Deep anterior lamellar keratoplasty for keratoconus: Elements for success

Marco Pellegrini[1,2,3], Angeli Christy Yu[1,2,3], Massimo Busin[1,2,3]

Access this article online

Quick Response Code:

Website: www.saudijophthalmol.org

DOI: 10.4103/sjopt.sjopt_100_21

Abstract:

Advanced keratoconus may require keratoplasty when the patient can no longer achieve functional vision with glasses and contact lenses. Deep anterior lamellar keratoplasty (DALK) has become the surgical treatment of choice due to its undisputed advantages over penetrating keratoplasty including the reduced risk of intraoperative complications, the absence of endothelial immune rejection, and the longer graft survival. Albeit "big-bubble" DALK still represents the most popular surgical method, several modifications have been developed over the years. This allowed standardization of the technique, with improved success rates and clinical outcomes. This review presents an overview on the literature on DALK surgery for keratoconus. We discuss state-of-the art surgical techniques, current evidence on the clinical outcomes and complications as well as possible future directions.

Keywords:

DALK; Deep anterior lamellar keratoplasty; Keratoconus

Introduction

Keratoconus is a progressive ectatic disorder in which the cornea assumes a conical shape due to thinning and protrusion. This leads to irregular astigmatism, myopia, and visual impairment.[1] Keratoplasty is usually required in advanced stages of the disease when the patient can no longer achieve functional vision with glasses and contact lenses.[2]

Penetrating keratoplasty (PK) has been considered the mainstay of surgical treatment for decades.[3] More recently, deep anterior lamellar keratoplasty (DALK) has become an alternative to PK, with the advantages of eliminating the risk of endothelial rejection and avoiding the complications associated with open-sky surgery.[4]

Despite these undisputed advantages, the uptake of DALK among corneal surgeons has been relatively slow, particularly in the U.S.[5] Longer surgical time, steep learning curve, and low patient volume and have been reported as the most important barriers to adoption of DALK.[6] Nevertheless, recent innovations in surgical technique, instrumentation and tissue preparation allowed standardization of DALK, with improved success rates even for inexperienced surgeons.[7]

This review provides an update on lamellar keratoplasty for keratoconus. Three key aspects will be covered: The rapidly changing techniques of modern lamellar surgery; the current evidence on the clinical outcomes and complications; the possible future developments in this evolving specialty.

Surgical Technique

Different techniques to perform DALK have been proposed, including layer-by-layer manual dissection, pneumatic dissection, and viscoelastic-assisted dissection.[8-10] The method of pneumatic dissection through injection of a "big bubble" described by Anwar[9] represents the most popular surgical method. The technique involves partial-thickness trephination of the corneal stroma followed by forceful injection of air into the deep stroma through a needle or cannula to form a "big bubble" [Figure 1a and b]. After anterior keratectomy, the roof of the bubble is then incised under viscoelastic protection and

[1]Department of Translational Medicine, University of Ferrara, [2]Department of Ophthalmology, Ospedali Privati Forlì "Villa Igea" [3]Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO), Forlì, Italy

Address for correspondence:
Prof. Massimo Busin, Ospedali Privati Forlì 'Villa Igea', Forlì 47122, Italy.
E-mail: mbusin@yahoo.com

Submitted: 03-May-2021
Accepted: 20-Dec-2021
Published: 11-Jul-2022

How to cite this article: Pellegrini M, Yu AC, Busin M. Deep anterior lamellar keratoplasty for keratoconus: Elements for success. Saudi J Ophthalmol 2022;36:36-41.

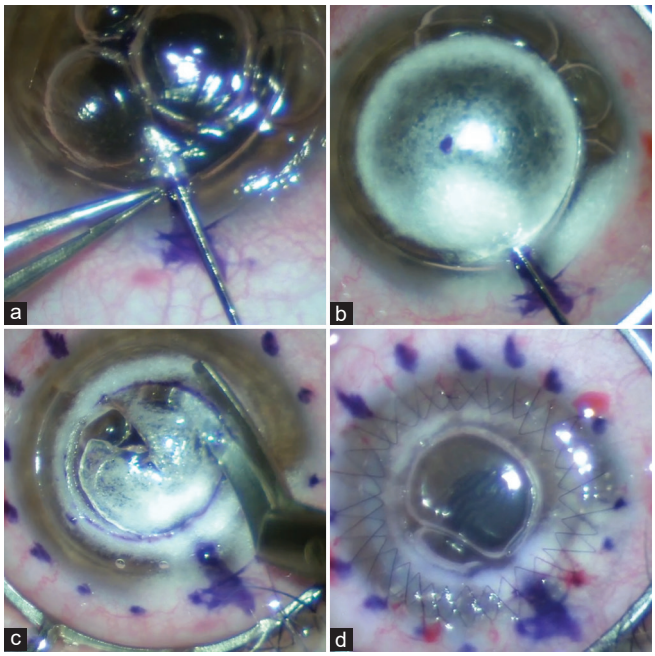

Figure 1: Surgical technique for deep anterior lamellar keratoplasty. After 9 mm partial thickness trephination, a Fogla cannula is inserted at the base of trephination and advanced centripetally (a); air is injected into the deep stroma to obtain a big bubble (b); after anterior keratectomy, the roof of the bubble is excised with corneal scissors limiting the stromal clearance to the central 6 mm optical zone (c); the graft is sutured into place using 16-bite double running sutures (d)

