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CLINICAL INVESTIGATION

Impact of new lamellar techniques of keratoplasty on eye bank activity

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Abstract
Background Deep anterior lamellar keratoplasty (DALK) has become an increasingly popular alternative to penetrating keratoplasty in patients with stromal corneal pathologies. The main advantages of DALK are: prevention of long-term endothelial loss, elimination of allograft reaction and short topical steroid treatment with lower risks of glaucoma, cataract and infection. Because this technique enables surgeons to use corneal grafts with low endothelial density, the aim of this paper was to determine whether this type of innovation has had a significant impact on eye bank activity.
Methods We reviewed our corneal graft activity over a 40-month period and assessed the proportion of deep lamellar and penetrating keratoplasties. During the same period, we also evaluated our eye bank activity and recorded the utilisation of grafts with endothelium abnormalities, which were only suitable for lamellar techniques.
Results Deep lamellar keratoplasty represented 29.8% (85 out of 285) of corneal transplantations. Forty-eight percent of all corneas stored at the local eye bank were unsuitable for penetrating keratoplasty; 36.6% of those were not suitable for endothelial deficiencies. Among these, 72.7% were used for DALK and 27.3% were rejected. This permitted a 24.5% increase in corneal grafting activity. In contrast, Descemet's membrane was removed at the time of surgery in 12% of corneas with healthy endothelium, which was used for deep lamellar keratoplasty.
Conclusions Deep anterior lamellar keratoplasty development and close collaboration between eye banks and surgeons can induce a significant increase in corneal grafting. This could be a partial solution in countries confronted with corneal graft shortages.

Keywords Keratoplasty · Corneal transplantation · Eye banks · Tissue and organ procurement

Introduction

Stromal corneal pathologies, keratoconus in particular, currently represent approximately one-third of indications for keratoplasty [1, 8, 16, 17, 25, 35]. In these indications, deep anterior lamellar keratoplasty (DALK) has become an increasingly popular alternative compared with penetrating keratoplasty (PK) [3, 4, 6, 12, 13, 19–21, 23, 30, 31, 33]. In this procedure, the corneal stroma first needs to be totally excised, leaving only the bare Descemet's membrane (Fig. 1a). In a second stage, Descemet's membrane and the endothelial cell layer are entirely and delicately removed from the donor graft (Fig. 1b). The donor's full-thickness stroma is then positioned against the Descemet's membrane of the recipient and sutured using standard techniques. The result is that no scar is formed between the recipient's and the donor's corneas (Fig. 1c). Visual function has been reported to be identical to that after

