Descemet membrane endothelial keratoplasty with stromal rim (DMEK-S) in complicated patients
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Purpose. To evaluate the outcomes of the hybrid technique of posterior lamellar keratoplasty (Descemets' membrane endothelial keratoplasty with stromal rim, DMEK-S) in eyes with multiple ocular pathologies.

Methods. A retrospective case control study of the consecutive group of all eyes with combined ocular pathologies which underwent DMEK-S keratoplasty. We evaluated the number of pre- and post-operative complications; uncorrected distance visual acuity (UDVA); corrected distance visual acuity (CDVA) and endothelial cell density (ECD). The first group (Group 1 - 100 eyes) was compared to a control group of eyes (Group 2 – 145 eyes) without combined ocular pathologies, which were operated throughout the same time period. Comparisons were made in the 12th month of the follow-up.

Results. Both the UDVA and the CDVA statistical values 12 months after the surgery were significantly better in Group 2. ECD was comparable in both groups. The number of complications during surgery was considerably higher in Group 1, where a certain type of complication occurred in 15 eyes (15%), while in Group 2 this complication occurred only in 9 eyes (6.2%). In Group 1 a slightly higher number of rebubbling cases (52% vs. 48.3%) occurred, as well as more than twice as many cases of primary graft failure (34% vs. 15.7%) compared to Group 2.

Conclusion. DMEK-S - hybrid endothelial transplantation in complicated eyes in the evaluated group of patients led to a noticeable improvement of visual acuity. When compared to surgeries in uncomplicated eyes, DMEK-S results in a higher rate of postoperative complications, especially graft detachment and primary failure.

Key words: DMEK-S, lamellar keratoplasty, endothelial dystrophy, endothelial transplantation

INTRODUCTION
There are currently several types of lamellar endothelial transplantation available for patients with endothelial dysfunction, such as bullous keratopathy, Fuchs endothelial dystrophy, posterior polymorphous endothelial dystrophy, iridocorneal endothelial syndrome, and corneal endothelial failure after perforating keratoplasty (PK) or lamellar keratoplasty.

The two most frequently used techniques of lamellar endothelial transplantation are DSAEK (Descemet stripping automated endothelial keratoplasty) where the lamella consists of deep stromal layers, Descemet's membrane (DM), and endothelium1; and DMEK (Descemet' s membrane endothelial keratoplasty) where the lamella consists only of DM and endothelium2,3.

Since 2007 the most commonly used method within our department has been the DMEK-S method, where a hybrid lamella is transplanted. Hybrid lamella consists of DM and endothelium in its central part, without the presence of stroma, while in peripheral areas there is a rim of deep stromal layers. The big-bubble technique was used for the DM separation4. The hybrid lamella theoretically combines the advantages of both previously mentioned techniques, i.e. a relatively easy manipulation (DSAEK) and an outstanding postoperative visual acuity after successfully performed surgeries (DMEK) (ref.5-8).

A lot of studies have evaluated the results of these techniques, however the authors usually compare the data of uncomplicated patients, such as eyes with no other ocular pathalogy than endothelial dysfunction. Though many of these patients indicated for the endothelial transplantation stated, that they had previously suffered from other eye diseases or underwent some other eye surgeries.

Performing a surgery on eyes affected in this manner is often more demanding than the standard techniques and therefore may bring multiple complications, both during surgery and in the postoperative period.

The aim of this study is to compare the results of DMEKS (visual acuity, frequency of complications during and after surgery) in complicated and uncomplicated patients.

MATERIALS AND METHODS
This study is a retrospective evaluation of a consecutive group of all patients with combined ocular pathologies who underwent DMEK-S keratoplasty at the Ophthalmology Department of Kralovske Vinohrady...
Teaching Hospital and the 3rd Medical Faculty of Charles University, Prague, from January 2007 to March 2015.

The first group of eyes (Group 1) was compared to the second group (Group 2), which was operated throughout the same time period, but without combined ocular pathologies influencing the surgery, the postoperative process of healing, and the postoperative visual acuity.

In the Group 1 we also individually evaluated results in subgroups of eyes (n ≥ 10 eyes) with different eye conditions - after pars plana vitrectomy (PPV), with anterior chamber intraocular lens (AC IOL), eyes after PK, eyes after glaucoma surgery and eyes with pseudoexfoliative syndrome (PEX).

We evaluated the number of intra- and post-operative complications; uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) in decimal values; endothelial cell density (ECD) in cc/mm².

Differences between the two groups, as well as differences between individual sub-groups and Group 1, were evaluated using Student’s unpaired t-test. Differences with P ≤ 0.05 were evaluated as statistically significant.