the remaining stroma is excised using blunt scissors [Figure 1c]. Finally, the donor tissue is punched and sutured into place using interrupted or running sutures [Figure 1d].[11,12]

To maximize the likelihood of pneumatic dissection, the cannula should be inserted as deep as possible, with over 90% success rate if air is injected within 100 μm of the posterior corneal surface.[13] The feeling of decreased tissue resistance to the advancement of the cannula usually indicates that depth is appropriate. Pupil dilation and use of the intraoperative red reflex may also help to judge the depth of dissection.[14] To standardize this surgical step, preoperative anterior segment optical coherence topography (OCT) is useful to map corneal thickness and calibrate the trephine within 100 μm from the thinnest pachymetric value at the site of trephination.[15,16] This allows insertion of the cannula at the appropriate depth, thus limiting the required centripetal advancement to 1–2 mm.[16]

The separation plane obtained with pneumatic dissection may differ, with three possible bubble types: type 1 bubble starts at the center, extends centrifugally, and consists of a plane of separation between the stroma and the pre-Descemet's layer; type 2 bubble starts at the periphery, extends centripetally and consists of a plane of separation between the pre-Descemet's layer and the Descemet's membrane; finally, both types can coexist to form a mixed-bubble.[17,18] Type 2 bubbles are very fragile due to the floor consisting only of Descemet's membrane, and this results in a high rate of perforation and conversion to PK.[19] Moreover, they are associated with increased risk of postoperative double anterior chamber formation.[20] Older age and advanced stages of keratoconus were recently recognized as important predictors of type 2 bubble formation.[21]

When pneumatic dissection fails, viscoelastic may be injected into the stromal tunnel used for pneumatic dissection to obtain a viscobubble.[22,23] Although retained viscoelastic in the interface may transiently reduce visual acuity in the 1st month after surgery, the long-term outcomes are comparable to those obtained with pneumo-\dissection.[23] In case viscoelastic-assisted dissection also fails, careful layer-by-layer manual dissection may be attempted.[24] This technique is associated with increased risk of perforation but can achieve good visual outcomes if the residual stromal bed is <20 μm.[25]

Performing large 9 mm DALK offers several advantages including providing superior refractive outcomes with more regular astigmatism[11,26] and maximizing removal of the ectatic with lower risk of late recurrence of ectasia.[27] Following large trephination, removal of the deep stroma may be limited to the central 6 mm optical zone.[11] This reduces the risk of perforation during hand dissection when the bubble does not reach the trephination. Moreover, the crown of deep stroma surrounding the central optical zone protects from inadvertent recipient bed perforation during suturing and confers higher mechanical stability due to the large surface of contact between the host and donor tissue.[11] Figure 2 shows a representative case of a patient with keratoconus treated with 9 mm DALK with clearance of a 6-mm optical zone.

Intraoperative macroperforation of the Descemet's membrane may require conversion to PK in 15%–35% of cases.[28-31] Occurrence of a type 2 bubble, manual dissection, presence of scarring and surgeon inexperience have been identified as independent risk factors for the need to conversion of intended DALK to PK.[31] Should conversion to PK be required, rather than a 9-mm PK, a two-piece mushroom keratoplasty may be performed.[32] This technique minimizes the endothelial transplant to the posterior 6 mm lamella while benefitting from the refractive advantages of a large 9 mm anterior lamella with excellent 5-year visual outcomes.[33]

Clinical Outcomes

One of the potential concerns of DALK is the presence of a graft-host interface which may cause light scattering and affect vision.[34] Studies comparing the visual outcomes after PK and DALK have been inconsistent.[35-43] Early reports documented inferior visual outcomes with DALK.[35-37] However, advancement in surgical techniques have allowed to obtain a thin residual stroma and a smooth interface with improved vision.[9,34,42] Three randomized controlled trials comparing big-bubble DALK and PK have demonstrated similar visual outcomes of the two procedures [Table 1].[38,39,43]

Although several studies have shown comparable short-term graft survival between DALK and PK,[35,40,41,44] patients with

Table 1: Randomized controlled trials comparing big bubble deep anterior lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus

