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CURRENT TRENDS IN CORNEAL TRANSPLANTATION

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Summary

Corneal transplantation, as full-thickness transplantation, is an old surgical procedure which has been successfully performed for more than 100 years. However, in a last decade significant changes in surgical technique(s) have been implemented. The reason for such changes is the current trend to replace only the diseased part of the recipient cornea, not the whole cornea. Therefore, if the anterior part of the recipient cornea is opaque, the method of choice to treat such patient is anterior lamellar keratoplasty in which we can preserve the healthy recipient endothelium and thus decrease the chance of graft rejection. If the corneal disease involves posterior part of the recipient cornea, we use posterior lamellar keratoplasty, sparing the anterior part of the recipient cornea and thus improving speed and quality of visual recovery since the problem of high astigmatism caused by corneal sutures is solved. The advantages of lamellar transplantation are numerous: faster visual recovery, decreased rate of corneal graft rejection, preservation of the integrity of the globe, no suture-related problems (in case of posterior lamellar grafts), avoidance of complications related to "open-sky" surgery, theoretical possibility to use one donor cornea for two recipients and the use of local instead of general anaesthesia. Of course, there are also some disadvantages of such surgeries: increased early endothelial cell loss, detachment of the posterior lamellar grafts, vascular or epithelial in-growth into lamellar plane, and uncertain fate of lamellar grafts in a long follow-up. In this review the most frequently performed methods of corneal transplantation are presented, together with main advantages and disadvantages of different surgical techniques.

Keywords: anterior lamellar keratoplasty; superficial anterior lamellar keratoplasty; deep anterior lamellar keratoplasty; posterior lamellar keratoplasty; deep lamellar endothelial keratoplasty; Descemet stripping automated endothelial keratoplasty; Descemet's membrane endothelial keratoplasty.

INTRODUCTION

Penetrating keratoplasty (PK) or full thickness corneal transplantation has been a gold standard for the treatment of many corneal diseases for over a century, since

dr. Eduard Zirm performed the first successful PK in a human eye in 1905. Although PK in a low-risk corneal diseases had the best outcome regarding graft survival rate among all transplantations, clinicians soon became aware of some undesirable postoperative consequences of PK. These include: high astigmatism induced by the placement of corneal sutures causing prolonged visual rehabilitation despite the presence of completely clear corneal graft, unpredictable refractive outcome, and an increased vulnerability to eye trauma for many years after surgery. Therefore, many corneal surgeons posed themselves a logical question: why should we transplant an entire cornea and damage the structural integrity of the globe, when in many corneal diseases only one corneal layer is sick and need replacement? Already in 1950 dr. Jose Barraquer proposed lamellar transplantation of the posterior cornea (in which only the diseased part of the cornea is replaced by a donor tissue) in case of endothelial diseases, but due to the techniqual difficulties in performing lamellar transplantation it took time for this type of surgery to be widely accepted [1,2]. Since that time various techniques of lamellar transplantations had been utilized to treat corneal diseases at the proper location of the disease itself; meaning that only the anterior part of cornea is replaced if the diseases is present in the anterior corneal layers (anterior keratoplasty), or only the posterior part of the cornea if the corneal disease involves posterior part of the cornea – endothelium (posterior keratoplasty). In this review, the most widely accepted surgical approaches of lamellar corneal transplantations are presented.

ANTERIOR LAMELLAR KERATOPLASTY (ALK)

In this type of surgery the anterior diseased part of the cornea is replaced by a donor tissue, while posterior stroma and/or Descemet membrane and endothelium of the recipient cornea is preserved. Depending on the fact whether corneal disease involves only anterior stroma or gets deeper into stromal layers we can use two different surgical approaches: a) Superficial Anterior Lamellar Keratoplasty (SALK) if the disease involves only the superficial part of corneal stroma, and b) Deep Anterior Lamellar Keratoplasty (DALK) if we need to replace total or near-total corneal stroma. The main advantage of ALK is preservation of the healthy recipient endothelium and thus decreased risk of graft rejection, better preservation of structural integrity of the globe and decreased chance of intraoperative complications involved with „open-sky" procedures [3]. However, there are also disadvantages of such procedures such as interface scarring or „haze", residual corneal pathology, epithelial ingrowth and potential vessel ingrowth into the interface (in vascularised corneas) limiting patient's quality of vision.

