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ORIGINAL ARTICLE

Exploring corneal strength: Comparative analysis of big bubble and manual lamellar dissection in deep anterior lamellar keratoplasty

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Abstract

Purpose: To compare the long-term visual outcomes and corneal biomechanical properties following deep anterior lamellar keratoplasty (DALK) using either the big bubble (BB) technique or manual lamellar dissection (MLD) in patients with advanced keratoconus. In addition to evaluate the relationship between residual stromal bed (RSB) thickness and post-operative visual and biomechanical parameters in MLD-DALK eyes, and to assess the reliability of intraocular pressure (IOP) measurements.

Methods: A total of 78 eyes from patients with keratoconus who underwent DALK (43 BB-DALK, 35 MLD-DALK) and completed 18 months of post-operative follow-up were retrospectively analyzed. Corneal hysteresis (CH), corneal resistance factor (CRF), cornea-compensated IOP (IOPcc), Goldmann correlated IOP (IOPg), and best-corrected visual acuity (BCVA) were assessed. In the MLD group, RSB thickness was measured using anterior segment OCT. Biomechanical assessments were performed using the Ocular Response Analyzer.

Results: At 18 months, CH and CRF were comparable between groups ($p>0.05$), as were BCVA and other topographic parameters. The mean RSB thickness in the MLD group was 75.8±27.7 µm, with no significant correlation between RSB and visual or biomechanical metrics. In both groups, IOPcc was significantly higher than IOPg ($p<0.01$), though IOP readings were not correlated with RSB thickness.

Conclusion: MLD-DALK offers similar visual acuity and biomechanical outcomes to BB-DALK and is a viable alternative when BB formation fails. Clinicians should consider using measurements IOPcc for accurate post-operative monitoring, as traditional methods may underestimate true IOP in DALK patients.

Keywords: Big bubble; corneal hysteresis; deep anterior lamellar keratoplasty; manual lamellar dissection.

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Deep anterior lamellar keratoplasty (DALK) is a surgical technique frequently employed to treat keratoconus, a progressive disorder where the cornea thins and protrudes outward. This method selectively replaces the damaged anterior corneal layers while keeping the healthy endothelial structure intact, offering a less invasive option. DALK is ideal for keratoconus as it removes abnormal corneal tissue and substitutes it with a donor cornea, correcting the irregular corneal shape and enhancing vision.[1-3]

The conventional surgical technique used in DALK for keratoconus involves creating a "big bubble" (BB) within the corneal stroma, typically using the Anwar BB technique.[4] This gas-filled cavity facilitates separation of the anterior from the posterior corneal layers, allowing precise removal of diseased tissue while preserving the endothelium. When BB (type 1 bubble) formation is unsuccessful, alternative techniques, such as manual lamellar dissection (MLD), can be employed, providing a viable option for successful transplantation while preserving posterior stromal integrity, although this approach often results in variable residual stromal bed (RSB) thickness. Depending on the type of bubble achieved, the graft may be positioned either directly on Descemet's membrane (type 2 bubble) or on the pre-Descemet/Dua's layer (type 1 bubble), and then sutured in place.[5]

An ocular response analyzer (ORA) is a diagnostic tool used to assess the biomechanical properties of the cornea.[6] It measures corneal hysteresis (CH) and corneal resistance factor (CRF), which represents the ability of the cornea to absorb and dissipate energy during the application and removal of force.[7] In keratoconus, the cornea typically exhibits reduced CH due to its weakened structure. By measuring the CH and other parameters, the ORA provides valuable information for diagnosing and monitoring keratoconus.[8,9] After DALK, the biomechanical properties of the cornea may be altered by surgical intervention and healing.

Only a few reports have investigated differences between BB and MLD techniques in DALK. Akdemir *et al*.[10] compared CH and CRF values in BB-DALK and MLD-DALK and found no significant differences. However, their study did not include a quantitative assessment of RSB thickness, which may influence post-operative biomechanics. Other studies also lacked a detailed analysis of the relationship between RSB and corneal biomechanics.

Therefore, in this study, we aimed to compare long-term visual and biomechanical outcomes between BB-DALK and MLD-DALK, while additionally incorporating anterior segment OCT–based RSB thickness measurements in MLD cases. To our knowledge, this is the milestone study to investigate whether residual stromal thickness correlates with visual function, CH, and intraocular pressure (IOP) parameters, thereby addressing an important gap in the present literature.

The aim of this study was to evaluate whether RSB, measured by anterior segment optical coherence tomography (AS-OCT), influences post-operative visual acuity, corneal biomechanics, and IOP, and to determine whether MLD-DALK provides comparable outcomes to BB-DALK in advanced keratoconus.

