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Corneal endothelial cell loss following Deep Anterior Lamellar Keratoplasty

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Abstract:

Purpose: evaluating the alterations in endothelial cell density and gauge the visual results after performing deep anterior lamellar keratoplasty .
Setting: Memorial institute for ophthalmic research and KasrAlainy Faculty of Medicine, Cairo University
Methods: A prospective interventional study where 30 eyes from 30 patients were enrolled to undergo deep anterior lamellar keratoplasty (DALK).The technique employed either the big bubble technique or lamellar dissection .The main goal was to evaluate the variations in endothelial cell density by utilizing a non-contact specular microscope before surgery, after 6 weeks and after 6 months. Furthermore, the study also aimed to evaluate the visual outcomes measured before the surgery, at 6 weeks postoperatively, and at 6 months postoperatively.
Results: Significant decrease in endothelial cell density was observed during the entire follow-up duration of the study. The preoperative cell density decreases significantly from 2905.5±119.5 to 2374.8±113.5after 6 weeks (p=0.000). Subsequently there was significant decline to 1894±113.2 at 6 months (p=0.000). Regarding visual outcome ,it showed significant improvement.
Conclusion: DALK is associated with significant decrease in the endothelial cell density at 6 weeks and 6 months postoperatively and visual outcomes show significant improvement.
Keywords: keratoplasty, DALK, endothelial loss, keratoconus

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Introduction:

For a considerable period, Penetrating keratoplasty (PKP) has been the favored treatment for advanced stages of keratoconus[1]. Nevertheless, over the past decade,

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the rise in surgical techniques has commanded to the increased utilization of deep DALK as a popular substitute in managing keratoconus[2].Despite achieving similar visual outcomes in various studies, DALK presents several advantages over PKP. These advantages include the conservation of globe integrity, early suture removal, lack of endothelial rejection, and a low rate of chronic endothelial cell loss [3].

In the absence of any ocular conditions, the endothelial cells shows annual loss at a rate or 0.6% approximately [4]. However, following PKP, the rate of corneal endothelial cell loss exceeds the physiological rate leading to collective cell loss of >50% within the initial decade after surgery. These findings suggest that the host ocular environment compromises the endurance of donor endothelial cells after the initial surgical trauma[5]. In comparison to PKP, DALK has been accompanied with lower levels of endothelial cell . This may be attributed to the reduced surgical trauma in DALK compared to PKP, as well as the absence of endothelial cell rejection in patients undergoing DALK [6]. While there are several reports confirming that endothelial cell loss following DALK is similar to the physiological cell loss observed two years after surgery, few reports have discussed the surgically induced endothelial cell loss due to challenges in preoperative imaging of endothelial cell density[7].

Our objective was to investigate the extent of endothelial cell loss following DALK during the postoperative period, specifically at 6 weeks and 6 months after the surgery.

Methods:

A prospective, interventional study conducted in accordance with the principles outlined in the Declaration of Helsinki and approved by the Ethics Committee at KasrAlainy Faculty of Medicine, Cairo University.

The study was conducted by a single surgeon at the Memorial Institute of Ophthalmic Research. It included 30 consecutive cases that require DALK, including cases of keratoconus and cases with faint superficial corneal opacities. Preoperative and postoperative endothelial data were collected at 6 weeks and 6 months after the surgery. The main outcome was measuring the endothelial cell

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density loss over the follow up period. The secondary outcome was measuring the visual acuity at the two time points.

The study will include patients who meet the following criteria:

- Primary procedure
- Clear graft during follow-up
- Keratoconus or other corneal opacities that allow imaging by specular microscopy.
- Preoperative endothelial cell density not less than 2000 cells/mm2
- Minimum postoperative follow-up of 6 months
- Uncomplicated surgery

The exclusion criteria are as follows:

- Corneal ulcer or kerato-uveitis
- Corneal opacities that do not allow imaging by specular microscopy.
- Repeated keratoplasty
- Documented rejection episode during follow-up
- Intraocular inflammation, uveitis, or uncontrolled glaucoma

Preoperative measurements were of UCVA, BCVA, manifest refraction, corneal tomography and specular microscopy. Visual function, refraction, and topography will be retested at 1.5 months and 6 months after surgery. Specular microscopy was repeated at the 1.5- and 6-month follow-up visits.

