Original Article

Microkeratome-assisted ultrathin Descemet's stripping automated endothelial keratoplasty: A randomized trial comparing single-pass versus double-pass technique

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Purpose: To compare the outcomes of two techniques, for preparation of microkeratome-assisted ultrathin grafts for Descemet's stripping automated endothelial keratoplasty (DSAEK). **Methods:** The study involved 20 eyes of 20 patients with pseudophakic bullous keratopathy, randomized into two groups. Group 1 eyes underwent microkeratome-assisted DSAEK using the single-pass technique for lenticule preparation, whereas group 2 eyes underwent microkeratome-assisted DSAEK using the double-pass technique. Patients were followed up till 6 months, postoperatively. Best-corrected visual acuity (BCVA) at final follow-up was considered as the primary outcome measure, whereas graft thickness (GT) contrast sensitivity and endothelial cell loss were considered as the secondary outcome measures. A *P* value of <0.05 was considered as statistically significant. **Results:** Baseline characteristics of two groups were comparable. The mean central GT was comparable in both groups at 6 months follow-up [group 1: 98 ± 24.46 µm, group 2: 129 ± 31.46 µm (*P* = 0.18)]. Both groups fared equally in terms of BCVA (*P* = 0.33). Contrast sensitivity was significantly better in group 1 eyes (*P* = 0.045). A statistically significant negative correlation was found between postoperative BCVA and postoperative GT (*R* = −0.728, *P* = 0.016). The percentage endothelial cell loss was slightly higher in group 2 eyes, although not statistically significant. Two eyes in group 2 experienced complications during lenticule preparation. None of the eye experienced any complication in the postoperative period. **Conclusion:** Both techniques provided grafts with comparable thickness and endothelial cell loss and were associated with comparable BCVA, at final follow-up visit. The contrast sensitivity was, however, better in eyes receiving grafts prepared with the single-pass technique.

Key words: Double-pass technique, microkeratome, single-pass technique, ultrathin Descemet's stripping automated endothelial keratoplasty

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1660_18

Quick Response Code:

Descemet's stripping automated endothelial keratoplasty (DSAEK) is currently the most popular surgical procedure for visual rehabilitation of patients with endothelial pathologies.[1] The procedure involves transplantation of Descemet's membrane, endothelium, and a layer of deep stroma, creating an interface at the junction of donor and host stroma. The Descemet's membrane endothelial keratoplasty (DMEK) graft, on the other hand, is completely devoid of stromal tissue and therefore the surgical procedure offers a faster visual recovery with better visual outcomes and reduced rejection rates.[2-4] The procedure, however, has limitations in the form of a technically challenging donor tissue preparation and higher rate of intraoperative as well as postoperative complications, compared to a standard DSAEK procedure.[2-4]

Neff *et al.* (2011) first reported a trend toward better visual acuity with thinner DSAEK grafts, which they defined as grafts with thickness ≤131 µm.[5] Subsequently, Busin *et al.* in a laboratory experiment described microkeratome-assisted double-pass technique for preparation of such thinner grafts, which they labeled as ultrathin (UT) DSAEK grafts.[6] The technique mainly comprised an initial debulking cut followed by a refinement cut to obtain the desired thickness. They also showed that the additional manipulation required to prepare UT grafts during the second cut did not adversely affect the endothelial cell loss. Similarly, authors in 2013 subsequently evaluated the clinical outcomes of UT DSAEK using microkeratome-assisted double-pass technique.[7] The visual outcomes were found to be comparable with those of DMEK and were better than those reported after the conventional DSAEK. The procedure had added advantages of easy graft preparation and tissue manipulation, compared to DMEK. The complication rates of UT DSAEK were similar to that of the

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Manuscript received: 03.10.18; Revision accepted: 06.04.19

Cite this article as: Sharma N, Hussain AY, Nagpal R, Rathi A, Maharana PK, Sinha R, *et al.* Microkeratome-assisted ultrathin Descemet's stripping automated endothelial keratoplasty: A randomized trial comparing single-pass versus double-pass technique. Indian J Ophthalmol 2019;67:1289-94.

standard DSAEK procedure, but were much less compared to DMEK. The procedure can also be safely performed in eyes where DMEK is difficult to perform, such as eyes with disorganized anterior segment anatomy, aphakia, and with significant corneal haze.