Materials and Methods

This retrospective, non-randomized, comparative study included 78 eyes diagnosed with keratoconus eligible for corneal transplantation. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ankara Bilkent City Hospital Ethics Committee (approval number: E-22-3135). Informed consent forms were obtained from all participants in the study. The selection of participants was based on the records of patients from Ankara Bilkent City Hospital- Corneal and External Diseases Services. To determine the appropriate sample size for this retrospective comparative study, a priori power analysis was conducted using G*Power 3.1.9.7 software. A medium effect size (Cohen's d=0.5) was predicted based on prior research that assessed corneal biomechanics following DALK procedures. The required sample size was determined to be 64 participants in total, with 32 participants in each group, with an alpha error probability of 0.05 and a desired statistical power of 0.80 for a two-tailed Mann–Whitney U test. Considering potential data exclusions and missing values, the study included 78 eyes (43 BB-DALK, 35 MLD-DALK), which exceeded the minimum sample size requirement and thereby ensured sufficient power to detect significant intergroup differences in CH and other biomechanical parameters. Participants included in both groups had severe keratoconus according to the Amsler-Krumeich classification. The groups were comparable in terms of pre-operative severity. Only patients aged >18 years who underwent a comprehensive eye examination and at least 18 months of post-operative follow-up were included. Exclusion criteria comprised Individuals with systemic illnesses or eye conditions other than keratoconus, such as cataracts, uveitis, glaucoma, trauma, vitreoretinal issues, dry eyes, or corneal infections. Patients who experienced graft rejection or Descemet's membrane perforation during

DALK were also excluded. All patients underwent thorough ocular examinations, including best-corrected visual acuity (BCVA), slit lamp examination, endothelial cell density with a specular microscope, and Pentacam topography (Oculus, Wetzlar, Germany), both before surgery and at specified post-operative intervals (1 week, 1 month, 3 months, 6 months, 12 months, and 18 months post-operatively). ORA (Reichert, Inc., Depew, NY, USA) was used to assess the corneal biomechanics 18 months post-operatively. The ORA provides two pressure-derived parameters, CH and CRF. Anterior segment photographs were recorded at all follow-up appointments. AS-OCT (Swept Source-OCT, Triton, Topcon, Japan) was utilized to measure the RSB thickness post-operatively (Fig. 1) in patients who underwent MLD-DALK. The measurements were performed in the central zone. Three consecutive measurements were performed, and the average value was computed to ensure accuracy. Furthermore, Figure 2 shows an OCT image of the BB-DALK surgery after 18 months without any RSB.

All surgeries were performed by one of the two experienced corneal surgeons (OEK and EEK). Under general anesthesia, partial-thickness trephination of the recipient cornea was performed, ensuring that it did not perforate the Descemet's membrane. Anwar's BB (Type 1 bubble) or MLD techniques were used to achieve a complete separation of the stroma from Descemet's membrane. For the BB group, conventional 8 mm diameter trephination was performed to a stromal depth between 60% and 80% using a suction trephine. Air was introduced using a 30-gauge needle angled at 45° with its bevel oriented downward. Following the formation of a large bubble, peripheral paracentesis was performed to reduce IOP. After the initial incision, a viscoelastic substance was introduced between the stroma and the layer preceding Descemet's membrane. The stroma was then segmented into four sections and delicately detached from the pre-Descemet's layer. If the BB formation failed despite two or three attempts, manual dissection of the stroma with blunt-tipped fine scissors and a blunt spatula was performed. At the end of both surgeries, an 8.5 mm donor cornea, excluding Descemet's membrane, was sutured in the recipient bed using 16 interrupted 10-0 nylon sutures. Moxifloxacin ophthalmic drops (Vigamox 0.5%; Alcon Laboratories Inc., Fort Worth, TX, USA) and dexamethasone ophthalmic drops (Maxidex 0.1%; Alcon Laboratories Inc.) were administered 6 times a day for 2 weeks post-operatively. After 2 weeks, the drops were adjusted according to the graft status at post-operative visits. All patients stopped receiving dexamethasone ophthalmic drops at the end of 1 year. The patients were assessed every week in the 1st month and every month in the 1st year. Ruptured and loose sutures were removed during routine examinations. At 12 months, all sutures were removed.

Data were analyzed using the Statistical Package for the Social Sciences software (version 25.0; IBM Corp, Armonk, NY, USA). Descriptive statistics were computed for all variables. For the analysis of continuous data, mean±standard deviation was used, while categorical variables were evaluated as the number of cases and percentages (%). The Mann–Whitney U test was employed to evaluate the significance of the difference between the mean values of the two groups. Statistical significance was set at $p<0.05$.

Results

Forty-three eyes with BB-DALK and 35 with MLD-DALK were included in this study. The demographic and topographic data of the patients are shown in Table 1 in terms of the pre-operative and post-operative 18-month periods.