Study	Country	Number eyes	Final BCVA	Corneal astigmatism
Javadi *et al*. 2011	Iran	42/35	0.18 versus 0.15 logMAR (NS)	3.89 verses 4.36 D (NS)
Cheng *et al*. 2011	Netherlands	28/28	0.39 versus 0.31 logMAR (NS)	3.57 verses 4.16 (NS)
Söğütlü Sari *et al*. 2012	Turkey	99/75	0.18 versus 0.14 logMAR (*P*=0.09)	3.16 verses 3.67 (NS)

BCVA: Best-corrected visual acuity, NS: Not significant

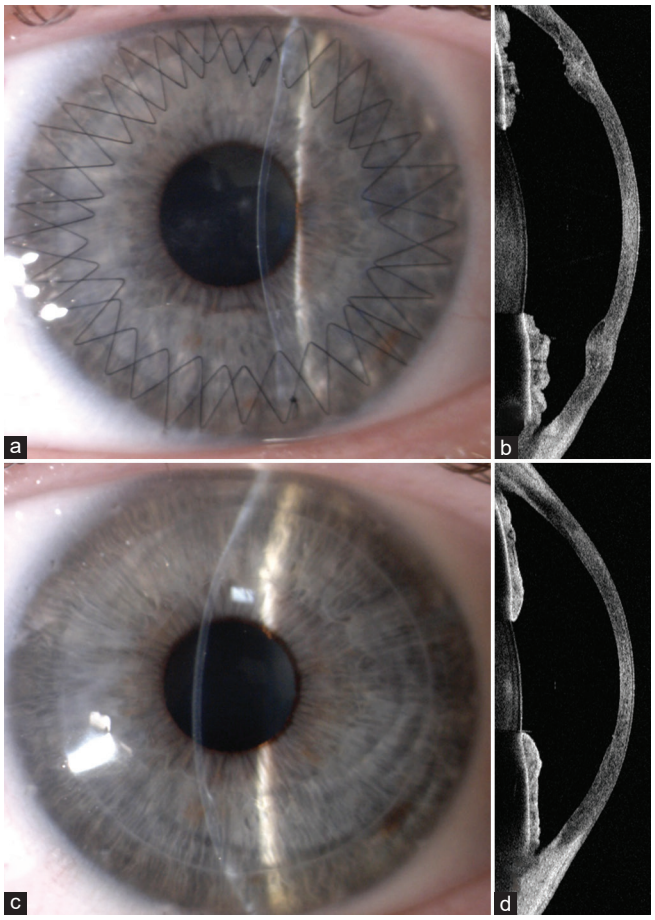

Figure 2: Representative case of a patient with keratoconus treated with deep anterior lamellar keratoplasty. 1 month postoperatively with both running sutures still in place (a); anterior segment optical coherence tomography showing the peripheral stromal shoulder surrounding the 6 mm central optical zone (b); 2 years postoperatively after complete suture removal (c); anterior segment optical coherence tomography showing disappearance of the peripheral shoulder due to stromal thinning and remodeling (d)

keratoconus undergoing keratoplasty are usually young, which makes long-term survival necessary. A recent large series demonstrated a significantly higher 10-year survival rate for DALK (94%) compared to PK (72%).[45] Moreover, based on the rate of endothelial cell loss, a statistical model was use to predict a median survival of 49 years for DALK versus 17 years for PK.[46]

Regarding refractive outcomes, most studies reported no significant differences between DALK and PK.[35,39-41] Nevertheless, high astigmatism is common after DALK, representing an important cause of suboptimal vision despite a clear graft.[47-49] Various interventions including photorefractive keratectomy,[50] laser *in situ* keratomileusis,[51] intrastromal corneal ring segments,[52] and manual[53] or femtosecond laser-assisted[54] relaxing incisions have been used to treat postkeratoplasty astigmatism. Our DALK technique with clearance of the deep stroma limited to the central 6 mm allows deep arcuate blunt relaxing incisions within the stepped graft–host junction with minimal risk of perforation.[53] In the presence of a cataract, phacoemulsification with toric intraocular lens implantation can be performed with good visual and refractive outcomes.[55,56]

One of the advantages of DALK over PK is the excellent safety profile. In particular, the potentially serious complications that can occur during the open sky surgery (e.g., iris prolapse, choroidal effusions, and expulsive hemorrhage) are avoided with DALK.[4] The risk of immune endothelial rejection is also eliminated. Moreover, since topical steroids are usually discontinued earlier after DALK, the incidence of steroid side effects is lower. In agreement with this, a recent meta-analysis demonstrated a reduced risk of cataract and intraocular pressure elevation after DALK compared to PK.[57]

Nevertheless, there are some complications that are unique to DALK such as intraoperative perforation of the Descemet's membrane which may lead to endothelial decompensation and/or postoperative detachment of the recipient bed with double anterior chamber formation.[58] Our group has previously reported that double anterior chamber formation may also occur without a perforation and is more frequent in scarred corneas and in case of occurrence a type 2 bubble.[20] In most cases, this complication requires rebubbling of the anterior chamber to reattach Descemet's membrane.