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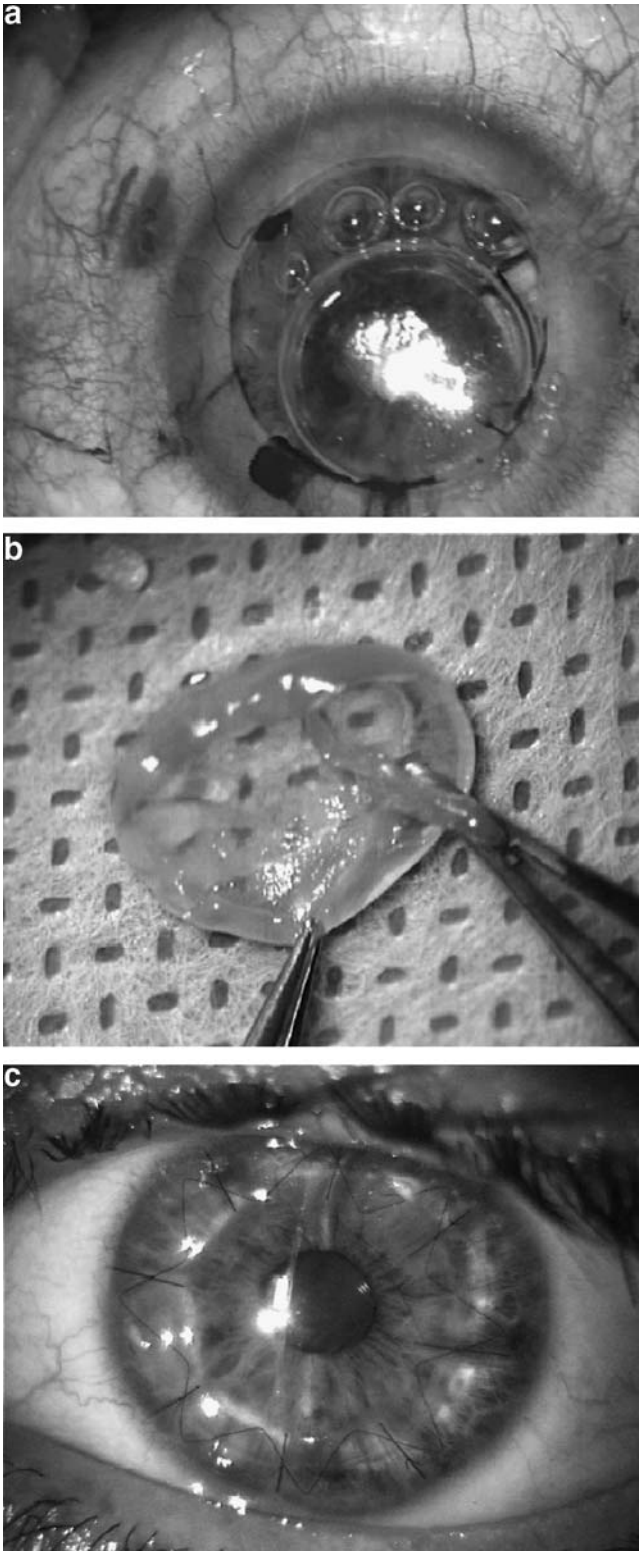

Fig. 1 Deep anterior lamellar keratoplasty (DALK). **a** Last stage of deep stromal dissection in the recipient. The air bubble in the anterior chamber confirms the presence of the sole, highly transparent Descemet's membrane. **b** Removal of Descemet's membrane in one piece from the donor's cornea. **c** Postoperative aspect 4 months after DALK

penetrating keratoplasty (PK) [4, 24, 29, 34]. As the recipient's endothelium remains intact, the main advantage of DALK is the absence of allograft reaction. Therefore, the duration of topical corticosteroid treatment is shortened with less risk of glaucoma, cataract, infection or epithelial defects. Another advantage is the prevention of long-term endothelial loss.

Another very important point is that this technique enables surgeons to use corneal grafts without having to consider endothelial quality. Therefore, a significant number of corneal grafts that routinely would have been discarded may now be proposed for our patients. This will undoubtedly enhance the profitability of eye banks.

As we had been performing DALK for 5 years in our centre, we undertook to reorganise the local distribution of our corneal grafts and to propose grafts with insufficient endothelial quality for patients with stromal pathologies.

The aim of this study was to determine whether this type of modification had a significant impact on eye bank activity.

Materials and methods

We reviewed the corneal graft activity of the Rouen University Hospital over a 40-month period (between May 2001 and August 2004) and determined the proportions of deep anterior lamellar keratoplasties and penetrating keratoplasties. During this period and whenever possible, we tried to propose corneal grafts with low endothelial density (<2,000 cells/mm^2) when patients required deep lamellar keratoplasty for a stromal pathology (keratoconus, keratitis sequelae, stromal dystrophies, etc.).