Another described method for preparing UT grafts involves the use of a microkeratome head, appropriately chosen, as per the standard nomogram based on the baseline donor corneal thickness.[8] The single slow pass technique described by Vajpayee *et al.* utilized a 400 µm microkeratome head to obtain thin donor lenticules and was found to be safe, efficacious, and repeatable.[9]

Both single-pass and double-pass techniques have separately been seen to produce thinner grafts, but to the best of our knowledge, till date no study has compared the outcomes and efficacy of these two techniques. This study prospectively evaluates the outcomes and complications of microkeratome-assisted single as well as double-pass technique, for preparation of UT DSAEK grafts.

Methods

The study was conducted at a tertiary care ophthalmic setup between December 2014 and 2015. A written and informed consent was obtained from all patients after explaining the nature and consequences of the study. Ethical clearance was obtained from the Institutional Review Board [Ref. no. IESC/T-412/28.11.2014]. The study adhered to the tenets of Declaration of Helsinki.

The study was taken up as a pilot project involving a small set of 20 patients. Twenty eyes of 20 patients with pseudophakic bullous keratopathy with a stable posterior chamber intraocular lens were enrolled and randomized into two groups. Eyes with deep stromal scarring, high or irregular astigmatism, end-stage glaucoma, retinal pathology, and those with no light perception or inaccurate projection of rays were excluded. Randomization was performed using a random number table. A table of 20 random numbers was generated by randomly selecting numbers from within the range of 1–2, allowing duplicate numbers. Group 1 eyes underwent microkeratome-assisted UT DSAEK, with grafts prepared using the single-pass technique. Group 2 eyes underwent microkeratome-assisted UT DSAEK, with grafts prepared using the double-pass technique.

The parameters which were evaluated preoperatively included uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), anterior chamber depth (ACD), and the position and stability of intraocular lens. An ultrasound B scan (EZ Scan AB 5500+, Sonomed Inc., Lake Success, NY, USA) was done for posterior segment evaluation in eyes where fundus examination was not possible clinically.

The parameters which were evaluated postoperatively included UCVA, BCVA, intraocular pressure using Tonopen AVIA (Reichert Technologies, New York, USA), contrast sensitivity using the Pelli-Robson chart (Precision Vision, LaSalle, USA), endothelial cell count using specular microscope (SP-3000P; Topcon, Europe), and central as well as mid-peripheral graft thickness (GT) using anterior segment optical coherence tomography [(Visante, Carl Zeiss Meditec, Inc, Dublin, CA, USA)]. BCVA at final follow-up visit was considered as the primary outcome measure, whereas central GT, contrast sensitivity, and percentage endothelial cell loss were taken as the secondary outcome measures.

Surgical technique

All surgeries were performed by a nonblinded single surgeon (NS). The donor tissue was first prepared, followed by the host bed. The donor corneoscleral button stored in McCarey-Kaufman (MK) medium was mounted on an artificial anterior chamber (AAC) (Moria, Antony, France) with infusion bottle kept at a height of 120 cm above the level of AAC and tubing clamped at a distance of 50 cm from the point of entry into the AAC. Graft was dissected using a microkeratome (Moria, Antony, France) with an appropriate cutting head.

Single-pass technique

After ensuring adequate pressure in the AAC system, central and mid-peripheral corneal thickness measurements were taken using an ultrasonic pachymeter (Micropach, 200P+; Sonomed, Lake Success, NY, USA). The mid-peripheral measurements were taken at a distance of 7 mm from the center of cornea. The corneas were not dehydrated in any of the case. Corneal epithelium was debrided. A 400-micron microkeratome head was chosen and first-pass was performed at a deliberately slow speed, lasting for 10–15 s. The anterior cap was removed and residual stromal bed was measured using microscope-integrated optical coherence tomography. The AAC was carefully disassembled, avoiding any trauma to the endothelium.

Double-pass technique

Here, the microkeratome head was appropriately chosen, in order to have a residual stromal bed thickness of < 130 µm. Corneal epithelium was debrided. The first-pass or the debulking cut was performed according to the nomogram described in Table 1. The first-pass was performed at a constant speed, lasting for 10–15 s. The residual stromal bed was then measured with ultrasound pachymetry. The second-pass or the refinement cut was done in accordance with a separate nomogram [Table 2]. The dissection was started at a site 180° away from the site of initiation of first dissection.

Table 1: Nomogram for the initial debulking cut of double-pass technique of microkeratome-assisted UT DSAEK

Donor central corneal thickness (µm)	Microkeratome head (µm)
>600	300
500-600	250
400-500	200
<400	130

Table 2: Nomogram for the refinement cut of double-pass technique of microkeratome-assisted UT DSAEK

Residual stromal bed thickness (µm)	Microkeratome head (µm)
>235	130
216-235	110
190-215	90

The residual stromal bed thickness was measured using microscope-integrated optical coherence tomography.