Superficial Anterior Lamellar Keratoplasty (SALK)

The main indications for SALK are: stromal opacities located in the anterior stroma which may be caused by anterior stromal dystrophy (e.g. Reis-Buckler), degeneration (Salzmann nodular degeneration), infection, chronic inflammation or previous refractive surgery resulting in corneal scarring. Resection of the anterior diseased part of the recipient cornea can be performed by manual resection, with the help of microkeratome or femtosecondlaser [4,5]. If the femtosecondlaser is used to create the lamellar cut then the procedure is called femtosecond-laser assisted anterior lamellar keratoplasty or FALK. Depth of the anterior stromal opacity can be determined preoperatively by the use of anterior segment optical coherence tomography (OCT). Results obtained with manual resection are suboptimal due to the irregular interface and thus poor visual outcome, while better results are reported with microkeratome-assisted ALK [4]. After removal of the diseased part of the recipient cornea, a lamella of the same thickness is obtained from a donor cornea mounted onto the artificial anterior chamber, punched to the same size and sutured into the recipient bed. Reported complications of SALK are residual corneal pathology, haze, anisometropia, epithelial ingrowth and dry eye [5].

Deep Anterior Lamellar Keratoplasty (DALK)

The main indications for DALK are: deep stromal opacities which may be caused by herpetic or other infectious scars, chronic inflammation with scarring after corneal burns and keratokonus. In this procedure corneal surgeon aims to remove nearly all or all of the recipient corneal stroma, while preserving the healthy endothelium. The advantage of DALK is preservation of host endothelium and thus reduced incidence of graft rejection, faster visual rehabilitation as compared to PK, and lower incidence of serious complications such as expulsive haemorrhage or endophthalmitis. DALK was first described by dr. Anwar in 1972. when simple blade was used to dissect deep stromal layers from Descemet membrane (DM) [6]. The technique was further improved by Anwar and Teichmann in 2002 with so called „Anwar's big-bubble technique". In this technique 60-80% of stromal depth is removed and then an air-bubble is inserted deep into the stroma to dissect Descemet's membrane with endothelium from corneal stroma; carefully the remaining stroma is then dissected. Finally, donor graft without Descemet membrane/endothelium of same size or 0.25 mm oversized is sutured into place [7]. Although DALK brings very good visual and refractive outcomes and preservation of host endothelium, the techniques is not easy to perform and may be complicated with perforations of DM and consequent need for penetrating keratoplasty. The most common indication for

such surgery is keratoconus. Several studies have been made to compare postoperative results of DALK versus PK in keratoconus, and it has been shown that similar visual results will be obtained by both techniques; however it is important to bear in mind that in case of DALK recipient endothelium is preserved and thus the incidence of graft rejection is lower [8-11]. Therefore, in spite of the fact that DALK is more time-consuming and more difficult to perform as compared to PK, increasing number of corneal surgeons are choosing this technique for keratoconus patients in order to spare recipient endothelium in those mostly very young patients.

POSTERIOR LAMELLAR KERATOPLASTY (PLK) OR ENDOTHELIAL KERATOPLASTY (EK)

Posterior lamellar (PLK) or endothelial keratoplasty (EK) is the selective replacement of diseased endothelium with a healthy donor endothelium (either on Descemets membrane alone or together with a thin part of donor stroma). The most frequent indications for such surgery are: Fuchs dystrophy, pseudophakic bullous keratoplasty and decompensated corneal grafts. More and more surgeons are performing EK because it gives better results, faster visual rehabilitation and it is safer surgery compared to PK [12-17]. Endothelial keratoplasties are nowadays most widely accepted lamellar corneal transplantations; for example in a period between 2005 and 2008 the rate of EK in USA increased 10-folds, coming to the rate of 70% of all corneal grafts. The most widely performed type of EK in USA, called DSAEK, is representing 80% of all lamellar keratoplasties performed in that country today. In Europe, the number of EK is not as significant as in USA, but it is in a constant rise coming to the rate of 30% of all grafts in year 2011 (according to the data of European Eye Bank Association). As previously mentioned, dr. Jose Barraquer was the first to propose lamellar transplantation of the posterior cornea already in 1950, but his surgical technique was not widely accepted due to techniqual difficulties [1]. In 1998 dr. Melles invented a novel surgical technique for posterior lamellar keratoplasty. He had proposed that after stripping of the diseased recipient endothelium, donor lamella consisting of donor endothelium and thin stromal layer can be inserted through the small corneal opening, and then use an air-bubble to fixate the donor endothelial graft onto the recipient cornea (*Figure 1*). He had shown that the oedematous cornea can be cleared if provided with a new functioning endothelial cell layer via a posterior corneal graft [18-22]. In 2001, dr. Terry published results of „deep lamellar endothelial keratoplasty“ (DLEK) in first United States patients [23]. The procedure was also adopted by dr. Price who termed it „Descemet-Stripping with Endothelial