Key Issues Moving Forward

Over the past decade, several intraoperative OCT platforms capable of providing the surgeon with extra intraoperative information have become available. Some of the potential applications of intraoperative OCT for DALK are the capacity of assessing the depth reached by the cannula prior to pneumatic dissection,[13] the thickness of the residual stromal bed,[59] as well as confirming that pneumatic dissection has successfully occurred.[60] These information have been shown to be useful in aiding surgical decision-making.[61] However, the utility of intraoperative OCT is still limited by the shadowing produced by metal instruments, the motion artifacts, and the latency

between surgeon hand movements and image motion on the screen.

The femtosecond laser is a neodymium glass laser employing ultrashort pulse durations that allows making corneal incisions at the desired depth.[62] Several previous studies have described the use of the femtosecond laser during DALK to create lamellar side cuts[63-66] and an intrastromal channel for the air injection.[67-69] To date, the additional costs associated with this technology do not seem justified by the gains in patient outcomes. In fact, a recent comparative study demonstrated similar results of manual and femtosecond laser-assisted DALK in terms of visual recovery and corneal astigmatism.[70] However, a randomized clinical trial comparing manual and femtosecond laser-assisted DALK is currently ongoing (NCT03732599).

Several years after PK for keratoconus, ectasia can re-emerge in the recipient after a period of latency.[71] DALK can be performed in these eyes to selectively replace the diseased stroma while leaving the functional endothelium in place.[72] We have recently developed a technique for DALK by simple peeling of the PK graft without any need for lamellar dissection. The technique involves 9 mm trephination followed by opening of the stromal component of the old PK wound until a natural plane of separation is found. Stromal peeling can then be performed due to the lack of adherence between the stroma of the PK graft and the underlying layers. This technique results in excellent visual outcomes while minimizing endothelial cell loss.[73]

There is an overwhelming imbalance between corneal tissue availability and demand worldwide.[74] Since corneas preserved through hypothermic storage and organ culture remain viable only for 2 and 4 weeks, techniques that can extend storage are of great interest.[75-77] In the current scenario of COVID-19 pandemic, long-term preservation of unused corneas due to cancellation of elective surgery may be particularly important to avoid tissue wastage.[78,79] Silica gel dehydration allows preservation of donor corneal stroma with maintenance of thickness, transparency, and biomechanical properties after rehydration.[80] The Veneto Eye Bank Foundation is storing and distributing dehydrated corneas for possible use in DALK. A randomized controlled trial comparing the outcomes of DALK using dehydrated versus standard organ culture stored donor corneas is currently ongoing in our center (NCT04430244).

Alternative solutions to overcome the shortage of donor corneas include the use of biocompatible materials[81] and xenograft tissues.[82] Although *in vitro* and studies with collagen-based engineered matrices and synthetic polymers have shown promising results,[83] clinical data regarding the use of these materials are still lacking. Decellularized porcine corneas have the potential to provide a scaffold for host keratocyte migration without inducing immune rejection due to the elimination of major immunogenic components.[84] Three clinical trials evaluating DALK using decellularized porcine corneas reported improved corneal transparency and visual acuity in patients with fungal[85,86] and herpetic keratitis.[87] Nevertheless, xenotransplantation is associated with important ethical dilemmas and safety concerns due to the risk of xenojenic rejection and xenozoonosis.[82]

