Intraoperative and Early Postoperative Complications of Deep Anterior Lamellar Keratoplasty: A Focus on First 100 Consecutive Cases

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ABSTRACT

Purpose: To investigate the peri-operative and early postoperative complications of deep anterior lamellar keratoplasty (DALK) and to evaluate the learning curve needed to complete the DALK surgery.

Materials and Methods: We retrospectively analyzed the medical records of 100 eyes in 100 patients who underwent the DALK procedure due to different corneal diseases. Preoperative demographic and clinical features were evaluated along with the perioperative and early postoperative complications during the first 3 months.

Results: We performed the DALK procedure successfully in 83 patients (83%) and intra-operatively decided conversion to penetrating keratoplasty (PK) procedure in the other 17 eyes (17%). The rate of conversion to PK was 40% (10 eyes) in the first 25 cases, 8% (2 eyes) in the second 25 cases, 12% (3 eyes) in the third 25 cases, and 8% (2 eyes) in the last 25 cases. There was a big bubble formation in 65 eyes (65%). The most common intra-operative complication was Descemet's membrane perforation occurred in 26 (26%) of 100 patients, 11 of which were micro-perforation, and the remaining 15 eyes had macro-perforation. The most common postoperative complications were double anterior chamber in 8 of 83 eyes (9.6%) and early suture loosening in 8 of 83 eyes (9.6%).

Conclusion: The study demonstrated that in the first 25 cases, the rate of conversion to PK was higher, however, the success rate increases remarkably after the first 25 cases.

Keywords: Deep anterior lamellar keratoplasty, Big Bubble, keratoconus, corneal stromal dystrophies, corneal scars, penetrating keratoplasty.

INTRODUCTION

Deep anterior lamellar keratoplasty (DALK) has gained popularity to restore corneal transparency and curvature in patients with corneal-stromal pathologies if there is healthy endothelium including keratoconus, scars, stromal dystrophies, and degenerations.[1-4] DALK has advantages over penetrating keratoplasties (PK), including lower rejection risk, lower loss of endothelial cells, and reduced need for topical and systemic corticosteroids, on condition that the host's healthy corneal endothelium is preserved.[1-3] Besides its advantages DALK is a difficult and experience-required method by comparison to PK but according to the learning curve (LC) complications decrease significantly. On the other hand, there are some disadvantages of DALK surgery related to perioperative complications including lack of creating big bubble (BB), Descemet's membrane (DM) perforation, and early postoperative complications including double anterior chamber (AC), DM wrinkles, interface haze, stromal rejection of DALK procedure.[4,5] The purpose of our study is to investigate the perioperative and early postoperative complications of DALK procedure performed by a single surgeon and to evaluate the LC of DALK.

MATERIALS AND METHODS

Study design and population

A total of 100 patients who had undergone DALK between 2014-2020 at the Department of Ophthalmology of Gaziantep University, were evaluated retrospectively based on their medical charts and surgery videos. We obtained the approval of the local Ethics Committee and informed consent from all patients.

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Surgical procedure

All surgeries were performed by a single surgeon (NK) who was experienced in PK surgery under general anesthesia at the same hospital (Gaziantep University School of Medicine Hospital). We aimed to use a BB technique to expose the Dua's layer or DM with intrastromal air injection in all procedures described by Anwar and Teichmann in 2002. This technique provides corneal stromal dissection to obtain the pre-Descemetic or Descemetic plane of the cornea.[6] Afterward, Dua et al defined the different types of BB.[7] The most common one is the Type-1 BB that forms between the deep stroma and the pre-Descemets layer. Type-2 BB forms between the DM and the posterior surface of Dua's layer. Type-3 BB is the mixed form of type-1 and 2 BB. If we achieved type-1 BB we maintained the procedure. However, when a type-2 BB formation or BB failure was present, we made layer by layer manual lamellar dissection of stroma to uncover the DM or a level closest possible to the DM.