Keratoplasty – DSEK" [24]. At the beginning, lamellar cut of a donor cornea to obtain healthy donor endothelium was performed by manual lamellar dissection, but the lamellar interface was not smooth enough, so dr. Gorovoy started to perform lamellar cuts with an automated cutting system called microkeratome (usually used for LASIK in refractive surgery), and this procedure was named DSAEK (Descemets Stripping Automated Endothelial Keratoplasty) [25]. Later on, when the preparation method of donor posterior lamella became more standardized, many eye-banks trained their staff to do the lamellar cut in the eye bank and then deliver so called "pre-cut" donor tissue for DSAEK to the corneal surgeon. Most of the american corneal surgeons are using such a "pre-cut" tissue for their DSAEK cases, while in Europe DSAEK is still mostly performed in a way that surgeon prepares posterior corneal graft in the operating room prior to transplantation. From the clinical point of view, both methods of tissue preparation for DSAEK seam to perform equally. Advantages of DSAEK over penetrating keratoplasty are numerous: corneal astigmatism is much lower as compared to PK due to the lack of sutures (which are causing significant astigmatism in PK); therefore visual recovery is fast and most patients have usable vision within 6 weeks after operation, and some of them have excellent vision at just 1 week, especially with ultra-thin DSAEK grafts [26-28]. After PK the stable visual acuity does not occur for at least 6 months to a 1 year (*Figures 2 and 3*). Sometimes it takes even longer period and patients require hard contact lenses to help normalize their astigmatism; unfortunately many older patients find it difficult or impossible to wear lenses. One more advantage of all endothelial keratoplasties is that small incision that is made during the operation leaves almost entire thickness of the recipient cornea untouched. This results in normal tectonic strength of the eye with resistance to traumatic rupture for the rest of the patient's life, which is not the case in PK where a circular wound cuts out the entire corneal thickness. Consequently, this vertical and unstable PK wound never heals with significant strength and patients may have ruptured wounds and lose their eye from blunt trauma, even many years after PK. There are also disadvantages of endothelial keratoplasty such as detachment of the donor graft (which occurs most often with DMEK cases), and a question of endothelial cell density (ECD) loss which may lead to primary graft failure. Reported rates of primary graft failure after DSAEK are between 0% and 29%, and detachment rates are between 1% and 40% [28,29]. If detachment of the DSAEK graft occurs, the graft can almost always be re-attached by reinsertion of an air-bubble into the anterior chamber, but this means an additional surgery for the patient (*Figure 4*). ECD loss after DSAEK is usually between 24% and 40% at 6 months to 1 year, which is higher than the early cell loss reported in most recent PK series [29]. The early cell loss with DSEAK is not surprising because

it entails more donor tissue manipulation than PK. However, there is also a study showing that after 3-4 years endothelial cell loss was less in DSAEK than in PK [30].

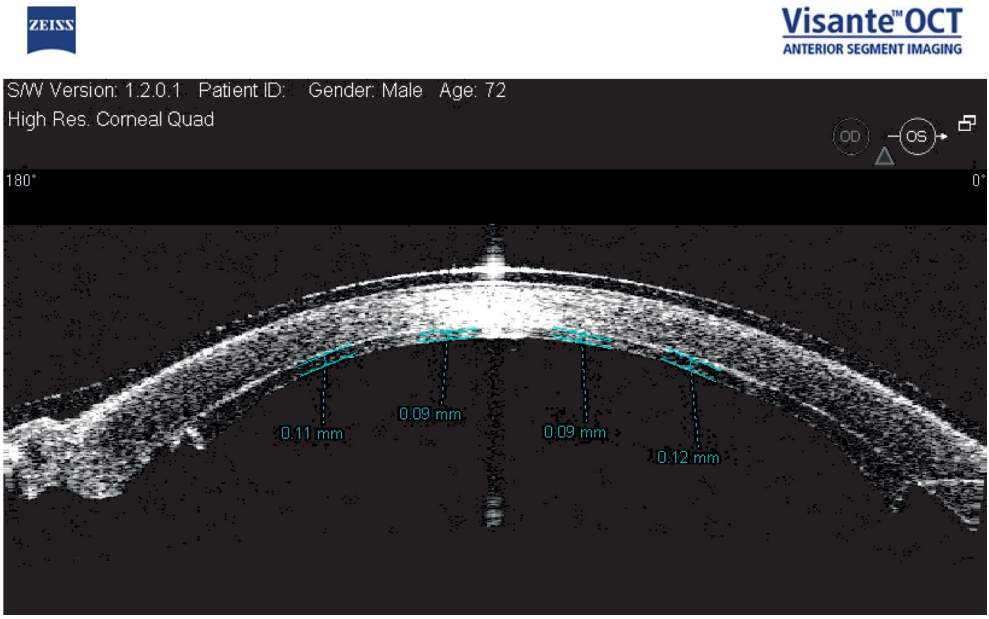

Figure 1. Posterior lamellar keratoplasty - anterior segment optical coherence tomography scan showing nicely adherent ultra-thin endothelial graft of 90μm thickness at first postoperative day.