Surgical technique

Deep anterior lamellar keratoplasty is performed using a modified "big bubble technique". Initially, a non-penetrating trephination 8 mm in diameter and with approximately 80% stromal thickness (measured beforehand by ultrasound pachymetry) is performed. Anterior stroma is then removed after manual lamellar dissection using a crescent knife, leaving only 20% of the posterior stroma. A 30-gauge needle, connected to a syringe filled with air is then inserted into the residual corneal stroma at the mid-periphery level with the bevel facing down. When the needle reaches the deep corneal layers, the plunger is vigorously depressed. In most cases, the air suddenly forms a large bubble with a circular outline, between Descemet's membrane and the deepest stroma. Another 30-gauge needle, attached to a syringe filled with viscoelastic substance is advanced into the air bubble. The viscoelastic substance is then injected to maintain the separation between the posterior stroma and

the Descemet's membrane. Thereafter, it is possible to make a large incision in the entire stroma using a sharp-tipped blade. The horizontal position of the needle prevents any perforation of Descemet's membrane with the blade. Once this initial incision is made, the remaining stroma can be easily dissected with scissors, which are engaged between the posterior stroma and Descemet's membrane. Finally, only the fully transparent Descemet's membrane must remain, ensuring optimal vision of the whole anterior chamber while maintaining its tightness. The graft is prepared from a whole cornea trephinated to 8 mm in diameter. Descemet's membrane is peeled off with forceps. Standard suturing techniques can be used: interrupted, running or combined interrupted running sutures with 10/0 nylon.

Management of corneal grafts distribution

In fact, deep lamellar dissection is a more difficult surgical technique than penetrating keratoplasty and the risk of perforating Descemet's membrane is always present. In such cases, reverting to standard penetrating keratoplasty is often necessary, requiring a corneal graft of high endothelial quality. Therefore, the surgical team will always schedule deep lamellar keratoplasty on a specific day and a penetrating keratoplasty on the next day, in order to provide a back-up corneal graft with high endothelial density in case of perforation. Every time the lamellar graft is used (91% of cases in this series), the other graft is used the next day for penetrating keratoplasty. When the lamellar graft cannot be used because of a perforation (9%), the other cornea with suitable endothelium is grafted. The eye bank is immediately informed, so as to prepare another graft for the second operation. The lamellar graft is sent back to the eye bank and will possibly be used later. The maximal preservation time at 31°C in our eye bank is set to 4 weeks for penetrating grafts and 5 weeks for lamellar grafts.

Results

Two hundred and eighty-five (n=285) keratoplasties were performed by one surgeon in our department during this 40-month period. Two hundred and three (n=203) of the 285 grafts came from our local cornea bank.

The operative indications for these 285 grafts are shown in Fig. 2.

In total, stromal pathologies represented 38.6% of graft indications (110 out of 285) including mainly keratoconus (22% of graft indications) and sequelae from infectious, viral or bacterial keratitis (14% of graft indications). Endothelial pathologies, however, represented 61.4% of indications (175 out of 285), beginning with pseudophakic or aphakic keratopathy (26% of indications), Fuchs dystrophy (15% of indications) and regraft (7% of indications).

Deep lamellar keratoplasty could be performed in 77.3% of stromal pathologies (85 out of 110) equivalent to 29.8% (85 out of 285) of all the keratoplasties performed over the duration of the entire study (Fig. 3). In fact, it was not possible to perform DALK in all cases with stromal pathology. In several cases, the surgical team routinely performs penetrating keratoplasty, i.e. in patients with keratoconus with a previous medical history of acute keratoconus with Descemet's membrane rupture (9 out of 110) or in sequelae of keratitis with endothelial density less than 1,000 cells/mm^2 (7 out of 110). Moreover, conversion to penetrating keratoplasty was necessary in 9 cases due to perforation (9.5%).

During that period 313 corneal grafts were collected and preserved in the local cornea bank, whereas 82 corneas still had to be imported from other French cornea banks to meet the demand for grafts (Table 1).

Fifty-two percent of retrieved corneas were suitable for penetrating keratoplasty (n=163) and 150 were not (47%). Fifty-five (36.6%) of these unsuitable corneas were inappropriate due to endothelial deficiencies, which is equivalent to 17.5% of all corneas retrieved. Among these, 72.7% (n=40) could be used for deep lamellar keratoplasties and 27.3% were eliminated either because no patient with stromal pathology was available at that time or because of excessive preservation time. As 203 keratoplasties were performed instead of 163, there was a 24.5% increase in corneal grafting activity.