All surgeries will be performed by the same surgeon at the same institution using the big-bubble technique described by Anwar and Teichmann[8]. (Figure 1,2)

If the surgeon was unable to achieve a big-bubble after multiple attempts, manual stromal dissection was performed using a blunt-tipped spatula dissecting the stroma layer by layer until the desired dissection was achieved.

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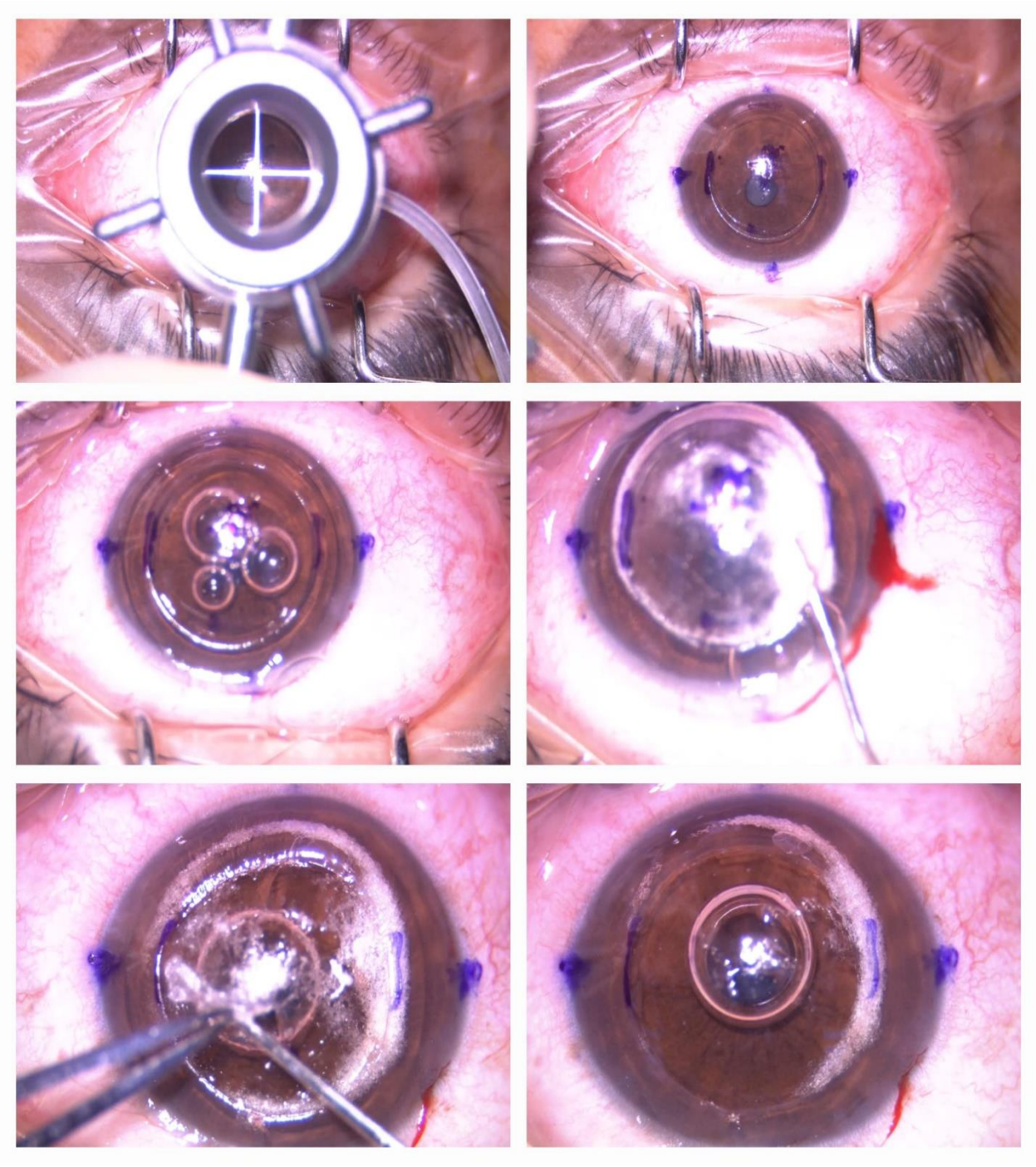