Donor corneal graft without DM-endothelial layer complex was sutured with 10-0 nylon sutures using interrupted or running suture techniques. We injected subconjunctival gentamicin and dexamethasone at the end of the operation and initiated routine topical medications including moxifloxacin, 1% prednisolone acetate, and sodium hyaluronate five times per day for 1 month in the postoperative period. Artificial tear and steroid drops were gradually reduced after 6 months from surgery.

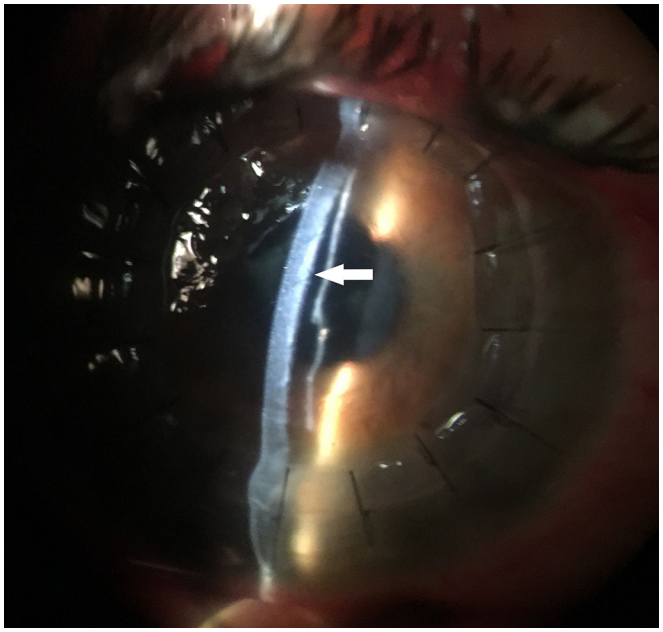

Figure 1: *Slit-lamp photograph showing double anterior chamber formation. White arrow shows pseudo anterior chamber (arrow).*

Ocular examination

Preoperative and postoperative eye examinations including visual acuity, refractive error, intraocular pressure (IOP), corneal topographic evaluation (Sirius, CSO, Italy), and fundus evaluation were carried out.

Outcome Measures and Study groups

1. A total of 100 patients were divided into 3 groups based on diagnosis as keratoconus (n=55), corneal dystrophia (n=16), and other corneal scars (n=29).

2. The cases were also classified into 4 groups (LC groups) based on the number and sequence of operations: Group 1q (first quartile:1-25 eyes), Group 2q (second quartile: 26 to 50), Group 3q (third quartile: 51 to 75), and Group 4q (fourth quartile: 76 to 100).

We evaluated preoperative demographic, clinical features and compared study groups regarding perioperative complications including, lack of creating BB, DM perforation, and early postoperative complications including, double AC, triple AC, Urrets-Zavalia syndrome (UZS), DM wrinkles, atopic sclero-keratitis, suture loose, intraocular pressure elevation, interface haze, and stromal rejection. Some of these complications are very rare such as triple AC and UZS. The triple AC is consists of two pseudo-chambers including, between the donor graft and