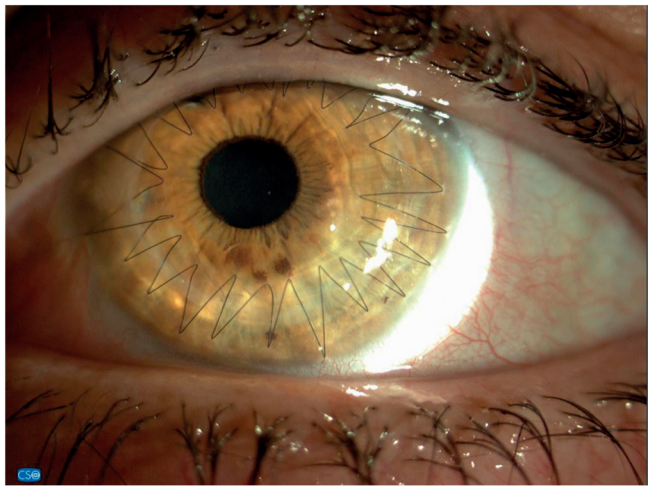

Figure 2. Clear corneal graft after penetrating keratoplasty at 6 months after surgery – uncorrected visual acuity is 50%, and best corrected visual acuity with a contact lens 100%.

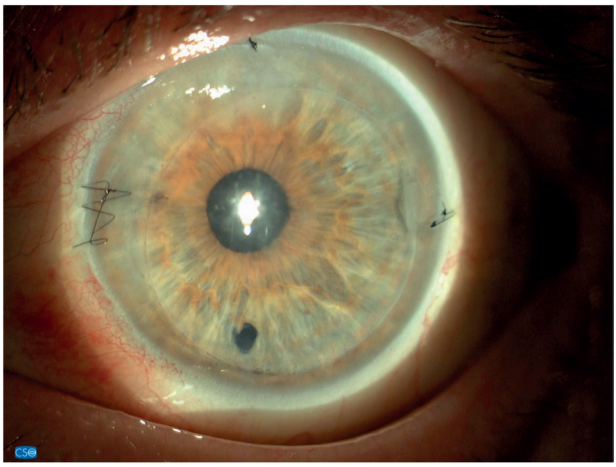

Figure 3. Endothelial graft after ultra-thin Descemet's Stripping Automated Endothelial Keratoplasty at 3 weeks after surgery – uncorrected visual acuity is 100%.

Figure 4. Posterior lamellar keratoplasty - anterior segment optical coherence tomography scan showing detached endothelial graft at three days after surgery. In such case it is necessary to place another air-bubble into the anterior chamber to reposition the graft.

Melles has investigated a further refinement of posterior lamellar transplantation and started with the transplantation of the Descemet's membrane alone; the procedure called Descemet's membrane endothelial transplantation or DMEK [31-34]. Main advantage of this procedure is that patients obtain better visual acuity in a quicker time-frame as compared to DSAEK, and that the graft rejection rate is significantly lower as compared to both DSAEK and PK [35,36]. However, the technique is technically more difficult with the reported graft detachment rate going up to 60%, and there is a general concern over higher endothelial cell density loss due to prolonged manipulation with such a thin donor graft. Price group made a prospective study comparing results of somewhat different approach - Descemet's membrane automated endothelial keratoplasty (DMAEK) with DSEK in 2011; study showed that DMAEK has a higher rate of postoperative air reinjections than DSEK and comparable 6-month endothelial cell loss [37]. In a recent study by dr. Kruse group in Germany it has been shown on a significant number of cases that DMEK provides faster and more complete visual rehabilitation when compared with DSAEK, without any significant differences concerning endothelial cell survival within a 6-month follow-up [38]. However, a long-time postoperative data on endothelial cell loss after DMEK are still lacking.