Conclusions

DALK represents the surgical procedure of choice for advanced keratoconus. The main advantages over PK include the reduced risk of intraoperative complications and the absence of endothelial immune rejections. Big-bubble DALK is still the most popular surgical method. Recent advances in the surgical procedure have allowed standardization of the technique with improved success rates even for inexperienced surgeons.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr., Guell JL, *et al.* Global consensus on keratoconus and ectatic diseases. Cornea 2015;34:359-69.
2. Garcia-Ferrer FJ, Akpek EK, Amescua G, Farid M, Lin A, Rhee MK, *et al.* Corneal Ectasia Preferred Practice Pattern®. Ophthalmology 2019;126:P170-215.
3. Parker JS, van Dijk K, Melles GR. Treatment options for advanced keratoconus: A review. Surv Ophthalmol 2015;60:459-80.
4. Reinhart WJ, Musch DC, Jacobs DS, Lee WB, Kaufman SC, Shtein RM. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty a report by the american academy of ophthalmology. Ophthalmology 2011;118:209-18.
5. Eye Bank Association of America. 2019 Eye Banking Statistical Report. Washington, DC, USA: Eye Bank Association of America; 2019. Available from: https://restoresight.org/wpcontent/uploads/2020/04/2019-EBAA-Stat-Report-FINAL.pdf. [Last accessed on 2021 Apr 15].
6. Thanitcul C, Mathews P, Woreta FA, Akpek EK, Varadaraj V, Srikumaran D. Surgeon preference for keratoplasty techniques and barriers to performing deep anterior lamellar keratoplasty. Cornea 2021;40:1406-12.
7. Myerscough J, Bovone C, Scorcia V, Ricci-Filipovic B, Leon P, Mimouni M, *et al.* Deep trephination allows high rates of successful pneumatic dissection for DALK Independent of surgical experience. Cornea 2019;38:645-7.
8. Anwar M. Technique in lamellar keratoplasty. Trans Ophthalmol Soc UK 1974;94:163-71.
9. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. J Cataract Refract Surg 2002;28:398-403.
10. Melles GR, Remeijer L, Geerards AJ, Beekhuis WH. A quick surgical technique for deep, anterior lamellar keratoplasty using visco-dissection. Cornea 2000;19:427-32.
11. Busin M, Leon P, Nahum Y, Scorcia V. Large (9 mm) deep anterior lamellar keratoplasty with clearance of a 6-mm optical zone optimizes outcomes of keratoconus surgery. Ophthalmology 2017;124:1072-80.
12. Busin M, Mönks T, Al-Nawaiseh I. Different suturing techniques variously affect the regularity of postkeratoplasty astigmatism. Ophthalmology 1998;105:1200-5.
13. Scorcia V, Busin M, Lucisano A, Beltz J, Carta A, Scorcia G. Anterior segment optical coherence tomography-guided big-bubble technique.