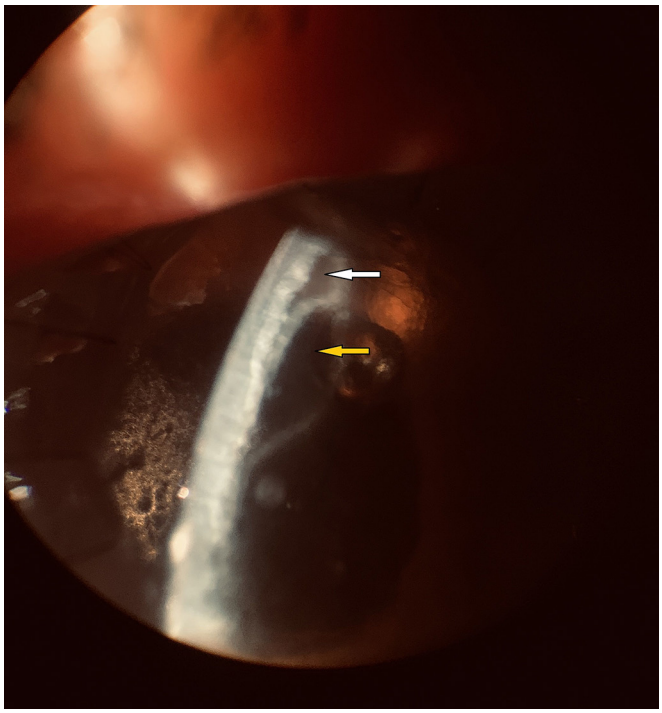

Figure 2: *Slit-lamp photograph showing triple anterior chamber formation, which consisting of two pseudo-chambers, between the graft and the Dua's layer (white arrow), and between the Dua's layer and the host Descemet's membrane (yellow arrow).*

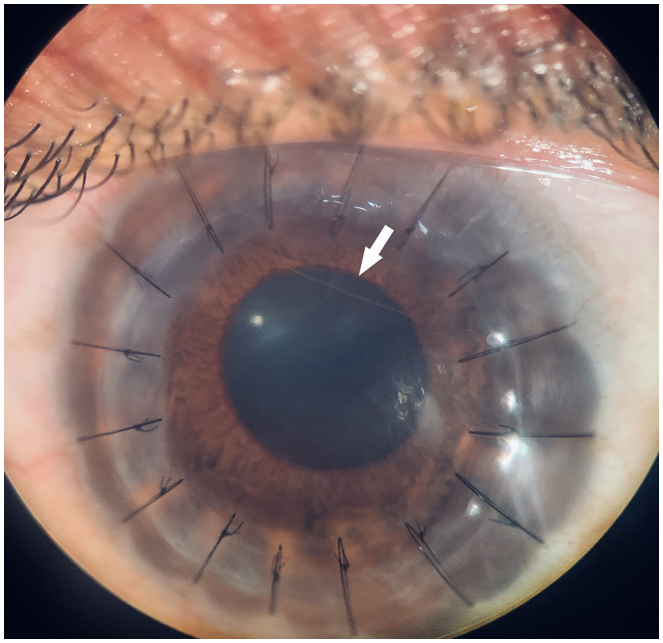

Figure 3: *The photo shows a superior Descemet's membrane wrinkle (arrow).*

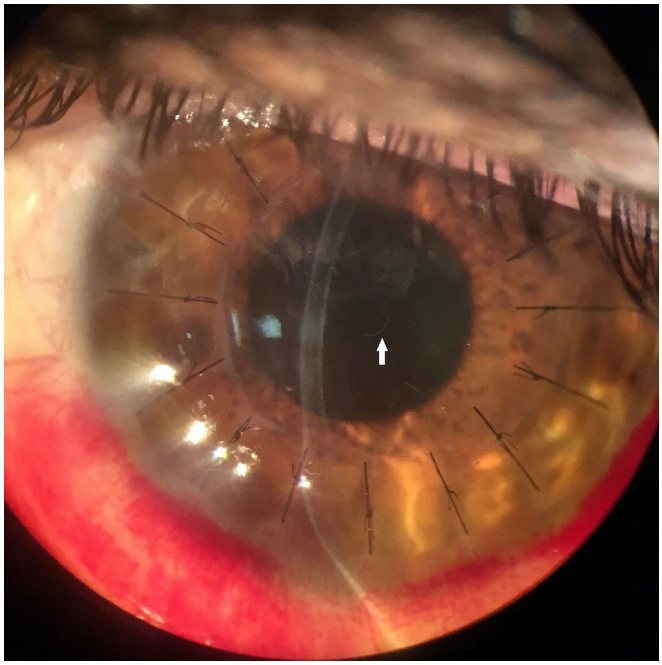

Figure 4: *A small fiber is seen in the donor-host interface (arrow).*

the Dua's layer, and between the Dua's layer and the host DM, along with the real AC.[8, 9] UZS is an uncommon but well-known complication associated with lamellar or PK.[10,11] It is characterized by fixed dilated pupil with iris atrophy.

