Recent years have witnessed a transformative shift in corneal transplantation, heralded by the introduction of deep anterior lamellar keratoplasty (DALK). DALK represents a novel approach, selectively replacing the affected corneal stroma while preserving the healthy endothelium. This technique circumvents many of the complications associated with PK, such as suprachoroidal hemorrhage, and offers a smoother postoperative course due to the absence of endothelial rejection. Moreover, DALK provides greater flexibility in donor tissue selection criteria. These advantages, coupled with reduced postoperative endothelial cell loss, position DALK as an attractive

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alternative to PK, particularly for patients at a heightened risk of graft rejections.[5,6]

DALK has demonstrated promising long-term visual outcomes across a spectrum of conditions, encompassing KC, stromal scars, corneal dystrophies, and herpetic keratitis.[7] Notably, it is the preferred choice for individuals with compromised mental capabilities (e.g. Down's or Turner's syndrome), as it mitigates the risk of graft rejection and ocular harm resulting from self-inflicted trauma or eye rubbing.[8] Conversely, cases involving ocular surface disorders like limbal stem cell failure are regarded as "relative" contraindications to DALK. However, the combination of ocular surface procedures with DALK has proven effective in facilitating visual recovery in such scenarios. With its reduced susceptibility to immune-based rejection, decreased dependence on topical medications, and a more straightforward approach to repeat DALK procedures, this technique offers enhanced prospects for graft survival compared to PK.[9]

This systematic review delves into the intricacies of DALK, exploring its diverse surgical methods and addressing the inherent challenges within each technique. Furthermore, it underscores the emerging developments and advantages of DALK when juxtaposed with PK. The review provides a comprehensive overview of the preoperative, intraoperative, and postoperative factors entailed in DALK procedures, with the ultimate aim of equipping ophthalmic surgeons with the knowledge needed to make informed decisions. By doing so, it strives to improve patient outcomes within the ever-evolving landscape of corneal transplantation.

Methods

A systematic and comprehensive search of the literature was meticulously conducted to identify relevant studies for this systematic review. Electronic databases, including PubMed, Cochrane, Web of Science, Scopus, and Embase, were extensively scrutinized to identify publications from January 2018 to July 2023. In addition, a supplementary search was carried out to ensure the inclusion of all pertinent studies. The search strategy was thoughtfully designed to encompass research related to DALK and its comparative analysis with PK in the treatment of corneal pathologies, with a specific emphasis on KC. The search strategy incorporated Medical Subject Headings terms and keywords to identify relevant publications. Figure 1 shows a visual representation of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This systematic review was prospectively registered in the PROSPERO International Prospective Register of Systematic Reviews (CRD42024497756).

Inclusion criteria encompassed original research articles, systematic reviews, and meta-analyses that involved human subjects, availability of relevant data, and adherence to the specified period. Exclusion criteria consisted of conference abstracts, studies lacking pertinent outcome data and relevance, and nonhuman subjects. To ensure the robustness of the review, two independent reviewers conducted the initial screening of identified studies. Subsequently, full-text of potentially relevant studies were subjected to thorough examination for eligibility.

Data extraction was conducted with precision, capturing essential study characteristics, patient demographics, surgical techniques employed, visual outcomes, graft survival rates, and complications. In instances where discrepancies in data extraction emerged, a consensus was achieved through discussion and evaluation.

A qualitative synthesis of the included studies was performed, with a specific focus on analyzing the fundamental aspects related to DALK in comparison to PK. This synthesis allowed for a comprehensive exploration of the advantages and limitations associated with DALK, particularly within the context of KC and other corneal pathologies. The review aimed to shed light on the intricate details of these surgical procedures, highlighting variations in outcomes and elucidating the key factors influencing graft survival and postoperative complications.