Host bed preparation

A peribulbar block was given using a 1:1 mixture of 0.5% bupivacaine and 2% lidocaine. A 9 mm mark was applied over the corneal surface using a DSAEK marker (Moria). A 23G anterior chamber maintainer connected to a balanced salt solution infusion line was inserted via a tunneled side port. The stained Descemet's membrane was then scored and stripped using a reverse sinskey hook. The donor lenticule was trephined using a disposable trephine, the size of which was chosen as per the white to white measurement of the eye. The lenticule was then transferred onto the Busin glide (Moria) and inserted via a tunneled 3.2 mm incision. After the donor lenticule was completely unfolded, air was injected into the anterior chamber to obtain a complete fill.

Postoperatively, 0.5% moxifloxacin hydrochloride eye drops were prescribed at a frequency of three times a day for the first 14 days. Prednisolone acetate; 1% eye drops were prescribed starting at a frequency of six times a day in the immediate postoperative period and then tapered off gradually. The patients were followed up at 1 week, 1 month, 3 months, and at 6 months after the surgery.

Statistical analysis was performed using SPSS 15 software. For quantitative variables, statistical significance was determined using nonparametric Wilcoxon signed-rank test, unpaired Student's *t*-test and Mann–Whitney *U*-test. Fisher's exact test was used to compare the significance of categorical variables. A *P* value of < 0.05 was considered as statistically significant.

Results

Baseline characteristics

The donor factors which were evaluated at baseline included age, death to preservation time, endothelial cell density, and central GT. Baseline host factors included mean age of patients and central corneal thickness. All these parameters were equally distributed among the two groups [Table 3]. The preoperative specular count values referred to the values measured before the microkeratome cut.

Visual acuity

LogMAR visual acuity was estimated preoperatively at 1 week, 1 month, 3 months, and at 6 months postoperative follow-up visit [Tables 4, 5 and Fig. 1]. Both UCVA and BCVA significantly improved at all follow-up time points in both groups. Comparing the two groups, the visual acuity values were comparable at all postoperative time points.

Spherical equivalent

The mean spherical equivalent values were comparable among the two groups, at all postoperative time points, with a trend toward progressive decrease in the amount of hyperopia [Fig. 2 and Table 6].

Contrast sensitivity

The contrast sensitivity was significantly better in group 1 eyes at all postoperative time points [Fig. 3 and Table 7]. Among the group 2 eyes, a statistically significant negative correlation as seen between contrast sensitivity and GT at 6 months follow-up ($R = -0.735$, $P = 0.015$).

Table 3: Baseline characteristics of two groups which underwent microkeratome-assisted UT DSAEK

	Group 1	Group 2	*P*
Donor parameters			
Age (mean±SD)	36.38±16.94	37.70±14.87	0.65
Death to preservative time (h) (mean±SD)	5.29±3.28	4.53±3.27	0.29
Specular count (mean±SD)	2495.33±278.94	2677.66±271.20	0.27
Mean central GT (μm)	172±34.12	155.3±51.13	0.40
Host parameters			
Mean age of patients			
Mean±SD	63.66±14.01	61.80±15.33	0.89
Range	49-77	46-76	
Central corneal thickness			
Mean±SD	615.5±39.62	631±55.93	0.48

Table 4: Mean LogMAR uncorrected visual acuity preoperatively and at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	Preoperative	1 week	1 month	3 months	6 months
Group 1	1.64±0.53	1.25±0.51	0.89±0.35	0.73±0.28	0.60±0.32
Group 2	1.78±0.53	1.48±0.32	1.04±0.30	0.88±0.31	0.75±0.18
P	0.13	0.22	0.5	0.5	0.8

Table 5: Mean LogMAR BCVA preoperatively and at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	Preoperative	1 week	1 month	3 months	6 months
Group 1	1.44±0.53	0.96±0.56	0.74±0.39	0.53±0.18	0.43±0.19
Group 2	1.75±0.53	1.24±0.32	0.85±0.41	0.75±0.22	0.64±0.15
P	0.07	0.27	0.52	0.4	0.33

Table 6: Mean spherical equivalent postoperatively at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	1 month	3 months	6 months
Group 1	0.92±1.08	0.67±0.98	0.53±0.90
Group 2	0.75±1.25	0.56±1.16	0.41±1.13
P	0.41	0.41	0.555

Central corneal thickness

The central corneal thickness was comparable in both groups at all follow-up time points [Table 8].