Data analyses

The SPSS for Windows software (version 16; SPSS Inc., Chicago, IL) was used for data analyses. A chi-square test was used to compare categorical variables between the groups. The one-way analysis of variance (ANOVA) was used to compare the means of two or more independent groups. $p < .05$ was considered statistically significant.

RESULTS

Demographic and preoperative details

A total of 100 eyes in 100 patients were included in this study. Overall, 47% were females and 53% were males. The mean age of the study population was 33±15 years. The indications for surgery were keratoconus (n=55), corneal dystrophia (n=16), and other corneal scars (n=29). The demographic characteristics are summarized in table 1.

Table 1: *Demographic and clinical features of the patients.*

	No
Number of Eyes/patients	100/100
Gender Female/Male	47/53
Age (years) Mean±Sd, Min-Max	33±15, 14-77
Primary diagnosis	
Keratoconus	55
Corneal stromal dystrophia	16
Corneal scars	29
Herpetic keratitis	16
Post-PRK scar	3
Infectious keratitis	2
Trauma	2
Chemical injury	1
Proparacaine toxicity	1
Unknown	4

Sd: standard deviation: PRK: photorefractive keratectomy

Peri-operative features

The peri-operative features are analyzed in all 100 patients and are summarized in tables 2 and 3.

Big-bubble formation

BB formations were present in 65 eyes (65%) including, type-1 BB, type-2 BB, and a mixed bubble in 42,16, 7 eyes; respectively. On the contrary, the BB formation was not observed in 35 eyes. We used the layer-by-layer manual dissection technique in 51 eyes in which BB formation was failed.

Table 3 shows the rates of bubble types in diagnostic groups. There were successful BB formations including in patients with keratoconus, corneal dystrophies, scars

Table 2: *Perioperative events and postoperative complications in learning curve groups.*

Case No	Overall	Learning curve groups				
		Group 1q	Group 2q	Group 3q	Group 4q	p
	100	First 25	26 to 50	51 to 75	76 to 100	
Indications						
Keratoconus	55	10	16	16	13	
Dystrophia	16	6	5	3	2	0.282
Stromal scar	29	9	4	6	10	
Gender						
Female/Male	47/53	13/12	13/12	10/15	11/14	0.781
Age (years)						
Mean±SD,	33±15	36±16	31±12	33±16	33±19	0.698
(min-max)	14-77	16-72	17-54	16-77	14-90	
Peri-op events						
Big-bubble formation	65	13 (52%)	19 (76%)	18 (72%)	15 (60%)	0.261
Type 1	42	6	12	13	11	
Type 2	16	5	6	2	3	0.483
Type 3	7	2	1	3	1	
Perforation	26	11 (44%)	5 (20%)	2 (8%)	8 (32%)	**0.030**
Micro	11	1 (4%)	4 (16%)	0 (0%)	6 (24%)	**0.026**
Macro	15	10 (40%)	1 (4%)	2 (8%)	2 (8%)	**0.001**
DM Rupture	1	0	0	1	0	0.387
Conversion PK	17	10 (40%)	2 (8%)	3 (12%)	2 (8%)	**0.005**
Completed DALK	83	15 (60%)	23 (92%)	22 (88%)	23 (92%)	
Post-op complications						
Double AC	8	1	1	3	3	0.537
Triple AC	1	0	1	0	0	0.387
Stromal rejection	1	1	0	0	0	0.387
Post-DALK ASK	2	1	1	0	0	0.564
Descemet's wrinkles	5	1	1	3	0	0.257
Early suture loose	8	0	1	3	4	0.233
Interface opacity	2	0	0	0	2	0.106
Intraocular pressure	4	0	1	1	2	0.555
elevation	1	1	0	0	0	0.387
Interface filament	2	0	0	0	2	0.106
UZS						