Results

DALK is a surgical technique that entails the excision of a substantial portion of the corneal tissue while preserving the Descemet's membrane (DM) and the corneal endothelium. Subsequently, a donor corneal graft is sutured in place, excluding the DM layer from the grafting process.[8] DALK offers versatility as it can be adapted to address complex cases involving intracorneal ring segments,[9,10] prior radial keratotomy procedures,[11] anterior lamellar keratoplasty,[12] and even cases where patients have previously undergone Descemet's stripping automated endothelial keratoplasty surgeries.[9] Notably, in instances where patients have a history of PK, stromal replacement can be accomplished by delicately peeling the stromal layer along a naturally occurring separation plane.[13]

Anesthetic approach

For the majority of patients, DALK can be safely conducted as an outpatient procedure under the supervision of monitored anesthesia care. Various anesthesia approaches, including retrobulbar or peribulbar anesthesia employing agents such as

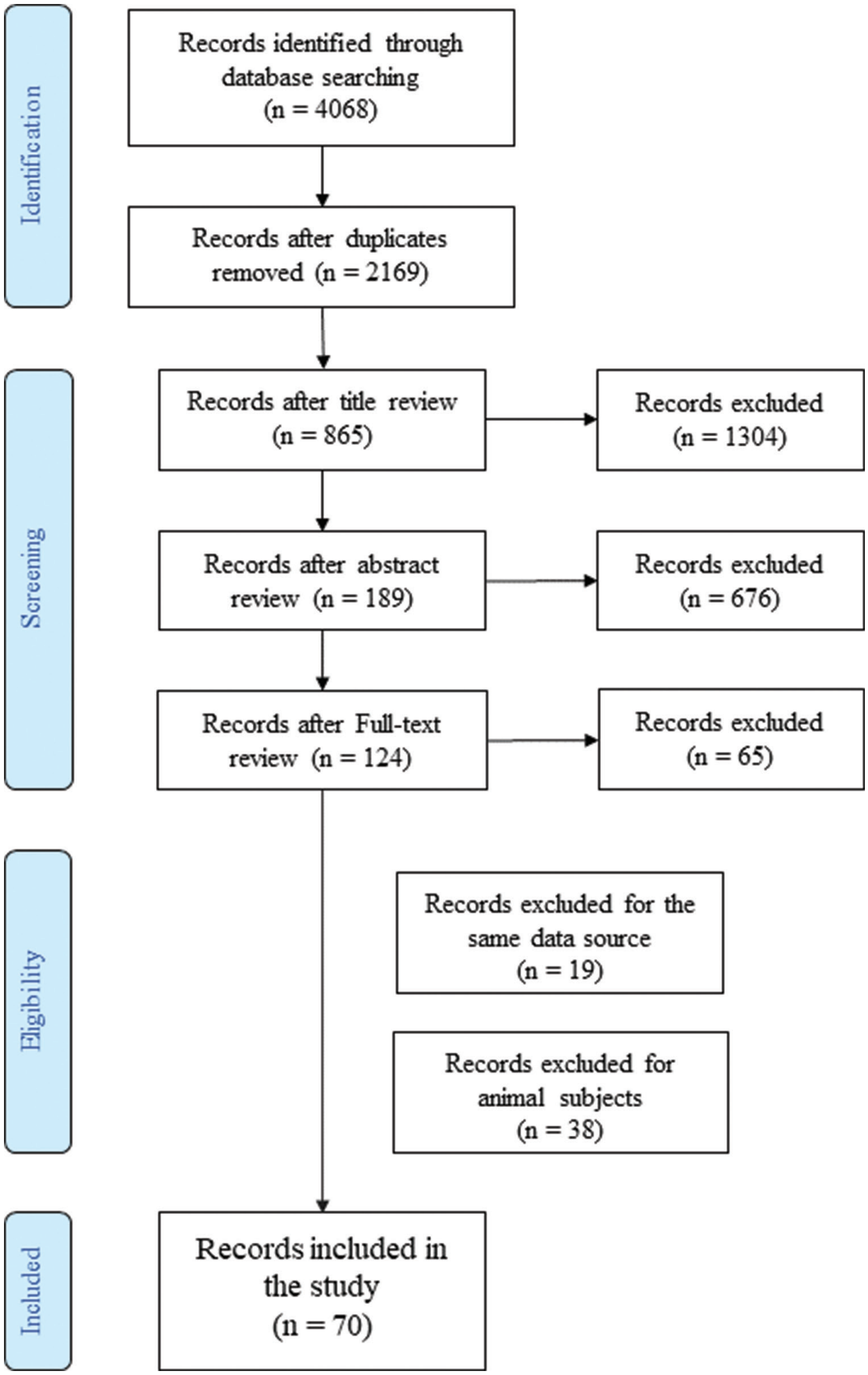

Figure 1: Preferred reporting items for systematic reviews and meta-analyses

bupivacaine, a combination of bupivacaine and mepivacaine, or lidocaine, are generally effective for this purpose. Nevertheless, there are specific scenarios, such as cases involving young individuals, individuals with mental or hearing impairments, those with communication challenges, repeat surgeries, or sensitive procedures, where the use of general anesthesia may become necessary. In situations where neither general anesthesia nor ophthalmic regional blocks are the preferred choices, local anesthesia in the form of blocks can present a viable alternative, albeit with certain limitations in its application.[14]

Preparation of donor corneal tissue

The quality of the donor corneal tissue emerges as a noncrucial factor influencing the clinical outcomes of DALK. For optimal DALK outcomes, donor corneas meeting specific criteria can be deemed safe. These criteria include donor corneas from individuals aged ≤88 years, possessing endothelial cell densities ≥1000 cells/mm², having preservation times of <2 weeks when cold storage is employed, or preservation times ≤35 days for organ culture. In addition, a preservation time postsplit before grafting of ≤96 h is considered safe for DALK procedures. It is noteworthy that donor tissue quality obtained through the corneoscleral disc excision technique is on par with that acquired through whole-globe enucleation. Both organ culture preservation and 4°C storage methods are deemed suitable for preserving donor tissues designated for DALK procedures.[15] Table 1 provides an overview of the preoperative considerations of DALK.

Host cornea trephination

The choice of trephine size in DALK should align with the extent of corneal pathology to prevent excessively large trephination. Studies suggest that using same-size donor grafts in DALK results in reduced myopia, and optical outcomes for KC are comparable to PK. The surgeon has various trephine options, including handheld and vacuum models. Proper center marking of the host cornea ensures trephine centration. The depth of trephination should be carefully verified to avoid excess pressure and prevent full-thickness trephination.[8]

Removal of superficial corneal layers