RESULTS

Group 1 examined 100 eyes of 66 patients with the mean age of 69±14 years (minimum age was 22 years; maximum age was 93 years). Types of ocular pathologies recorded in Group 1 are described in detail in Table 1. There were more than one ocular pathologies in some eyes, which were included in several sub-groups evaluating the individual risk factors.

Different types of complications occurred in 15 eyes during the surgery: graft turning over, bleeding, loosening of lens ligament, flat anterior chamber, herniation of vitreous body, presence of silicon oil in anterior chamber, lamella graft in vitreous cavity, miosis.

From various postoperative complications in Group 1 graft detachment occurred in 52 eyes (52%). In these 52 eyes the rebubbling was performed once in 29 eyes, twice in 15 eyes, three times in 5 eyes, and four times in 3 eyes. In 34% of the cases a primary graft failure occurred, resulting in the absence of postoperative corneal clearance. In 4 cases a repeated endothelial dysfunction and corneal oedema occurred after a period of successful corneal clearance (secondary graft failure).

Postoperative increase of intraocular pressure was recorded in 11 eyes, exceeding the value of 24 mmHg. In 7 out of these 11 eyes the intraocular pressure continued to increase even after completing the steroid therapy. Therefore, this condition was identified as a secondary glaucoma developed de novo (2 eyes) or as a secondary decompensated glaucoma of a different type, already present in the preoperative phase: juvenile glaucoma (1 eye), pseudoexfoliative glaucoma (1 eye), primary open-angle glaucoma (1 eye), and secondary glaucoma after different eye surgery (2 eyes).

In the treatment of this glaucoma a change in conservative therapy was sufficiently effective in 5 patients, while in 2 patients the glaucoma surgery using Ex-Press...

A mini glaucoma shunt was performed (Alcon Laboratories, Fort Worth, TX, USA).

Transplant rejection occurred in 1 patient, 18 months after surgery.

A number of other complications occurred in Group 1, always in 1 patient. These were: mild keratitis, epiretinal membrane, retrolental membrane, pupiloplegia, cystoid macular edema, subluxation of intraocular lens (IOL), newly developed wet form of age-related macular degeneration, cataract, branch retinal vein occlusion, luxation of IOL into vitreous cavity, and candida corneal ulcer (due to overall immune deficiency). The frequencies of postoperative complications in Group 1 and 2 are summarized in Table 3.

In the comparative Group 2 were 145 eyes with single ocular pathology of 102 patients with the mean age of 72 ± 10 years (minimum age was 42 years; maximum age was 91 years).

A certain type of complication occurred in 9 eyes during surgery: graft turning over in 6 eyes, pronounced intraoperative floppy iris syndrome (IFIS) in 1 eye, shallow anterior chamber in 1 eye, and in 1 eye a reimplantation of the lamellae due to the graft being pushed out of the anterior chamber by irrigation flow.

Postoperative results are summed up in Table 2. Twelve months after surgery UDVA was 0.58 ± 0.26, CDVA was 0.81 ± 0.22, ECD was 1187 ± 508 bb/mm² which represents a decrease of 60 ± 17%.

From various postoperative complications in Group 2 a graft detachment occurred in 70 eyes (48.3%). Out of these 70 eyes the rebubbling was performed once in 51 eyes, twice in 11 eyes, three times in 6 eyes, and four times in 2 eyes. In 22 cases (15.7%) a primary graft failure occurred, while secondary graft failure occurred in 5 cases: in one case after 3 months, in two cases after 6 months, in two cases after 12 months.

In 12 eyes with normal preoperative values of intraocular pressure, a postoperative increase in the intraocular pressure was recorded. In 10 eyes intraocular pressure increase continued, even after completing the steroid therapy. Therefore, this condition was identified as a secondary glaucoma. In 2 cases the glaucoma surgery was performed-deep sclerectomy with T-Flux implant (Carl Zeiss Meditec, Germany).

Other postoperative complications included: transplant rejection in 2 eyes, one 3 months, and one 12 months after surgery.

Nd: YAG laser capsulotomy was necessary in 4 eyes due to posterior capsular opacification, and a cataract developed in 1 phakic eye, recommended for surgery.

When comparing Group 1 (complicated patients) with Group 2 (uncomplicated patients), both UDVA and CDVA values 12 months after surgery were statistically significantly better in Group 2. ECD was comparable in both groups.

As expected, the number of perioperative complications were considerably higher in Group 1 where a certain type of complication occurred in 15 eyes (15%), while in Group 2 only in 9 eyes (6.2%).

In Group 1 a slightly higher (statistically insignificant) number of rebubbling cases (52% vs. 48.3%) occurred, as well as more than twice as many cases of primary graft failure (34% vs. 15.7%, statistically significant) compared to Group 2. The numbers of the remaining types of complications were roughly the same in both Groups.