In reality, process optimisation could have enabled us to perform 40+15 DALK, i.e., 55 DALK and 217 corneal grafts. This would have resulted in an increase in corneal grafting activity of 33% instead of 24.5%.

In contrast, Descemet's membrane was removed at surgery from 12% of corneas with healthy endothelium (20 out of 163), which were used for deep lamellar keratoplasty.

The DALK performed using graft with low endothelial density (n=40) represented 66% of the DALK from local corneas (n=60) and 47% of all the DALK performed (n=85).

Final best corrected acuity was 0.62, 12 months after DALK (range 0.3 to 1). Suture abscesses occurred in two cases and responded well to medical therapy. One eye presented with reversible stromal rejection 6 months after DALK and responded well to topical corticosteroids. Clinical data, including those for DALK and PK, are reported in Table 2.

Discussion

At present, more than a third of the cornea specimens collected and preserved in cornea banks are unsuitable for

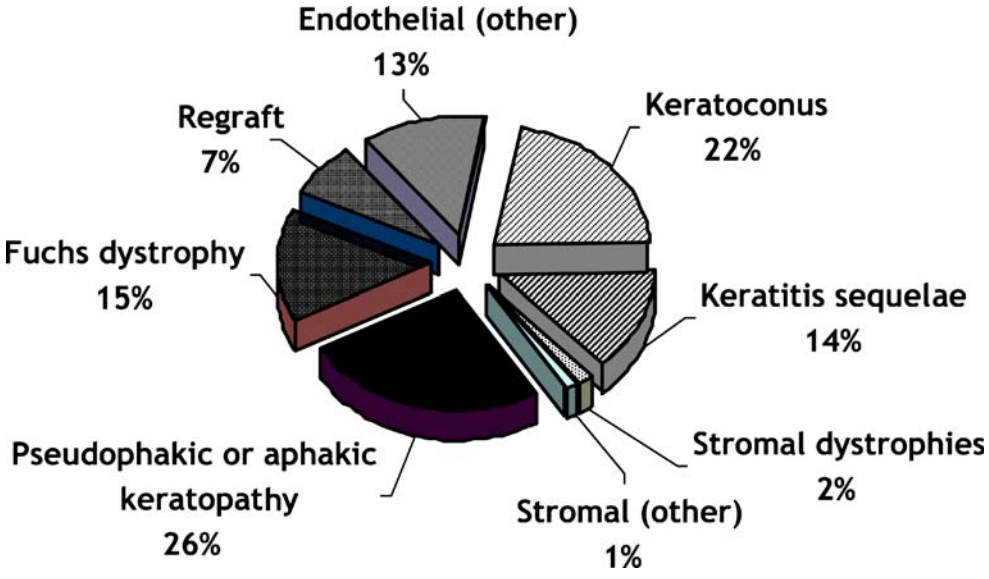

Fig. 2 Operative indications for keratoplasties (penetrating and lamellar)

grafting because of the positive serology of the donors, graft contamination or poor endothelial quality. In 2003, the mean rate of unsuitable corneas was reported to be 46% in France [10] and 37.6% on average in 66 European cornea banks [9]. It is therefore necessary to maintain a high rate of cornea collection to be able to perform grafts in all patients on waiting lists and comply with the safety criteria accepted by all. Such a necessary activity will incur costs that will necessarily impact the cost of each healthy graft. Indeed, in the present system, widely used in the USA and western Europe, customers of the bank pay the "production costs" of the cornea. The more corneas that have been eliminated, the more expensive the suitable ones will be. Furthermore, the need to collect more grafts than the number of patients waiting will also be detrimental to countries or regions in which collection rates are low [5, 11, 14, 15, 22, 26].