When addressing deeper corneal scars or conditions affecting the DM, it is advisable to opt for manual dissection. In instances involving KC, it is recommended to remove the outer 2/3 of the corneal lamella. This step facilitates precise needle or cannula placement for procedures such as air injection or viscodissection in the posterior stromal layers.[8] Table 2 outlines the intraoperative considerations of DALK.

Suturing techniques

Several suturing techniques can be utilized in DALK, and their depth may vary slightly compared to PK to achieve the best possible alignment between the host DM and the donor corneal button. It is advisable to remove sutures after 12–15 months to prevent wound separation and ensure favorable outcomes. Research has indicated that there is no substantial difference in postkeratoplasty

Table 1: Preoperative considerations of deep anterior lamellar keratoplasty

Preoperative Factor	Consideration
Age	Older patients are less likely to experience graft rejection due to weaker immune systems
	DALK is especially advantageous for patients with KC, who are generally younger
	For pediatric patients (>5 years), DALK has an edge over traditional PK due to lower graft failure rates. However, in very young patients (<5 years), DALK's graft failure rates are comparable to PK[16]
Co-morbidities	Prior to corneal transplantation, any ongoing inflammation or infection should be addressed, as these factors increase the risk of graft failure[17]
Crystalline lens status	The presence of a cataract affecting vision should be evaluated
	If feasible, correct the cataract before DALK. If the corneal condition doesn't permit safe cataract surgery, perform DALK first to avoid complications[18]
Cataract surgery	After DALK settles (usually 1 year postoperative), cataract surgery can be considered to correct astigmatism using a toric IOL. Simultaneous DALK and phacoemulsification is possible in cases where a type-1 big bubble is achieved. DALK involving Dua's layer allows safe phacoemulsification[19,20]
IOP	Maintaining optimal IOP levels emerges as a pivotal factor for achieving successful outcomes in DALK. Effective IOP management, whether through medical or surgical means, is a prerequisite before contemplating DALK procedures. In cases involving patients with severe ocular co-morbidities, the implementation of a glaucoma tube device may be necessary to regulate and stabilize IOP levels[21]
Retinal status	Prior to DALK, assess macula and retina status using indirect ophthalmoscopy
	In cases where a clear view is hindered, techniques like OCT or ultrasound B-scan can be used. Potential acuity meter testing aids in estimating postoperative visual potential[8]
Recipient-related factors	A comprehensive assessment of the eyelids and ocular surface represents a critical aspect of ensuring favorable graft outcomes, particularly in scenarios involving ocular surface disorders. This evaluation encompasses techniques such as staining and impression cytology. Furthermore, it is imperative to actively manage concurrent surface conditions like exposure keratitis, dry eye, and meibomian gland dysfunction. Surgical interventions aimed at correcting lid margin and tarsal plate issues have been shown to significantly contribute to the enhancement of graft survival rates[17,22]
Meibomian gland dysfunction	Manage meibomian gland dysfunction with lid hygiene, antibiotics, corticosteroids, and oral doxycycline as needed[23]
Limbal stem cell deficiency	In cases of limbal stem cell deficiency with normal endothelium, DALK offers the advantage of performing both stem cell and corneal transplantation simultaneously
	Various transplantation techniques can be employed[24]