Visual acuity and endothelial loss 12 months after surgery in individual sub-groups of Group 1 were similar and comparable with the results for Group 1 as a whole. The only statistically significant difference was a higher endothelial loss in the sub-group of patients after PK (P=0.0075). The rest of the differences were not statistically significant.

Among the postoperative complications a graft detachment with the necessity of rebubbling occurred most commonly in the sub-group of patients after PK (60%) and after glaucoma surgery (58.3%). Primary failure occurred noticeably more often in the sub-group of patients with aphakia (71.4%), while in the sub-group of patients after glaucoma surgery its percentage was the lowest (16.7%), coming close to the results of the Group 2 with uncomplicated eyes (15.7%). The frequencies of graft detachment and primary failure were similar in the rest of the sub-groups.

**DISCUSSION**

Results of endothelial transplantation in complicated patients are only rarely published and the numbers of patients involved are relatively limited. Most of the studies available are focused on DSAEK type of surgery and each study usually looks at a specific comorbidity.

Most of the published studies describe results and frequencies of complications in patients with AC IOL.

<p>| Table 3. Comparing the numbers of individual postoperative complications in Groups 1 and 2. |
|-----------------------------------------------|-----------------------------------------------|
| Complicated eyes, n=100 | Uncomplicated eyes, n=145 |</p>
<table>
<thead>
<tr>
<th>Number</th>
<th>%</th>
<th>Number</th>
<th>%</th>
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<tbody>
<tr>
<td>Rebubbling</td>
<td>52</td>
<td>52</td>
<td>70</td>
</tr>
<tr>
<td>Primary failure</td>
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<td>34</td>
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<td>Secondary failure</td>
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<td>11</td>
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<td>10</td>
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<tr>
<td>Rejection</td>
<td>1</td>
<td>1</td>
<td>3</td>
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IOP = Intraocular pressure
or with aphakia. Some studies also include an exchange of the AC IOL for a posterior chamber intraocular lens (PC IOL).

Shah described results at six months after DSAEK with IOL exchange combined surgery in the group of 19 eyes. No dislocations or primary graft failures occurred; the mean CDVA value was 0.42 and mean donor cell loss at 6 months was 33% (ref. 9).

Similar group of patients with DSEK (Descemet stripping endothelial keratoplasty) combined with AC IOL removal and scleral fixation of a PC IOL was described by Wylegala. The study group consisted of 11 eyes and the follow-up was 19.3 months. Lamella detachment occurred in 3 eyes, corneal rejection was observed in 1 eye. The mean CDVA value was 0.36; mean ECD value was 2048 bb/mm². Endothelial cell loss was 36% (ref. 10).

Velez, in a total of 9 aphakic eyes with simultaneous DSEK and retro pupillary fixed iris claw lens (Artisan), states the minimum visual acuity of 0.25 at six months after the surgery11.

Hsu compared outcomes and difficulties of DSAEK in complicated cases with IOL exchange, aphakia, or AC IOL implants (30 eyes) with a group of uncomplicated DSAEK cases (109 eyes). Of the 30 complicated DSAEK cases, 14 eyes underwent IOL exchange, 5 AC IOLs were not removed, 5 eyes remained aphakic, and 5 eyes had IOL exchange done before or after DSAEK. One eye had an iris-supported phakic IOL removed, followed by cataract extraction with IOL implantation at the time of DSAEK. In group of complicated cases only 27.6% of patients achieved a CDVA value of 0.5 and better, compared to 94.4% in the other group of patients without visually significant comorbidities. 60% of the complicated eyes achieved a CDVA value of 0.29 and better. Of the 30 complicated cases, 5 (16.7%) had graft detachments and 5 (16.7%) developed IOL dislocations. Primary graft failure occurred in 3 cases (10%) (ref. 12).

Ang evaluated an endothelial cell loss in 18 eyes, which underwent DSAEK while retaining AC IOL, and compared it to the results of a control group with PC IOL left in place. The endothelial cell loss at 1 year was 31.9±21.3% in the DSAEK with AC IOL group compared to 24.5±21.2% in the DSAEK group; however, this figure was significantly greater in the DSAEK with AC IOL group at 3 years compared to the DSAEK group (55.3±29.2% vs 33.3±20.8%) (ref. 13).

Elderkin evaluated the frequency of complications in a group of 11 patients with corneal decompensation and AC IOL who underwent DSAEK. Six patients had a temporary suture to secure their graft. There was 1 graft dislocation postoperatively and 1 primary graft failure among those 11 patients14.

Most authors agree that the results in complicated patients are slightly worse and the frequency of complications is higher, when compared to the results in eyes without other ocular copathology.