Ophthalmology 2013;120:471-6.
14. Scorcia V, Lucisano A, Pietropaolo R, Savoca Corona V, Scorcia G, Busin M. Red reflex-guided big-bubble deep anterior lamellar keratoplasty: A simple technique to judge dissection depth. Cornea 2015;34:1035-8.
15. Riss S, Heindl LM, Bachmann BO, Kruse FE, Cursiefen C. Pentacam-based big bubble deep anterior lamellar keratoplasty in patients with keratoconus. Cornea 2012;31:627-32.
16. Busin M, Scorcia V, Leon P, Nahum Y. Outcomes of air injection within 2 mm inside a deep trephination for deep anterior lamellar keratoplasty in eyes with keratoconus. Am J Ophthalmol 2016;164:6-13.
17. Dua HS, Faraj LA, Said DG, Gray T, Lowe J. Human corneal anatomy redefined: A novel pre-Descemet's layer (Dua's layer). Ophthalmology 2013;120:1778-85.
18. Abdelkader A, Kaufman HE. Descemetic versus pre-descemetic lamellar keratoplasty: Clinical and confocal study. Cornea 2011;30:1244-52.
19. Goweida MB. Intraoperative review of different bubble types formed during pneumodissection (big-bubble) deep anterior lamellar keratoplasty. Cornea 2015;34:621-4.
20. Myerscough J, Bovone C, Mimouni M, Elkadim M, Rimondi E, Busin M. Factors predictive of double anterior chamber formation following deep anterior lamellar keratoplasty. Am J Ophthalmol 2019;205:11-6.
21. Scorcia V, Giannaccare G, Lucisano A, Soda M, Scalzo GC, Myerscough J, *et al.* Predictors of bubble formation and type obtained with pneumatic dissection during deep anterior lamellar keratoplasty in keratoconus. Am J Ophthalmol 2020;212:127-33.
22. Muftuoglu O, Toro P, Hogan RN, Bowman RW, Cavanagh HD, McCulley JP, *et al.* Sarnicola air-visco bubble technique in deep anterior lamellar keratoplasty. Cornea 2013;32:527-32.
23. Scorcia V, De Luca V, Lucisano A, Carnevali A, Carnovale Scalzo G, Bovone C, *et al.* Results of viscobubble deep anterior lamellar keratoplasty after failure of pneumatic dissection. Br J Ophthalmol 2018;102:1288-92.
24. Bhatt UK, Fares U, Rahman I, Said DG, Maharajan SV, Dua HS. Outcomes of deep anterior lamellar keratoplasty following successful and failed 'big bubble'. Br J Ophthalmol 2012;96:564-9.
25. Ardjomand N, Hau S, McAlister JC, Bunce C, Galaretta D, Tuft SJ, *et al.* Quality of vision and graft thickness in deep anterior lamellar and penetrating corneal allografts. Am J Ophthalmol 2007;143:228-35.
26. Seitz B, Langenbucher A, Küchle M, Naumann GO. Impact of graft diameter on corneal power and the regularity of postkeratoplasty astigmatism before and after suture removal. Ophthalmology 2003;110:2162-7.
27. Yoshida J, Murata H, Miyai T, Shirakawa R, Toyono T, Yamagami S, *et al.* Characteristics and risk factors of recurrent keratoconus over the long term after penetrating keratoplasty. Graefes Arch Clin Exp Ophthalmol 2018;256:2377-83.
28. Gadhvi KA, Romano V, Fernández-Vega Cueto L, Aiello F, Day AC, Allan BD. Deep anterior lamellar keratoplasty for keratoconus: Multisurgeon results. Am J Ophthalmol 2019;201:54-62.
29. Donoso R, Díaz C, Villavicencio P. Comparative study of keratoconus between Anwar's deep anterior lamellar keratoplasty versus converted penetrating keratoplasty. Arch Soc Esp Oftalmol 2015;90:257-63.
30. Huang OS, Htoon HM, Chan AM, Tan D, Mehta JS. Incidence and outcomes of intraoperative descemet membrane perforations during deep anterior lamellar keratoplasty. Am J Ophthalmol 2019;199:9-18.
31. Myerscough J, Roberts H, Yu AC, Elkadim M, Bovone C, Busin M. Five-year outcomes of converted mushroom keratoplasty from intended deep anterior lamellar keratoplasty (DALK) mandate 9-mm diameter DALK as the optimal approach to keratoconus. Am J Ophthalmol 2020;220:9-18.
32. Busin M, Madi S, Scorcia V, Santorum P, Nahum Y. A two-piece microkeratome-assisted mushroom keratoplasty improves the outcomes and survival of grafts performed in eyes with diseased stroma and healthy endothelium (An American Ophthalmological Society Thesis). Trans Am Ophthalmol Soc 2015;113:T1.
33. Myerscough J, Friehmann A, Bovone C, Mimouni M, Busin M. Evaluation of the risk factors associated with conversion of intended deep anterior lamellar keratoplasty to penetrating keratoplasty. Br J Ophthalmol 2020;104:764-7.