A number of efforts have been made to improve the profitability of cornea banks: new preservation laboratories with known standards and the implementation of truly surgical collection theatres, the aim being to reduce the graft contamination rate; serological tests have also been

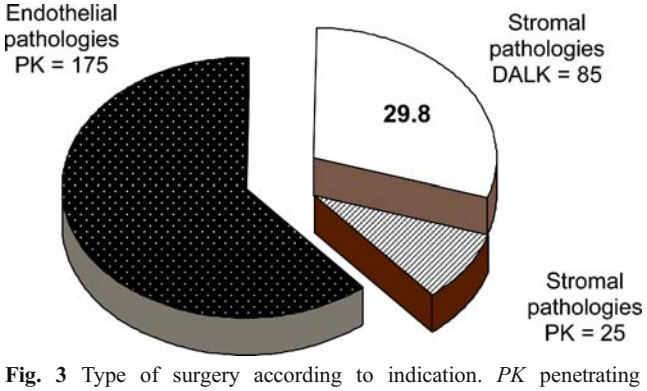

Fig. 3 Type of surgery according to indication. *PK* penetrating keratoplasty, *DALK* deep anterior lamellar keratoplasty

refined to significantly reduce the number of false-positive results. Nevertheless, a large number of grafts are still being rejected because of low endothelial density, i.e. below 2,000 cells/mm^2 in most cornea banks [9, 32]. The corneas rejected for endothelial reasons in our series represented 17.5% of all the corneas preserved, a figure close to that of 16.86% reported in 2003 by French cornea banks [10], and 36% of all the corneas rejected versus 28% on average in European banks [9]. In total, endothelial failure is responsible for approximately one-third of graft rejections. Since the new development of lamellar surgery it has been known that these corneas can be grafted in patients with no endothelial pathology. Several series have thus shown that DALK produced the same visual results as those of a penetrating keratoplasty and at the same time reduced risks of rejection and maintained high endothelial density [4, 24, 29, 34]. Best corrected visual acuity (BCVA) was reported to be superior to 0.5 in 76–89% of cases [2, 4, 7] 6 months after DALK for keratoconus. In a prospective, randomised clinical trial, Shimazaki et al. found that DALK was superior with regard to its safety, such as preventing continuous decreases in endothelium or increases in intraocular pressure [29]. In this series, the PK group showed a tendency towards faster recovery in BCVA than the DALK group, but the difference was not statistically significant [29]. In contrast, Panda et al. reported a BCVA of 0.5 or more in 70.8% and 62.5% of the DALK and PK groups respectively after 1 year, which was not significant [24]. According to Panda et al., the mean endothelial cell count was 2,233 cells/mm^2 and 2,219 cells/mm^2 6 months and 1 year respectively after DALK, which was not significant. The mean cell count of the donor eyes used for PK was 1,902.8 cells/mm^2 after 6 months, and 1,579 cells/mm^2 after 1 year [24]. All the values showed highly significant changes (p<0.001).

Table 1 Eye bank activity and repartition of corneal grafts according to the type of surgery. *DALK* deep anterior lamellar keratoplasty, *PK* penetrating keratoplasty

	Number of corneal grafts	Corneal grafts used for PK	Corneal grafts used for DALK	Discarded corneas
Valid corneas in local corneal bank	163	143	20	0
Non-valid corneas in local corneal bank	150			
Endothelial deficiency	55	0	40	15
Other causes of non valid corneas	95	0	0	95
Imported corneas from other banks	82	57	25	
Total	395	200	85	110

During that procedure, the surgeon removes the recipient's entire stroma to leave only Descemet's membrane. He then stitches a corneal graft after removing Descemet's membrane in one piece. Thus, there is no interface between graft and Descemet's membrane, which may impair postoperative visual recovery. The surgical difficulty of this operation remains a limiting factor of its development, but techniques are gradually becoming more refined and precise, and there is no question that the procedure will eventually replace the standard penetrating keratoplasty in all non-endothelial pathologies. Such a generalisation would also help to improve cornea bank profitability insofar as non-endothelial pathologies represent a non-negligible part of graft indications.