IOL=Intraocular lens, DALK=Deep anterior lamellar keratoplasty, IOP=Intraocular pressure, OCT=Optical coherence tomography

Table 2: Intraoperative considerations of deep anterior lamellar keratoplasty

Intraoperative Factor	Considerations
Extensive emphysema	Inadequate needle placement can lead to emphysema of the posterior corneal lamella
Inability for big bubble	If big bubble can't be achieved, manual dissection techniques can be employed or microbubble incision may be used as a rescue technique[25]
Achieving double bubble simultaneously	Inadequate needle placement during the procedure can lead to the simultaneous formation and rupture of both type 1 and type 2 bubbles. Even if the type 2 bubble bursts into the anterior chamber, it is possible to preserve the integrity of the initial type 1 bubble. Following this, the surgery proceeds with the removal of the posterior lamella flap and subsequent suturing[25]
DM perforation	DALK's frequent complication is DM perforation. Various measures like suturing, stromal patching, fibrin glue, or conversion to manual dissection can be used for management. The size and timing of perforation matter
	Most microperforations can be managed by tamponade and controlled air injection. Peripheral air injection is a modification that increases big bubble formation. Macroperforations may require conversion to full thickness PK for better outcomes. Double anterior chamber may arise postoperative from microperforation, resolving spontaneously. Retained host DM can cause detachment, which can often self-reattach. Failed air tamponade or double chamber due to DM perforation might resolve well[26-29]
Correct bubble identification	Identifying bubble type in pneumatic dissection is crucial
	Type 2 bubble is a risk for double chamber and conversion to PK
	Type 2 bubble is fragile due to thin DM, favoring dissection techniques[30-33]
Recipient-related factors	Intact donor epithelium on day 1 improves graft outcome. For patients suffering from ocular surface disorders, keeping donor epithelium intact is beneficial
	Gentle donor DM removal and proper suturing ensure smooth graft migration and tear meniscus maintenance[34,35]
Graft rejection	Treatable etiologies of graft failure after DALK
	Intraoperative DM perforation
	Postoperative DM nonattachment
	Interface wrinkling
	Interface haziness

DM=Descemet's membrane, DALK=Deep anterior lamellar keratoplasty, PK=Penetrating keratoplasty

astigmatism in advanced KC patients when employing various suturing methods after suture removal.[36] Table 3 provides an overview of the postoperative considerations of DALK.

Progress in corneal imaging and surgical instruments has enhanced the traditional big-bubble technique. The use of anterior segment optical coherence tomography has enabled accurate measurements and guided trephination [Figure 2]. Increasing the diameter and depth of trephination has shown to enhance the success rate of big-bubble formation, particularly in large-diameter DALK procedures.[43,44] These findings collectively provide a comprehensive overview of the key aspects of DALK, from preoperative considerations to intraoperative techniques and postoperative care, highlighting its adaptability and potential benefits in the treatment of various corneal pathologies.