34. Fontana L, Parente G, Sincich A, Tassinari G. Influence of graft-host interface on the quality of vision after deep anterior lamellar keratoplasty in patients with keratoconus. Cornea 2011;30:497-502.
35. Watson SL, Ramsay A, Dart JK, Bunce C, Craig E. Comparison of deep lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus. Ophthalmology 2004;111:1676-82.
36. Funnel CL, Ball J, Noble BA. Comparative cohort study of the outcomes of deep lamellar keratoplasty and penetrating keratoplasty for keratoconus. Eye 2006;20:527-32.
37. Coster DJ, Lowe MT, Keane MC, Williams KA; Australian Corneal Graft Registry Contributors. A comparison of lamellar and penetrating keratoplasty outcomes: A registry study. Ophthalmology 2014;121:979-87.
38. Söğütlü Sari E, Kubaloğlu A, Ünal M, Piñero Llorens D, Koytak A, Ofluoglu AN, *et al.* Penetrating keratoplasty versus deep anterior lamellar keratoplasty: Comparison of optical and visual quality outcomes. Br J Ophthalmol 2012;96:1063-7.
39. Javadi MA, Feizi S, Yazdani S, Mirbabaee F. Deep anterior lamellar keratoplasty versus penetrating keratoplasty for keratoconus: A clinical trial. Cornea 2010;29:365-71.
40. Shimazaki J, Shimmura S, Ishioka M, Tsubota K. Randomized clinical trial of deep lamellar keratoplasty vs**.** penetrating keratoplasty. Am J Ophthalmol 2002;134:159-65.
41. Han DC, Mehta JS, Por YM, Htoon HM, Tan DT. Comparison of outcomes of lamellar keratoplasty and penetrating keratoplasty in keratoconus. Am J Ophthalmol 2009;148:744-51.e1.
42. Feizi S, Javadi MA, Jamali H, Mirbabaee F. Deep anterior lamellar keratoplasty in patients with keratoconus: Big-bubble technique. Cornea 2010;29:177-82.
43. Cheng YY, Visser N, Schouten JS, Wijdh RJ, Pels E, van Cleynenbreugel H, *et al.* Endothelial cell loss and visual outcome of deep anterior lamellar keratoplasty versus penetrating keratoplasty: A randomized multicenter clinical trial. Ophthalmology 2011;118:302-9.
44. Jones MN, Armitage WJ, Ayliffe W, Larkin DF, Kaye SB**;** NHSBT Ocular Tissue Advisory Group and Contributing Ophthalmologists (OTAG Audit Study 5). Penetrating and deep anterior lamellar keratoplasty for keratoconus: A comparison of graft outcomes in the United kingdom. Invest Ophthalmol Vis Sci 2009;50:5625-9.
45. Arundhati A, Chew MC, Lim L, Mehta JS, Lang SS, Htoon HM, *et al.* Comparative study of long-term graft survival between penetrating keratoplasty and deep anterior lamellar keratoplasty. Am J Ophthalmol 2021;224:207-16.
46. Borderie VM, Sandali O, Bullet J, Gaujoux T, Touzeau O, Laroche L. Long-term results of deep anterior lamellar versus penetrating keratoplasty. Ophthalmology 2012;119:249-55.
47. Elkadim M, Myerscough J, Bovone C, Busin M. Astigmatism orientation after deep anterior lamellar keratoplasty for keratoconus and its correlation with preoperative peripheral corneal astigmatism. Cornea 2020;39:192-5.
48. Feizi S, Zare M. Current approaches for management of postpenetrating keratoplasty astigmatism. J Ophthalmol 2011;2011:708736.
49. Romano V, Iovieno A, Parente G, Soldani AM, Fontana L. Long-term clinical outcomes of deep anterior lamellar keratoplasty in patients with keratoconus. Am J Ophthalmol 2015;159:505-11.
50. Bilgihan K, Ozdek SC, Akata F, Hasanreisoglu B. Photorefractive keratectomy for post-penetrating keratoplasty myopia and astigmatism. J Cataract Refract Surg 2000;26:1590-5.
51. Kovoor TA, Mohamed E, Cavanagh HD, Bowman RW. Outcomes of LASIK and PRK in previous penetrating corneal transplant recipients. Eye Contact Lens 2009;35:242-5.
52. Arantes JC, Coscarelli S, Ferrara P, Araújo LP, Ávila M, Torquetti L. Intrastromal corneal ring segments for astigmatism correction after deep anterior lamellar keratoplasty. J Ophthalmol 2017;2017:8689017.
53. Elkadim M, Myerscough J, Bovone C, Busin M. A novel blunt dissection technique to treat modified deep anterior lamellar keratoplasty (DALK)-associated high astigmatism. Eye (Lond) 2020;34:1432-7.
54. anNakhli F, Khattak A. Vector analysis of femtosecond laser-assisted astigmatic keratotomy after deep anterior lamellar keratoplasty and penetrating keratoplasty. Int Ophthalmol 2019;39:189-98.