Therefore, it is rather rare to see results such as those published by Shpitzer, who retrospectively compared patients who underwent DSAEK and had a retained AC IOL, with patients who underwent DSAEK and had a PC IOL. There were 11 eyes with an AC IOL and the authors found no significant differences between the groups in terms of perioperative complications, change in visual acuity, graft survival, and endothelial cell loss15.

In our sub-group of patients with AC IOL the mean visual acuity at 12 months was 0.41 ± 0.24, thus comparable or even better than in published studies. This difference can be explained by generally better results for visual acuity after DMEK type of surgery compared to DSAEK and DSEK.

On the other hand, a significantly higher frequency of postoperative complications was recorded, especially of graft detachment (42.8% in eyes with AC IOL and 57.1% in aphakic eyes) and primary graft failure (42.8% and 71.4%, respectively). Furthermore, endothelial cell loss was slightly higher in our group compared to published results (39 ± 24%).

In the case of aphakic eyes our method, i.e. DMEK-S combined with IOL implantation, turned out to be quite risky. It would probably be more appropriate to separate the two surgeries: perform IOL implantation first and the endothelial transplantation after that as a separate surgery, because of the lower frequency of complications in the sub-group of patients with AC IOL.

A group of 20 vitrectomized eyes selected for DMEK was described by Yoeruk. Seven eyes had a history of anterior vitrectomy and 14 eyes of PPV. Twelve months after surgery the CDVA was 0.25 and ECD was 1241 ± 155 bb/mm² on average16.

In our sub-group of patients after PPV mean CDVA after a 12-month follow-up was significantly better (0.40±0.34), while ECD was lower (1097±631 bb/mm²). A specific type of complication in eyes after PPV, which was also once recorded in our sub-group, would be the unwanted dislocation of the donor graft into the posterior segment.

A series of this complication associated with DSAEK was described by Afshari et al. In 6 of 8 eyes PPV was used to remove the dislocated graft. Their study concluded that better postoperative results seem to be associated with the prompt removal of the posteriorly dislocated graft17.

Mitry et al. evaluated results of patients who underwent DSAEK after failed PK. It was a multicentre study that included 246 eyes with the median follow-up of 17 months. In total, 19.1% (47 of 246) of DSAEK grafts failed. Authors identified the following significant preoperative risk factors for failure: young recipient age, previous filtration surgery, and rejection episodes before PK failure. Authors came to conclusion that DSAEK after failed PK combines greater wound stability and reduces suture-related complications, with visual outcomes and graft survival rates comparable to those of a second PK (ref. 18).

Chaurasia notes primary graft failure in 22.2% and visual acuity of 0.33 and better in 63% of eyes in a group of 27 eyes with DSEK for failed penetrating keratoplasty (PK) (ref. 18).

Lee described results of a group of 8 eyes with DSAEK after PK. Seven of the patients showed an improvement in CDVA, while the average CDVA acuity 6 months post-
operatively was 0.1. Graft detachment occurred in 4 eyes (50%) and 1 eye experienced graft failure.

Covert published similar results in 7 patients: average visual acuity was 0.31; graft detachment occurred in 3 eyes and primary failure in 3 eyes (42.9 %) (ref.21).

In our sub-group of patients after PK a relatively good visual acuity was achieved (0.35±0.23), however endothelial loss in this sub-group was by far the highest among all studied types of comorbidities (2180 ± 203). It was even statistically significantly higher than that for the whole of Group 1. This is probably also related to a higher rate of postoperative complications in our sub-group: 60% of graft detachments and 30% of primary failures.

CONCLUSION

DMEKS – hybrid endothelial transplantation in complicated eyes led in our group of patients to a marked improvement of visual acuity. After successful surgeries the resulting visual acuity is higher than that in published data for comparable patients after DSAEK.

When compared with surgeries in uncomplicated eyes and in complicated eyes after DSAEK, DMEK-S results in a high rate of postoperative complications, especially graft detachment and primary failure.

In aphakic eyes we consider DMEK-S combined with AC IOL implantation as unsuitable.

When choosing the optimal surgery technique, the surgeon must always individually evaluate possible pros and cons of a given type of surgery.

ABBREVIATIONS

AC IOL, anterior chamber intraocular lens; CDVA, corrected distance visual acuity; DM, Descemet’s membrane; DMEK, Descemet’s membrane endothelial keratoplasty; DMEKS, Descemet’s membrane endothelial keratoplasty with stromal rim; DSAEK, Descemet stripping automated endothelial keratoplasty; DSEK, Descemet stripping endothelial keratoplasty; ECD, endothelial cell density; IOL, intraocular lens; PC IOL, posterior chamber intraocular lens; PK, penetrating keratoplasty; PPV, pars plana vitrectomy; UDVA, uncorrected distance visual acuity.

Author contributions: PS: literature search; PS, MV: manuscript writing; DK: data collection; PS, MV, DK: data analysis, final approval

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REFERENCES