Discussion

Currently, DALK is classified into two primary types: pre-Descemetic DALK, where a portion of the posterior stroma is retained along with the DM, and Descemetic DALK, which involves dissection up to the DM. Several techniques have been developed for deep lamellar dissection in DALK, including pneumatic dissection, the big-bubble DALK (BB-DALK) technique, hydrodelamination, viscoelastic-assisted dissection, the Melles technique, and femtosecond laser-assisted techniques.[45]

Big-bubble-deep anterior lamellar keratoplasty technique

The BB-DALK technique has gained significant popularity, particularly in patients with KC and stromal scars. Its worth noting that the ratio of scar depth to minimal corneal thickness can serve as a predictor for DM perforation.[46] Pneumatic dissection based on air movement within the corneal stroma can create type 1 and type 2 bubbles. Successful pneumatic dissection relies more on proper air injection depth than the distance of the cannula from the cornea center.[47] Challenges in BB-DALK include achieving precise cannula placement near the DM and overcoming adhesions in scar tissue. Modifications have been introduced to enhance the formation of the big bubble.[48]

Manual dissection technique

The manual dissection technique involves injecting air into the anterior chamber to visualize the posterior corneal stroma. This method is suitable for thick corneal scars, such as those resulting from infection or hydrops. Proper trephine size and depth are crucial, and the layers are dissected to the pre-Descemetic level. While it is considered safe for pediatric cases, it may not always guarantee functional recovery due to amblyopia.[49] Air-assisted manual dissection has demonstrated efficacy

Table 3: Postoperative considerations of deep anterior lamellar keratoplasty

Postoperative Factor	Considerations
Visual rehabilitation	Visual recovery postsurgery may extend beyond a year
	Patients might require additional interventions such as spectacles, lenses, or surgeries such as keratorefractive surgery or intraocular surgery[8]
Shallow DM detachments	Minor detachments of DM often resolve on their own
	Larger detachments may necessitate surgical intervention, involving fluid drainage or air/gas injection
Graft rejection	
Interface complications	Surgical interface complications include DM perforation, double chamber formation, wrinkling, and haziness
	DM perforation risk depends on surgical techniques, conditions, and surgeon experience[29]
Epithelial abnormalities	Maintaining graft epithelial integrity is crucial for clarity
	Abnormalities include punctate keratopathy, filamentary keratitis, and defects
	Recognition and treatment are vital for graft longevity[37]
Donor-related factors	Donor-related factors such as diabetes, storage media, and quality influence graft epithelium. Longer preservation time may increase epithelial defects. Appropriate tissue selection is important[38]
Recipient-related factors	The recipient's ocular surface health, eyelid conditions, and tear film quality impact graft epithelial health
	Preexisting dry eye and limbal stem cell deficiency can hinder recovery
Surgical factors	Surgical technique affects graft epithelium
	Proper alignment and sutures are vital for epithelial healing
	Incorrect suturing can hinder healing and graft integration[36]
VKC	Patients with VKC have a higher risk of graft rejection
	Surgery should be scheduled during quiescent periods, and careful postoperative monitoring is essential[8]
Corneal graft neovascularization	Corneal neovascularization, often caused by various conditions, can lead to graft failure and rejection
	Strategies such as anti-VEGF therapies and laser treatments help control vascularization[39]
Postoperative care	Graft epithelial healing is facilitated by postoperative care, including discontinuing harmful eye drops, using antibiotics, lubricants, and artificial tears, and sometimes using contact lenses[40,41]
Recurrence of HSK	DALK for HSK is beneficial but carries a risk of recurrence
	Prophylactic oral acyclovir for a year helps minimize recurrence risk, but follow-up is necessary[42]

VKC=Vernal keratoconjunctivitis, HSK=Herpes simplex keratitis, VEGF=Vascular endothelial growth factor, DM=Descemet's membrane, DALK=Deep anterior lamellar keratoplasty

in cases of scarring due to inflammation and fibrosis, with confocal microscopy supporting comparable results.[8,50]

Hydrodelineation and viscodissection techniques

Hydrodelineation involves injecting a balanced salt solution into the stroma to induce localized thickening and is employed when the big-bubble technique is unsuitable. Subsequent layer-by-layer dissection follows.[8,51] Viscodissection involves the creation of deep dissection using sharp or blunt instruments, creating a posterior stromal nick, or utilizing forceps before injecting an ophthalmic visco-surgical device (OVD) with a blunt cannula. The OVD fills the gaps between the deep stroma, thus easing the dissection process.[52,53]