55. Wade M, Steinert RF, Garg S, Farid M, Gaster R. Results of toric intraocular lenses for post-penetrating keratoplasty astigmatism. Ophthalmology 2014;121:771-7.
56. Lockington D, Wang EF, Patel DV, Moore SP, McGhee CN. Effectiveness of cataract phacoemulsification with toric intraocular lenses in addressing astigmatism after keratoplasty. J Cataract Refract Surg 2014;40:2044-9.
57. Liu H, Chen Y, Wang P, Li B, Wang W, Su Y, *et al.* Efficacy and safety of deep anterior lamellar keratoplasty vs. penetrating keratoplasty for keratoconus: A meta-analysis. PLoS One 2015;10:e0113332.
58. Den S, Shimmura S, Tsubota K, Shimazaki J. Impact of the descemet membrane perforation on surgical outcomes after deep lamellar keratoplasty. Am J Ophthalmol 2007;143:750-4.
59. De Benito-Llopis L, Mehta JS, Angunawela RI, Ang M, Tan DT. Intraoperative anterior segment optical coherence tomography: A novel assessment tool during deep anterior lamellar keratoplasty. Am J Ophthalmol 2014;157:334-41.e3.
60. Myerscough J, Friehmann A, Busin M, Goor D. Successful visualization of a big bubble during deep anterior lamellar keratoplasty using intraoperative OCT. Ophthalmology 2019;126:1062.
61. Au J, Goshe J, Dupps WJ Jr**.**, Srivastava SK, Ehlers JP. Intraoperative optical coherence tomography for enhanced depth visualization in deep anterior lamellar keratoplasty from the PIONEER study. Cornea 2015;34:1039-43.
62. Han SB, Liu YC, Mohamed-Noriega K, Mehta JS. Application of femtosecond laser in anterior segment surgery. J Ophthalmol 2020;2020:8263408.
63. Price FW Jr**.**, Price MO, Grandin JC, Kwon R. Deep anterior lamellar keratoplasty with femtosecond-laser zigzag incisions. J Cataract Refract Surg 2009;35:804-8.
64. Farid M, Steinert RF. Deep anterior lamellar keratoplasty performed with the femtosecond laser zigzag incision for the treatment of stromal corneal pathology and ectatic disease. J Cataract Refract Surg 2009;35:809-13.
65. Li S, Wang T, Bian J, Wang F, Han S, Shi W. Precisely controlled side cut in femtosecond laserassisted deep lamellar keratoplasty for advanced keratoconus. Cornea 2016;35:1289-94.
66. Kopani KR, Page MA, Holiman J, Parodi A, Iliakis B, Chamberlain W. Femtosecond laser-assisted keratoplasty: Full and partial-thickness cut wound strength and endothelial cell loss across a variety of wound patterns. Br J Ophthalmol 2014;98:894-9.
67. Liu YC, Wittwer VV, Yusoff NZ, Lwin CN, Seah XY, Mehta JS, *et al.* Intraoperative optical coherence tomography-guided femtosecond laser-assisted deep anterior lamellar keratoplasty. Cornea 2019;38:648-53.
68. Lucisano A, Giannaccare G, Pellegrini M, Bernabei F, Yu AC, Carnevali A, *et al.* Preliminary results of a novel standardized technique of femtosecond laser-assisted deep anterior lamellar keratoplasty for keratoconus. J Ophthalmol 2020;2020:5496162.
69. Pedrotti E, Bonacci E, De Rossi A, Bonetto J, Chierego C, Fasolo A, *et al.* Femtosecond laser-assisted big-bubble deep anterior lamellar keratoplasty. Clin Ophthalmol 2021;15:645-50.
70. Salouti R, Zamani M, Ghoreyshi M, Dapena I, Melles GR, Nowroozzadeh MH. Comparison between manual trephination versus femtosecond laser-assisted deep anterior lamellar keratoplasty for keratoconus. Br J Ophthalmol 2019;103:1716-23.
71. Bergmanson JP, Goosey JD, Patel CK, Mathew JH. Recurrence or re-emergence of keratoconus – What is the evidence telling us? Literature review and two case reports. Ocul Surf 2014;12:267-72.
72. Lake D, Hamada S, Khan S, Daya SM. Deep anterior lamellar keratoplasty over penetrating keratoplasty for host rim thinning and ectasia. Cornea 2009;28:489-92.
73. Bovone C, Nahum Y, Scorcia V, Giannaccare G, Spena R, Myerscough J, *et al*. Stromal peeling for deep anterior lamellar keratoplasty in post-penetrating keratoplasty eyes. Br J Ophthalmol 2020:bjophthalmol-2020-316653.
74. Gain P, Jullienne R, He Z, Aldossary M, Acquart S, Cognasse F, *et al.* Global survey of corneal transplantation and eye banking. JAMA Ophthalmol 2016;134:167-73.
75. Busin M, Halliday BL, Arffa RC, McDonald MB, Kaufman HE. Precarved lyophilized tissue for lamellar keratoplasty in recurrent pterygium. Am J Ophthalmol 1986;102:222-7.
76. Arffa RC, Busin M, Barron BA, McDonald MB, Kaufman HE. Epikeratophakia with commercially prepared tissue for the correction of aphakia in adults. Arch Ophthalmol 1986;104:1467-72.
77. Chaurasia S, Das S, Roy A. A review of long term corneal preservation techniques: Relevance and renewed interests in the COVID-19 era. Indian J Ophthalmol 2020;68:1357-63.
78. Busin M, Yu AC, Ponzin D. Coping with COVID-19: An Italian perspective on corneal surgery and eye banking in the time of a pandemic and beyond. Ophthalmology 2020;127:e68-9.
79. Parekh M, Ferrari S, Romano V, Myerscough J, Jones G, Griffoni C, *et al*. Impact of COVID-19 on corneal donation and distribution. Eur J Ophthalmol 2022;32:NP269-NP270.
80. Romano V, Levis HJ, Gallon P, Lace R, Borroni D, Ponzin D, *et al.* Biobanking of dehydrated human donor corneal stroma to increase the supply of anterior lamellar grafts. Cornea 2019;38:480-4.
81. Doillon CJ, Watsky MA, Hakim M, Wang J, Munger R, Laycock N, *et al.* A collagen-based scaffold for a tissue engineered human cornea: Physical and physiological properties. Int J Artif Organs 2003;26:764-73.
82. Yoon CH, Choi HJ, Kim MK. Corneal xenotransplantation: Where are we standing? Prog Retin Eye Res 2021;80:100876.
83. Matthyssen S, Van den Bogerd B, Dhubhghaill SN, Koppen C, Zakaria N. Corneal regeneration: A review of stromal replacements. Acta Biomater 2018;69:31-41.
84. Hashimoto Y, Funamoto S, Sasaki S, Negishi J, Honda T, Hattori S, *et al.* Corneal regeneration by deep anterior lamellar keratoplasty (DALK) using decellularized corneal matrix. PLoS One 2015;10:e0131989.
85. Zhang MC, Liu X, Jin Y, Jiang DL, Wei XS, Xie HT. Lamellar keratoplasty treatment of fungal corneal ulcers with acellular porcine corneal stroma. Am J Transplant 2015;15:1068-75.
86. Zheng Q, Zhang Y, Ren Y, Zhao Z, Hua S, Li J, *et al.* Deep anterior lamellar keratoplasty with cross-linked acellular porcine corneal stroma to manage fungal keratitis. Xenotransplantation 2021;28:e12655.
87. Zheng J, Huang X, Zhang Y, Wang Y, Qin Q, Lin L, *et al.* Short-term results of acellular porcine corneal stroma keratoplasty for herpes simplex keratitis. Xenotransplantation 2019;26:e12509.