Having in mind that DSAEK is surgically much safer and easier then DMEK, and that the thinner endothelial grafts may bring quicker and better visual recovery [39-43], dr. Busin suggested so-called „ultra-thin DSAEK" as, in his opinion, currently optimal surgical approach for patients in need for endothelial lamellar transplantation [44]. The difference to conventional DSAEK is that ultra-thin donor tissue preparation for endothelial keratoplasty is made with a double-pass microkeratome; first cut is usually made with a microkeratome head of 250 to 350 μm and the second one with a 50 to 130μm head (depending on the thickness of the donor corneal tissue) [45]. This technique combines advantages of DSAEK (easier manipulation with the endothelial graft and consequently decreased endothelial cell loss) with the advantages of DMEK (thin grafts bring better vision) [46].

CONCLUSION

Corneal transplantation has changed dramatically since its early days over 100 years ago, when the gold standard of surgery was full thickness penetrating keratoplasty (PK). In a last decade many new surgical options have been proposed to treat patients with corneal diseases. The main standard of care nowadays is to remove only the diseased part of the recipient cornea and to replace it with a donor corneal lamella. The options for such a general idea are numerous, and it is up to a cor-

neal surgeon to choose an optimal surgical option for each individual patient. All the previously described surgical methods of lamellar corneal transplantation have their great advantages, but also their limitations that we must be aware of. Finally, the growing number of lamellar cases performed worldwide does not mean that PK becomes an obsolete technique, since there are still a significant number of patients having corneal diseases involving all corneal layers, and for which PK will remain the only way to regain their vision.

Abbreviations: PK- penetrating keratoplasty, ALK- anterior lamellar keratoplasty, SALK – superficial anterior lamellar keratoplasty, DALK – deep anterior lamellar keratoplasty, PLK- posterior lamellar keratoplasty, EK- endothelial keratoplasty, DLEK- deep lamellar endothelial keratoplasty, DSAEK - Descemet stripping automated endothelial keratoplasty; DMEK- Descemet membrane endothelial keratoplasty.

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Sažetak

Suvremeni trendovi u transplantaciji rožnice

Transplantacija rožnice vrlo je stara kirurška metoda koja se uspješno primjenjuje već više od 100 godina. U posljednjih desetak godina nastupile su velike promjene glede kirurških metoda koje se primjenjuju prilikom transplantacije rožnice. Razlog za tako drastične promjene jest suvremeni trend da se prilikom transplantacije zamijeni samo onaj oboljeli sloj primateljeve rožnice, a ne puna debljina rožnice. Takav kirurški zahvat naziva se slojevita ili lamelarna transplantacija rožnice. Ako je samo prednji dio bolesnikove rožnice zahvaćen bolešću, metoda izbora pri liječenju bit će prednja slojevita (lamelarna) transplantacija, pri kojoj se sačuva zdravi primateljev endotel, a time se i smanji šansa za odbacivanje transplantata. Ako je bolest rožnice zahvatila stražnji dio rožnice, primjenjuje se stražnja slojevita transplantacija kojom se postiže znatno brži oporavak i bolja kvaliteta vida negoli kod perforativne keratoplastike (PK) jer se izbjegava problem astigmatizma koji se nužno javlja kod PK radi postavljanja šavova rožnice. Brojne su prednosti slojevite transplantacije: brži oporavak vida, manja šansa za odbacivanje transplantata, očuvanost integriteta bulbusa, nema problema vezanih uz šavove rožnice (vrijedi za stražnju slojevitu transplantaciju), izbjegavanje komplikacija vezanih za rad na „otvorenom" oku, teoretska mogućnost uporabe jedne donorske rožnice za dva bolesnika (ako istog operativnog dana imamo bolesnika kojem radimo prednju lamelarnu i bolesnika predviđenog za stražnju lamelarnu transplantaciju) te mogućnost primjene lokalne (ili potencirane) anestezije umjesto opće anestezije. Naravno da postoje i problemi koji se mogu javiti kod takvih operacija, a to su: povećan rani gubitak endotelnih stanica rožnice, odljepljenje stražnjeg endotelnog transplantata, urastanje krvnih žila ili epitela u sloj između primateljeve i donorske lamele rožnice te nedovoljno informacija glede dugoročne sudbine lamelarnih transplantata. U ovom preglednom članku prikazane su danas najčešće upotrebljavane metode slojevite transplantacije rožnice, zajedno s njihovim prednostima i manama u odnosu na standardni PK.

Ključne riječi: prednja slojevita (lamelarna) transplantacija; površna prednja slojevita transplantacija; duboka prednja slojevita transplantacija; stražnja slojevita transplantacija, duboka stražnja slojevita transplantacija; automatizirana endotelna transplantacija uz ljuštenje Descemetove membrane; endotelna transplantacija Descemetove membrane.

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