Figure 1: Surgical steps of DALK using big bubble technique till barring of the Descemet's layer of the cornea.

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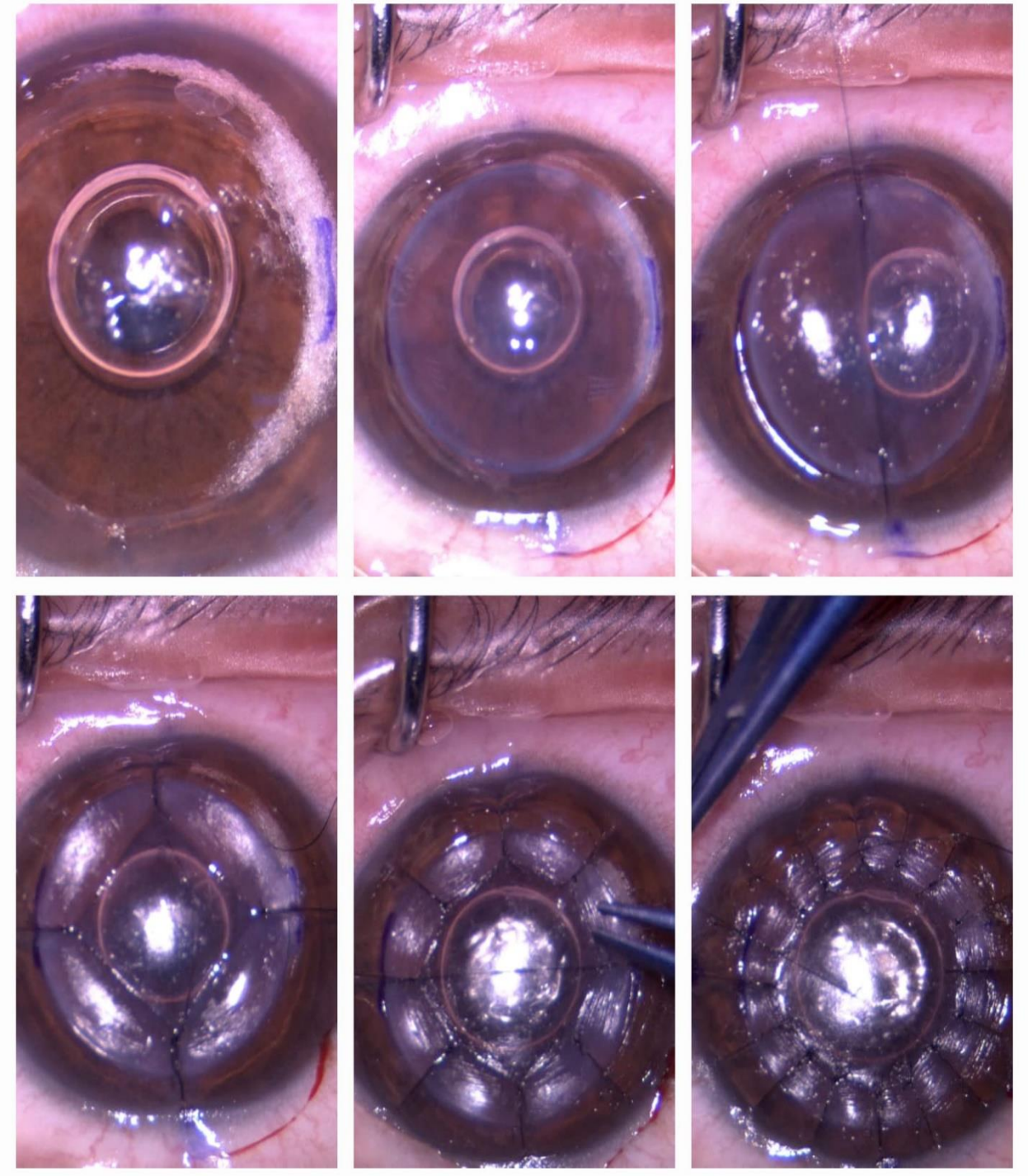