Femtosecond laser-assisted deep anterior lamellar keratoplasty

Femtosecond laser-assisted DALK provides precise tissue depth identification and aids in creating the big bubble by injecting air at a predetermined pre-Descemet plane. This approach leads to improved wound fitting, which in turn accelerates the healing process and reduces astigmatism. For some practitioners, it is considered technically simpler and more effective than manual DALK. In the initial reports, zigzag incisions were even employed to achieve specific wound configurations.[54-56]

The versatility of surgical techniques in DALK underscores the adaptability of the procedure to different clinical scenarios. BB-DALK, manual dissection, hydrodelineation, viscodissection, and femtosecond laser-assisted DALK, each offers distinct advantages and considerations, making them valuable tools in the surgeon's armamentarium for addressing a wide range of corneal pathologies. The choice of technique should be guided by the specific characteristics of the patient's condition and the surgeon's expertise.

Comparison between deep anterior lamellar keratoplasty and penetrating keratoplasty

While DALK offers numerous advantages over PK for treating corneal pathologies like KC, it is important to note that graft failure in DALK can result from nonimmunologic factors, such as persistent postoperative double anterior chamber, haziness of the surgical interface, graft epithelial abnormalities, infectious keratitis, recurrence of primary pathology within the graft (including corneal dystrophies), graft vascularization, and scarring. In addition, subepithelial and stromal graft rejection may still occur postoperatively, potentially leading to lamellar graft failure.[8] Unlike PK, which often relies on immunosuppressive therapy to mitigate endothelial graft rejection, DALK's graft