Central and peripheral GT

Both central as well as peripheral GT values were comparable in both groups at all time points [Fig. 4 and Tables 9, 10]. The central GT values were higher both preoperatively as well as at 6 months postoperatively, although with no significant difference.

Endothelial cell density

The postoperative endothelial cell density in eyes with group 1 was slightly higher with a lesser percentage endothelial cell loss at 6 months follow-up. The difference was, however, not significant statistically [Table 11].

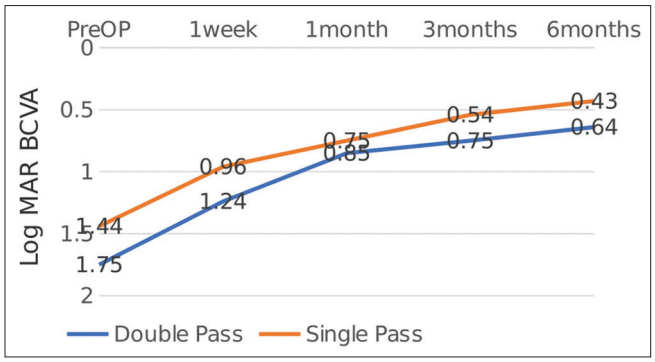

Figure 1: Line diagram demonstrating LogMAR BCVA, preoperatively and postoperatively at various time points following single-pass and double-pass techniques of microkeratome-assisted UT DSAEK

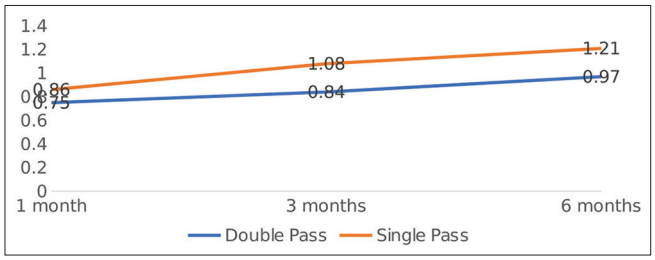

Figure 3: Line diagram demonstrating change in contrast sensitivity postoperatively at various time points following single-pass and double-pass techniques of microkeratome-assisted UT DSAEK

Table 7: Mean contrast sensitivity values postoperatively at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	1 month	3 months	6 months
Group 1	0.86±0.32	1.08±0.21	1.21±0.22
Group 2	0.73±0.46	0.84±0.25	0.97±0.13
P	0.07	0.019	0.045

Correlation between GT and BCVA

Spearman's rho correlation analysis was performed to determine a relationship between postoperative BCVA with intraoperative as well as postoperative GT. Postoperative BCVA was found to negatively correlate with both intraoperative ($R = -69$, $P = 0.008$) as well as postoperative GT ($R = -0.728$, $P = 0.016$).

Complications

Graft preparation was successful in 100% eyes belonging to group 1. In group 2, one eye had an irregular cut during the initial debulking stage and another eye experienced perforation during the refinement cut. These donor corneas were not transplanted and excluded from the study. No major postoperative complications such as graft detachment, graft infection, graft rejection, or failure were observed during the study period.

Discussion

The study compared the outcomes of two techniques for preparation of UT grafts for microkeratome-assisted DSAEK. Grafts prepared with both the techniques; single as well as the double-pass technique, provided comparable outcomes

Figure 2: Line diagram demonstrating change in spherical equivalent values postoperatively at various time points following single-pass and double-pass techniques of microkeratome-assisted UT DSAEK

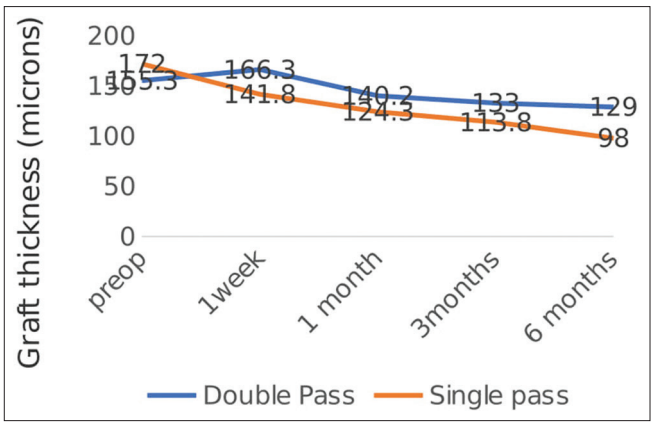

Figure 4: Line diagram demonstrating change in central GT values preoperatively and postoperatively at various time points following single-pass and double-pass techniques of microkeratome-assisted UT DSAEK

in terms of postoperative visual acuity, GT, and endothelial cell loss. Grafts prepared with the single-pass technique were associated with lesser intraoperative complications and better postoperative contrast sensitivity.