Figure 2: suturing of the graft on the Descemet with 16 interrupted 10/0 nylon sutures

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After the surgery, patients were prescribed topical medications for postoperative care. They received Moxifoxacin eye drops 5 /day for 30 days to prevent infection. Additionally, they were given topical prednisolone eye drops stating 5 times per day for 30 days ,which were tapered over 2 to 3 months. Topical lubricants were also administered to aid in the healing of the corneal epithelium. In cases of nonhealing epithelial defects, bandage contact lenses were fitted as a treatment measure. Follow-up examinations were scheduled at specific intervals: 1 , 3 , 7 , and 30 days postoperatively, as well as at 3 months and 6 months after the surgery. These follow-up visits allowed for monitoring of the patient's progress and assessment of the surgical outcome.

Statistical analysis:

Data was collected, revised, coded, and entered to the statistical package for social science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. Also, qualitative variables were presented as numbers and percentages. Z score was used to determine whether two populations statistically significant from each other, if =0 identical to mean.

Results:

This study included 30 eyes of 30 patients who underwent DALK operations at Memorial institute for ophthalmic research. The mean age was 28.90 ± 1. 093. Females were 20(66.6%) and the males were 10(33.3%). (Table 1,2)

Table 1: Males & Females correspondence

Gender	Frequency	Percent
F	20	66.6 %
M	10	33.3 %
Total	30	100.0 %

Table 2: Patients age

Variable	Mean ± SD	95% CI	Range	IQR	Median	SD
Age	28.90 ± 1.093	26.67 - 31.13	26	9	28.5	5.99

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The indications of DALK in 28 Patients was keratoconus and 2 patients had stromal opacities. Successful big bubble was achieved in 15 (50 %) with mean K of 64 diopters and in 5 (16.6 %) of mean K of 75 diopters. Descemet membrane perforation occurred in 2 cases **(6.66%)**. Graft-host interface opacities were recorded in 3 cases (10%) where dissection was done manually**.** In our study, Descemet's folds occurred in 10 patients (30%) with preoperative mean central K> 65 diopters, which disappeared spontaneously in 5 of the once the compressive effect of sutures was released. Poor final visual outcome associated with marked graft host interface opacities was observed in one patient (3%). Delayed re-epithelialization (beyond two weeks after surgery) occurred in one patient (3%).

Data analysis showed statistically significant improvement of visual outcome as the mean BCVA improved from 1.620 to 1.430 (LogMar) at 6 weeks and further improvement occur at 24 weeks to 0.780 (LogMar)**.** There was statistically significant change over the post-operative period (p=0.001). (table 3)

Table 3 :BCVA changes in logMar

Variable	Mean ± SD	95% CI	Range	IQR	Median	SD	P Value	
							Age	Gender
Pre operative	1.620 ± 0.098	1.42-1.82	2	0.2	1.5	0.54	0.283	0.793
Post 6weeks BCVA (LogMar)	1.430 ± 0.07	1.267-1.593	2.3	0.2	1.4	0.43	0.289	0.348
Post 24weeks BCVA (LogMar)	0.780 ± 0.07	0.530-0.844	1.7	0.7	0.85	0.42	0.198	0.761
*P value < 0.05 is considered statically significant								
Comparison over Time period Post 6weeks BCVA - Post 24 weeks BCVA								
Z score	**P Value :** 0.001*							
-4.715								