LC: Learning curve, q: quartile, DM: Descemet's membrane, PK: Penetrating keratoplasty, DALK: Deep anterior lamellar keratoplasty, AC: Anterior chamber, UZS: Urrets Zavalia Syndrome, ASK: Atopic sclero-keratitis, Peri-op: Perioperative, Post-op: Postoperative

with a rate of 72.7%, 75%, and 44.8%; respectively. There was a statistically significant lower success rate in patients with the corneal scar as compared to in patients with keratoconus and corneal dystrophy (p=0.026). Moreover, the type-1 BB rate was higher in patients with keratoconus than in patients with dystrophy and scar, the difference was statistically significant (p<0.001). Table 2 shows the effect of LC on successfully formed BB. The successfully achieved BB rate was 52% in group 1q, 76% in group 2q, in 72% in group 3q, and 60% in group 4q (p=0.261).

Descemet's Membrane perforation

DM perforation occurred in 26 (%26) of 100 patients. The perforation rate was 20% (11 of 55), 37.5% (6 of 16), and 31% (9 of 29) in the keratoconus, corneal dystrophy, and scar groups; respectively (p=0.390). There was a statistically significant lower perforation rate in group 3q as compared to group 1q (p=0.008). The perforation rate was 40% (14 of 35 eyes) in patients with failed BB; whereas it was 18.4% (12 of 65 eyes) in patients with the presence of BB and the difference was statistically significant (p=0.030).

Table 3: *Perioperative events and postoperative complications in primary diagnosis groups.*

		Primary diagnosis groups			
	Overall	**Keratoconus**	**Dystrophia**	**Corneal Scars**	**p**
Case no	100	55	16	29	
Peri-op events					
BB- formation	(%)	(%)	(%)	(%)	
Overall	65 (65)	40 (72.7)	12 (75)	13 (44.8)	**0.026**
Type 1	42 (42)	33 (60)	5 (31.2)	4 (13.8)	**0.000**
Type 2	16 (16)	5 (9.1)	5 (31.2)	6 (20.7)	0.074
Type 3	7 (7)	2 (3.6)	2 (12.5)	3 (10.3)	0.333
Perforation	26 (26)	11 (20)	6 (37.5)	9 (31.0)	0.390
Micro	11 (12)	6 (10,9)	1 (6.2)	4 (13,8)	0.209
Macro	15 (14)	5 (9,1))	5 (31.3)	5 (17,2)	**0.019**
DM Rupture	1 (1)	1 (1.8)	0 (0)	0 (0)	0.662
Conversion to PK	17 (17)	7 (12.7)	6 (37.5)	4 (13.8)	0.058
Completed DALK	83 (83)	48 (87.3)	10 (62.5)	25 (86.2)	
Postop complications					
Double AC	8 (9.6)	0 (0)	2 (20)	6 (24)	**0.003**
Triple AC	1 (1.2)	0 (0)	0 (0)	1 (4)	0.290
Stromal rejection	1 (1.2)	0 (0)	0 (0)	1 (4)	0.290
Post-Keratoplasty ASK	2 (2.4)	2 (4.1)	2 (20)	0 (0)	0.434
DM wrinkles	5 (6.0)	3 (6.25)	0 (0)	2 (8)	0.321
Early suture loose	8 (9.6)	5 (11.1)	0 (0)	3 (12)	0.533
Interface opacity	2 (2.4)	0 (0)	0 (0)	2 (8)	0.082
IOP elevation	4 (4.8)	3 (6.25)	1 (6.2)	0 (0)	0.423
Interface filament	0 (0)	0 (0)	0 (0)	1 (3.4)	0.290
UZS	2 (2.4)	1 (2.1)	0 (0)	1 (4)	0.724