Stromal pathologies represented 40.3% of indications for keratoplasty in the latest French national waiting list published (keratoconus, keratitis sequelae, stromal dystrophies, etc.) [27], a figure very comparable with the 38.6% reported here. Likewise, analysing graft indications in other countries confirmed their modification since the improvement in cataract surgery and the reduced incidence of pseudophakic keratopathy. In a number of series, keratoconus has become one of the primary graft indications with 28.4% of indications in Israel [35], 23.5% in the UK [1], 11.4–24.2% in the USA [8, 18, 28] and 28.8% in France [16]. These figures are very close to the 22% described in our series.

However, proposing a low endothelial density graft in each patient with stromal pathology who is in need of a graft is not that simple. Indeed, DALK requires the recipient's entire corneal stroma to be removed to leave only Descemet's membrane in place. The difficulty of that procedure induces a non-negligible risk of perforation, mainly at the time of training. This risk of perforating Descemet's membrane varies between 0 and 39.2% according to studies and whether discrimination is made between microperforations not requiring conversion to perforating grafts and larger perforations that make that conversion necessary. Several factors are involved, including the operative technique in particular (fluid lamellar dissection, big bubble technique, intrastromal viscoelastic injection) and the surgeon's experience. When the perforation is small, it is often possible to fit a small graft without any endothelium. But when the perforation is large, it is absolutely necessary to have a graft of very high endothelial quality to perform a transfixing keratoplasty. For example, Amayem and Anwar reported conversion to penetrating keratoplasty in 8.4% of cases [2], Caporossi a rate of 11.1% [6], and Shimmura a rate of 16.6% [30]. The results are similar to the 9.5% of conversion to penetrating keratoplasty that we reported in our study, and which markedly confirms this peroperative occurrence in most series.

It is therefore out of the question to risk dispatching a low endothelial quality graft to the surgical team without providing a back-up graft with high endothelial density. Fortunately, generalisation of organ culture has definitely modified distribution in eye banks. It is now possible to transport grafts at room temperature for 48 h. Grafts are now carefully scheduled, choosing the most suitable time

Table 2 Clinical data 1 year after DALK and PK in patients with stromal pathologies

	DALK (85 patients)	PK1 (25 patients)	PK2 (18 patients)
Visual acuity	0.62±0.26	0.37±0.32 ($p<0.05$)	0.64±0.32 NS
Astigmatism	2.66±0.57	2.08±0.72 NS	2.5±1.12 NS
Complications	Reversible stromal rejection: 1 case Suture abscesses: 2 cases	Graft rejection: 1 case Reversible graft rejection: 1 case	Reversible graft rejection : 1 case

PK1 indicates 25 patients with the antecedent of stromal pathologies who benefited from PK (9 patients with a history of acute keratoconus with Descemet's membrane rupture, 7 patients with keratitis sequelae with endothelial density less than 1,000 cells/mm^2 and 9 patients in whom conversion to penetrating keratoplasty was necessary due to perforation)

PK2 indicates 18 patients with a previous medical history of stromal pathologies who benefited from PK (patients with keratitis sequelae with endothelial density less than 1,000 cells/mm^2 were excluded from PK1)

for both the surgeon and the patient. We elected to plan a lamellar operation followed 24 h later by a penetrating surgery. Two grafts were therefore prepared 24 h ahead of the first operating day: one with low endothelial density and a back-up graft with an endothelial density above 2,000 cells/mm^2. In more than 90% of cases, the second graft was fitted the next day during penetrating keratoplasty. Less than once out of ten times was the back-up graft used during the first operation and the cornea bank was immediately advised to provide another cornea the next day. Close cooperation is necessary between the tissue bank and the surgical team. Likewise, location proximity between teams or the quick availability of carriers are among many factors that will facilitate the procedure.

This study showed that the development of deep lamellar keratoplasty and close cooperation between eye banks and surgeons permitted a significant increase in corneal grafting without increasing procurement activity (24.5% in our centre).

This could be a partial solution in countries confronted with corneal graft shortages. In other countries in which the number of patients on waiting lists is decreasing, this type of organisation may have other advantages, such as more corneal grafts to export, less expensive corneal bank activity or more corneas for research.

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