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There was highly statistically significant change in endothelial count before and after 1.5 months of surgery (p=0) as well as before and after 6 months of surgery (p=0) and through the follow up period at the recorded 2-time intervals 6 and 24 weeks (p=0). (Table 4)

Table 4: Endothelium Count Preoperative, Post-operative 6 & 24 weeks

Variable	Mean ± SD	95% CI	Range	IQR	Median	SD	P Value	
							Age	Gender
Pre-Endo	2905.5 ± 119.5	2661-3149	2525	873	2721	654	0.019*	0.83
Post 6 weeks Endo	2374.8 ± 113.5	2142-2607	2230	1032	2182	621	0.005*	0.715
Post 24 weeks Endo	1894 ± 113.2	1662-2125	2196	1139	1662	620	0.006*	0.898
*P value < 0.05 is considered statically significant								
Comparison over Time period Pre Endo to Post 6weeks Endo								
Z score			**P Value**					
-4.782			0.000*					
Comparison over Time period Pre Endo to Post 24 weeks Endo								
Z score			**P Value**					
-4.782			0.000*					
Comparison over Time period Post 6 weeks Endo to Post 24 weeks Endo								
Z score			**P Value**					
-4.782			0.000*					

Mean endothelial count Pre-operative was 2,905.50 cells per mm^2, mean endothelial count at 6 weeks was 2,374.80 cells per mm^2, % loss = 18.3 % (530 cell loss) & mean endothelial count at 24 weeks was 1,894.27 cells per mm^2, % loss = 34.8 % (1011 cell loss). Consequently, Endothelial cell loss velocity calculated as [(t1 + t2) /2 = (ECD t2 − ECD t1) / (t2 − t1)] applies across 2 consecutive time periods along study as follows; Pre to 6 weeks post-operative endothelial velocity loss = (2374.8-2905.5)/ (6) = 88.36 cell loss per first 3 weeks and Post 6 weeks to 24 weeks post-

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operative endothelial velocity loss = (1894.27-2374.8)/ (18) = 26.69 cell loss per week after first 3 weeks.

Discussion:

Adequate density of corneal endothelial cells is crucial for the long-term effectiveness of any keratoplasty procedure[3].In the case of penetrating keratoplasty, studies have shown an initial loss of approximately 33%of endothelial cells within the first two years after surgery. Moreover, the rate of cell density decline continues to accelerate over the course of up to 20 years following the procedure[9-12.]

In DALK surgery, the extent of endothelial cell loss caused by allograft rejection significantly diminishes. According to Sugita et al. [9], the reduction in endothelial cell density after DALK surgery was 13% by the end of the first year. Van Dooren et al.[13] discovered that the density exhibited an 11% decline in the initial six months following DALK, with subsequent annual decreases of 1% to 2%. Remarkably, they also observed that the reduction in endothelial cell density was comparable to that of healthy corneas that had not undergone surgery[13]. Various factors have been proposed as potential causes for the notable decline in cell density after DALK surgery, including the injection of air into the anterior chamber during the perioperative phase and trauma to the recipient endothelium during deep stromal dissection[13,14].

In our study the endothelial cell loss in the first postoperative period (6weeks and 6months) was 18.3%and 34.8% respectively. There was significant improvement of visual outcome over the postoperative follow up period.

One of the limitations of our study was the relatively short duration of the follow-up period. To obtain a more comprehensive understanding of the rate of endothelial cell loss over time, we recommend conducting a long-term follow-up study. This would allow for a comparison between the rate of cell loss in our specific procedure and that observed in penetrating keratoplasty (PKP). Additionally, to enhance the statistical power and generalizability of our findings, we suggest increasing the sample size in future studies.

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Conflict of interest declaration:

The authors of this manuscript did not have any financial interest in the materials discussed within the study.

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