DM: Descemet's membrane, PK: Penetrating keratoplasty, DALK: Deep anterior lamellar keratoplasty, AC: Anterior chamber, UZS: Urrets Zavalia Syndrome, ASK: Atopic sclero-keratitis, IOP: Intraocular pressure, Peri-op: Perioperative, Post-op: Postoperative

DM micro-perforation occurred in 11 (11%) patients. One of which was converted to PK due to the enlargement of the perforation. There was no statistically significant difference between the diagnosis groups in the rate of micro-perforation occurrence (p=0.209).

We performed PK in 15 (15%) patients with macro-perforation and the macro-perforation rate was statistically significantly higher in the dystrophy group than other groups (p=0.019). Similarly, the macro-perforation rate was remarkably higher in group 1q when compared to other groups (p=0.001). In addition, a DM rupture was present during the type-1 BB formation before conversion to PK in one patient (1%) with keratoconus

Conversion to PK

We successfully carried out the DALK procedure in 83 patients (83%), but in 17 patients (17%) the surgery has converted to PK. There are various types of indications for conversion to PK including macro-perforation, enlargement of micro-perforation, and DM rupture in 14, 2, and one patient; respectively. Comparison of different groups showed that group 1q has a higher conversion rate than other groups and the difference is statistically significant (p=0.005).

Early Postoperative Complications

The post-operative complications were analyzed over 83 patients who had DALK operations.

Double Anterior Chamber

Double AC developed in 8 of 83 eyes (9.6%) on day 1 postoperatively. In two of 8 patients, double AC was resolved spontaneously. In six patients, SF6 tamponade was injected into the AC to restore DM attachment and graft transparency. There was a recovery in five of 6 eyes after SF6 injection. We performed PK in one patient with a persistent double AC. We diagnosed UZS syndrome

in two of 8 eyes after SF6 injection. The double AC rate was statistically significantly higher in the scar group when compared to the keratoconus or dystrophia group (**p=0.003**). There was micro-perforation in four of 8 patients with postoperative double AC and we could not generate BB so completed DALK with manual dissection, but there was no perforation in the other four patients, therefore, the BB was present without any detected complication. Two of them had type-2 BB, one of them had type-1 BB, and one of them had type-3 BB.

Triple Anterior Chamber

A triple AC was observed in one of 83 eyes (1.2%). As a result of failure regarding SF6 injection in this patient, we applied PK.

Urrets-Zavalia syndrome

UZS syndrome developed in two eyes (2.4%) after intracameral SF6 injection to treat double AC.

Descemet's Membrane wrinkles

We noticed DM wrinkle development in 3 cases with keratoconus and 2 eyes with corneal scars.

Suture loose

We performed resuturing after noticing loosened sutures within first postoperative month in 8 (9.6%) of all cases. We diagnosed keratoconus in five of 8 patients and corneal scar in the other three patients.

Intaocular pressure elevation

IOP elevation was seen in four eyes (3.6%) in the early postoperative period, and only fixed combination of dorzolamide/timolol drops were used.

Interface haze

A graft-host interface haze was observed in two of 83 patients (2.4%) in the early postoperative period. We carried out manual dissection in these two patients and they were in the corneal scar group.

Other postoperative complications

Atopic sclero-keratitis developed in two patients (2.4%) and systemic steroid treatment was used. A small filament of cotton fiber was observed in one of 83 eyes (1.2%) at the donor-host interface. Lastly, stromal rejection occurred in one patient (1.2%) after 3 months. All the complications were summarized in table 2 and 3 according to groups.

DISCUSSION

Although final visual acuity and graft survival incidence are similar between DALK and PK, complications and LC have some differences.[5] DALK surgery is a more challenging and time-consuming procedure as compared to PK. The success rate is associated with LC.[12-14] In the current study, we evaluated the intra-operative and early postoperative complications of the DALK procedure in the first 100 cases and investigated the effect of LC.