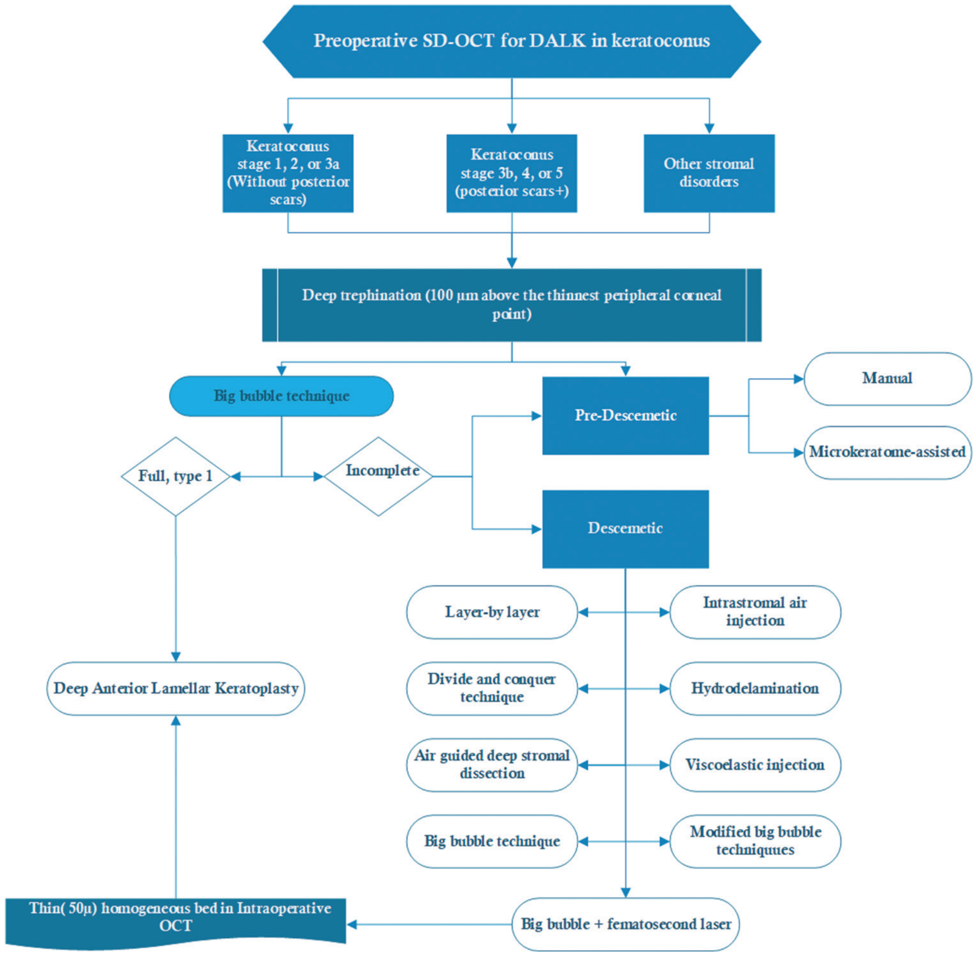

Figure 2: Preoperative optical coherence tomography-guided management for deep anterior lamellar keratoplasty in keratoconus. OCT = Optical coherence tomography, SD-OCT = Spectral domain OCT, DALK = Deep anterior lamellar keratoplasty

survival predominantly depends on optimizing the ocular surface to create a suitable environment for graft success. Effective management of interface-related complications and stromal graft rejection is crucial for achieving favorable visual and anatomical outcomes.[8]

Visual outcomes

Research findings on the comparison of visual outcomes between DALK and PK are varied. Some studies indicate similar outcomes between the two procedures,[57-60] while others suggest superior visual outcomes after PK.[61] Despite the distinct learning curve associated with DALK and the differences between DALK and conventional full-thickness PK, DALK still offers advantages over the latter, primarily in terms of avoiding graft failure due to endothelial rejection.[8]

Graft survival and complications

Existing literature demonstrates relatively similar outcomes in terms of graft survival and complications between DALK and PK among KC patients during the 3–8 years following surgery. Specifically, DALK failure rates range from 6.1% to 10%, while PK failure rates vary between 6.0% and 28%.[62,63] Notably, the incidence of rejection tends to be higher in PK, with no reported cases in DALK and a 6% rejection rate for PK.[64] Furthermore, postoperative cataract and glaucoma surgeries are more frequently necessary following PK than DALK.[65] A recent meta-analysis of clinical trials also found no instances of endophthalmitis or expulsive hemorrhage associated with DALK. Likewise, the rates of infectious keratitis are similar between DALK and PK in KC patients, ranging from 0% to 8% for DALK and from 0% to 5.8% for PK. Overall, postoperative complications such as cataracts, graft rejection, graft failure, high intraocular pressure, and corneal infection are more frequently observed in PK than in DALK.[66-68]

Advantages of deep anterior lamellar keratoplasty

DALK presents significant advantages when compared to traditional full-thickness PK, mainly due to its extraocular nature. By preserving the DM, DALK sidesteps the complications associated with open-sky surgery, thus maintaining the structural integrity of the eye.[8] In contrast to PK, DALK effectively eliminates the risk of immune-mediated endothelial graft rejection and the consequent graft failure, contributing to outstanding cumulative survival rates and anticipated higher endothelial cell densities.[63,69] These distinct advantages position DALK as an appealing choice for addressing corneal pathologies, particularly in scenarios like KC, where the threat of endothelial graft rejection significantly jeopardizes graft longevity.

Conclusion

DALK represents a versatile and valuable surgical approach for addressing a variety of corneal pathologies. The procedure's capacity to selectively replace the anterior corneal layers while preserving the DM and endothelium offers distinct advantages, particularly in cases of KC and stromal scars. Throughout this manuscript, we have explored the intricacies of DALK, including different surgical techniques such as the big-bubble technique, manual dissection, hydrodelineation, viscodissection, and femtosecond laser-assisted DALK. Each of these approaches presents unique strengths and considerations, providing ophthalmic surgeons with a range of tools to tailor their interventions to the specific needs of patients. The ongoing advancements in imaging technologies and surgical tools continue to refine and expand the capabilities of DALK, positioning it as a valuable option for achieving optimal corneal outcomes.

Key takeaways

- DALK offers a tailored approach to corneal pathologies by selectively replacing the anterior corneal layers
- Various surgical techniques, including the big-bubble technique, manual dissection, hydrodelineation, viscodissection, and femtosecond laser-assisted DALK, cater to diverse clinical scenarios
- The choice of DALK technique should be guided by the individual patient's condition and the surgeon's expertise
- Advances in imaging and surgical technologies continually enhance the precision and outcomes of DALK
- DALK remains a valuable tool in the ophthalmic surgeon's armamentarium for achieving successful corneal transplantation.

Data availability statement

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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Conflicts of interest

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