Hsu *et al.* reported increased risk of donor tissue loss due to intraoperative perforation with the use of double-pass technique.[10] Because the microkeratome is passed twice over the donor tissue, there is an increased likelihood of complications such as tissue perforation, greater amount of endothelial cell loss due to additional manipulation, and loss of good quality donor tissue. Busin *et al.* reported tissue loss in 2.8% of their eyes, due to complications occurring at the time of tissue preparation.[7] All complications occurred at the time of second-pass. In our study, two out of 12 donor tissues were rejected due to irregular cuts and perforations occurring at the time of tissue preparation. These two corneas were not utilized and excluded from the study.

The single-pass technique has been modified to achieve thinner grafts. Vajpayee *et al.* evaluated the efficacy of single slow-pass technique using standard 400 µm head and achieved thinner grafts in 100% eyes with a mean GT of 111 ± 17.62 µm (70–134 µm) at 6 months follow-up.[9] The authors in another study compared and suggested the use of 400 µm microkeratome head instead of 350 µm to achieve thinner grafts with better visual outcomes, without increasing the overall complication rate.[11]

In our study, the mean central GT at 6 months was higher with the double-pass technique, although not statistically significant. This suggests that both techniques can produce

Table 8: Mean central corneal thickness values (μm) postoperatively at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	1 week	1 month	3 months	6 months
Group 1	615.5±124.91	558.55±90.36	510.76±112.44	497.53±113.74
Group 2	690±144.05	625.9±128.42	541.1±73.17	508±69.37
P	0.06	0.07	0.18	0.56

Table 9: Mean central GT values (μm) postoperatively at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	1 week	1 month	3 months	6 months
Group 1	141.8±36.77	124.3±29.52	113.8±28.25	98±24.46
Group 2	166.3±43.9	140.2±39.14	133±31.77	129±31.46
P	0.91	0.28	0.08	0.18

Table 10: Mean peripheral GT values (μm) postoperatively at various time points following microkeratome-assisted UT DSAEK in group 1 and group 2

	1 month	3 months	6 months
Group 1	180.5±55.83	165.8±55.47	152±54.81
Group 2	202±36.49	185.6±28.86	172.5±17.11
P	0.28	0.21	0.32

Table 11: Preoperative and 6 months postoperative endothelial cell density values with % endothelial cell loss following microkeratome-assisted UT DSAEK in group 1 and group 2

	Preoperatively	6 months	% loss
Group 1	2495.33±278.94	1811.11±175	30.5±3.34%
Group 2	2677.66±271.20	1788.38±190.75	32.36±4.94%

UT grafts (<130 μm) although the grafts obtained with single-pass were further thinner than those obtained with the double-pass technique. Maier *et al*. reported better visual outcomes with grafts which were <120 μm, compared to grafts which were thicker than 120 μm.[12] In our study, similar BCVA and spherical equivalent was noted at all follow-up points in both the groups. We also found a statistically significant negative correlation between postoperative visual acuity and GT, suggesting better visual acuity in eyes with thinner grafts. We also found significantly better contrast sensitivity in eyes with grafts prepared by the single-pass technique. This could be attributed to the overall lower mean GT in these eyes.

It has been suggested that the double-pass technique may be associated with higher rate of endothelial cell loss compared to the single-pass technique. This has been attributed to the microkeratome head being passed twice over the donor cornea. Busin *et al*. reported a 33% rate of endothelial cell loss following double-pass UT DSAEK at 6 months follow-up, which stabilized by 1 year.[7] These values compared well with that reported after DSAEK as well as DMEK. In our study, we did not find any increased cell loss with the double-pass technique. One of the limiting factors in our study was the inability to measure endothelial cell counts following the final microkeratome pass and therefore the pre-keratome cut values were compared with the postoperative specular count values.

Conclusion

On the basis of our experience from this pilot study, it can be concluded that UT DSAEK grafts can be safely harvested using the single-pass technique with minimal adverse effects and efficacy, comparable with the double-pass technique. A study with a larger sample size and a longer duration of follow-up is, however, required to further validate the results.

Financial support and sponsorship

None of the authors have any proprietary or commercial interest in any material discussed in the article.

Conflicts of interest

There are no conflicts of interest among the authors.

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