The rate of conversion to PK was reported as 0.37%-60% based on the surgeon's experience.[12-15] In the present study, we carried out DALK in 83% of the patients and PK for the rest of the patients (%17). There are several reasons associated with the conversion of DALK to PK including type-2 bubble formation, manual dissection, corneal scar, and inexperienced surgeons.[13, 14] Myerscough et al reported that experienced surgeons (case >100) had lower PK conversion rates compared to inexperienced surgeons (case<10) (12.5% vs 54.6%).[13] In our study, conversion to PK was 40%, 8%, 12%, and 8% in the first, second, third, and last 25 cases, respectively. The conversion rate to PK was remarkably high in the first quarter compared to the other quarters.

In the literature, the BB rate was found to vary from 35% to 95% based on the surgical experience and corneal pathologies.[16-21] The overall successfully performed BB formation rate was 65% in our report. The BB formation rate was ranging between 56% and 90%, 70% and 81%, 38% and 76% in patients with keratoconus, corneal scarring, and corneal dystrophy, respectively in the literature.[7, 14, 16-24] We performed BB successfully with a rate of 72.7%, 75%, and 44.8% in patients with KC, CD, and CS respectively. Our results and previous reports demonstrated that the BB formation rate is lower in patients with deep corneal scars. These findings may result from tight junctions between deep stromal lamellae and the DM in cases with corneal scarring. The LC of DALK may influence the success rate of BB formation.[20, 25] In this study, the successfully performed BB rate was the lowest in the first 25 cases (52%) when compared to other quarters.

The main intra-operative complication of a DALK surgery is DM perforation up to 57% in the literature.[3, 6, 16, 17, 21, 25-27] The variable rates of perforation of DM may be associated with the diagnosis of patients, surgical technique, and surgeon's LC.[28, 29] In our study, we performed PK in 16 of 26(61.5%) patients with intra-operative DM perforation. In sub-group analyses, 1 of 11 eyes with micro-perforation, 15 of 15 eyes with macro-perforation, and one eye with DM rupture were converted from DALK surgery to PK. We caused perforations in 14 of 35 and 12 of 65 eyes with failed big-bubble and successfully achieved BB; respectively. The perforation rate was the highest in the first quarter (44%) and lowest in the third quarter (8%). We noticed the highest micro-perforation rate in group 4q whereas we

observed the lowest rate in group 3q. We attributed this finding according to the lower big-bubble formation rate which may be resulted from the high incidence of corneal scarring in group 4q. Although greater micro perforation rates, surgeries were completed as DALK with a higher rate rather than other groups due to increased surgical experience in group 4q (92%). A previous study found that the perforation rate is higher in patients with keratoconus.[30] Conversely, our study showed that the perforation rate is lower in eyes with keratoconus (20%) when compared to eyes with dystrophia (37.5%) or stromal scar (31%). Risk factors for perforation during DALK surgery include deep corneal stromal scarring, severe corneal ectasia, advanced thinning of the cornea, and inexperienced surgeon.[25, 31] Moreover, using a sharp instrument for deep lamellar dissections may increase the risk of inadvertent DM perforations. The DM perforation may occur during recipient trephination, air injection with a needle, deep stromal lamellar dissection, and saturation.[17, 32, 33]

One of the most common early postoperative complications associated with the DALK procedure is double AC formation due to the detachment of the DM, which is unique to DALK surgery.[5] In large series, postoperative double AC was observed in 48 of 591 (8.1%) eyes.[34] In our study, a double AC occurred in eight of 83 (9.6%) eyes. In sub-group analyses, we showed that double AC is not observed in any of 48 eyes with keratoconus, whereas detected in two of 10 eyes (20%) with dystrophia and in six of 25 eyes (24%) with a corneal scar. The most common risk factors for double AC after DALK are macro- and micro-perforations of the DM. In our study, four of 8 eyes (50%) with postoperative double AC had micro-perforation during surgery; however, we failed to detect any perforation in four eyes even after the repeated video reviewing. The type-2 BB formation is a risk factor for double AC formation even in the absence of peri-operative perforation and may be related to the fenestrations found between the origin of the trabecular meshwork and the termination of DM.[34, 35]

The triple AC is a rare complication. In the current study, triple AC was observed in one of 83 cases (1.2%). We performed an intracameral gas injection to resolve extra spaces of this patient and subsequently carried out PK.

UZS after DALK was reported in five of 263 (1.9%) eyes by Foroutan et al and eight of 106 (7.5%) eyes by Bozkurt et al.[10, 11] In general, UZS associated with DALK is a result of intracamerally injected of air/gas tamponade.[10, 11] It has been suggested that the air or gas bubble in the AC may cause a pupillary block and increased IOP related to pupillary block may cause iris ischemia and fixed dilated pupil.[10] In our study, the UZS developed in two eyes (2.4%) which we injected air tamponade postoperatively to resolve double AC.

The incidence of glaucoma after DALK surgery was reported up to 22.6%.[36-38] The steroid usage, presence of pre-existing glaucoma, increased intra-operative manipulation, and severe inflammation can contribute to an increase in the incidence of glaucoma in the post-operative period.[36-38] In our study, high IOP (>22 mmHg) was observed in four of 83 (4.8%) patients in the first 3 months after surgery and they were managed successfully with topical fixed combination of dorzolamide/timolol agents.

Suture-related complications may frequently occur after keratoplasty. A large cohort analysis showed that a premature loosening of sutures is diagnosed in 30% of eyes.[15] It has been shown that patients with severe keratoconus have an increased risk of suture-related complications.[39, 40] In our study, we diagnosed early suture loosening in eight of 83 (9.6%) eyes and re-sutured. Of these eight eyes, five (62.5%) were with keratoconus and three (37.5%) were with corneal scars.

DM wrinkle is another postoperative complication of DALK surgery. Ceylanoglu et al observed DM wrinkles in 54.8% of eyes after DALK surgery.[41] DM wrinkles are noticed in five out of 83 (6%) eyes including, three were with keratoconus and two were with a corneal scar in the current study. The reason for the higher rate of DM wrinkles in keratoconus patients may be that DM wrinkles are associated with high keratometry (K) values.[41]

Post-keratoplasty atopic sclera-keratitis is a host inflammatory response after keratoplasty in atopic patients.[42, 43] In our study, two patients (2.4%) had post-keratoplasty atopic sclera-keratitis which were improved with systemic steroid treatment.

Interface problems between the graft- host stroma after DALK surgery is a complication that may cause poor visual performance.[44] It occurs especially in the event of inadequate depth of posterior stromal dissection. In our study, a graft-host interface haze was observed in two of 83 eyes (2.4%) in the early postoperative period. These two cases were in the corneal scar group and manual dissection was performed on these patients.

The stromal graft rejection after DALK is a rare and mild complication[45], which is usually treated with topical steroid therapy without any severe sequel.[46] The stromal rejection rate reported in the previous series is up to 14%.[23, 47] In our study, stromal rejection occurred only one patient (1.2%) within the third month after surgery. The patient was managed with topical steroid therapy without any sequel.

Also, a small filament of cotton fiber was shown in one of 83 eyes (1.2%) in the donor-host interface after surgery without any adverse effects. Likely, it might be caused by a cotton sponge used during the graft preparation for DMEK surgery in a split keratoplasty surgery.

In conclusion, the results of this study demonstrate that the intraoperative complications of DALK surgery may be associated with surgical experience, whereas postoperative complications may be independent of LC. The complexity of the DALK procedure needs an LC to obtain successful outcomes. In the study, the first 25 attempts were more frequently (40%) converted into PK. However, a remarkable success (90.7% completed DALKs) was achieved following the first 25 procedures.

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