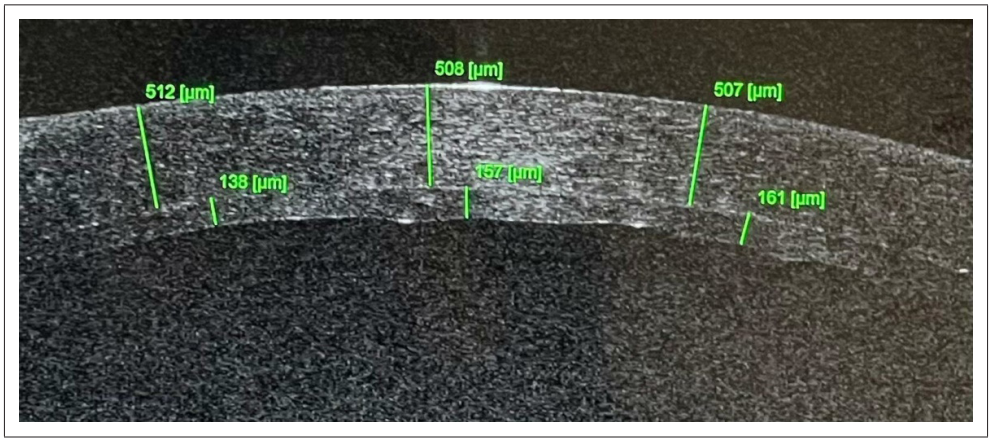

Fig. 1. Anterior segment optic coherence tomography image of a deep anterior lamellar keratoplasty with manual lamellar dissection technique patient, residual stromal bed thickness, and calculation method.

Table 1. Demographic data and comparison of pre-operative and post-operative 18th-month refractive and topographic outcomes between groups

Parameters	BB-DALK	MLD-DALK	*p*
Age (years)	38.58±16.11	44.08±18.42	0.219
Gender (F/M)	23/20	22/13	0.132
Pre-op manifest refraction (SE)	-7.71±3.81	-8.01±4.11	0.088
Pre-op Kmax (D)	68.80±8.12	66.71±7.25	0.486
Pre-op topographic astigmatism	6.21±2.88	5.59±3.01	0.221
Pre-op Central corneal thickness (µm)	418±41.12	403.12±38.33	0.337
Pre-op BCVA (logMAR)	0.96±0.83	1.02±1.02	0.552
Pre-op ECD (cell/mm^2)	2902±403.42	2874±48.12	0.712
Post-op manifest refraction (SE)	-0.23±4.17	-0.43±4.87	0.606
Post-op Kmax (D)	46.01±4.12	45.98±4.54	0.918
Post-op topographic astigmatism	3.87±3.45	3.32±3.76	0.590
Post-op Central corneal thickness (µm)	547.86±59.90	588.75±72.62	**0.019***
Post-op BCVA (logMAR)	0.56±0.37	0.67±0.34	0.096
Post-op ECD (cell/mm^2)	2171.79±605.84	2291.65±660.61	0.396

BB-DALK: Deep anterior lamellar keratoplasty with big bubble technique, MLD-DALK: Deep anterior lamellar keratoplasty with manual lamellar dissection technique, SE: Spherical equivalent, K: Keratometry, D: Diopters, BCVA: Best corrected visual acuity, ECD: Endothelial cell density. *Level of statistical significance $P<0.05$

Table 2. Corneal biomechanics values at post-operative 18th month

Parameters	BB-DALK	MLD-DALK	*p**
CH (mmHg)	8.01±1.90	8.68±1.94	0.123
CRF (mmHg)	9.03±2.24	9.66±2.19	0.173
IOPcc (mmHg)	20.50±6.47	19.93±4.29	0.833
IOPg (mmHg)	17.74±6.59	17.9±4.5	0.520

BB-DALK: Deep anterior lamellar keratoplasty with big bubble technique, MLD-DALK: Deep anterior lamellar keratoplasty with manual lamellar dissection technique, CH: Corneal hysteresis, CRF: Corneal resistance factor, IOPcc: Cornea-compensated factor, IOPg: Goldmann-correlated intraocular pressure

Graft survival rates were 100% in the BB-DALK and MLD-DALK groups at 18 months. Post-operative complications occurred in 5 eyes (6.9%) in the BB-DALK group (1 suture abscesses, 2 loose sutures) and 4 eyes (11.4%) in the MLD-DALK group (2 suture abscesses, 2 loose sutures) (p=0.97) during the follow-up period, patients presenting with loose sutures underwent suture removal and subsequent re-suturing. In cases where a suture abscess developed, the affected suture was removed, and following a 2-week course of topical moxifloxacin drops (Vigamox 0.5%; Alcon Laboratories Inc., Fort Worth, TX, USA) therapy leading to resolution of the abscess, re-suturing was performed.

Patients in both groups were pre-operatively classified as having severe keratoconus according to the Amsler-Krumeich criteria. Pre-operative severity was comparable between groups in terms of spherical equivalent (SE), BCVA, maximum keratometry (Kmax), central corneal thickness (CCT), and endothelial cell count. Post-operative SE, BCVA, Kmax, CCT, and endothelial cell count values were similar between the groups. In the MLD-DALK group, the average RSB was 75.85±27.70 µm. The mean CH, CRF, cornea-compensated IOP (IOPcc), and Goldmann-correlated IOP (IOPg) values of the BB-DALK and MLD-DALK eyes are shown in Table 2. The patients showed CH of 8.01±1.90 and 8.68±1.94 mmHg, CRF of 9.03±2.24 and 9.66±2.19 mmHg,

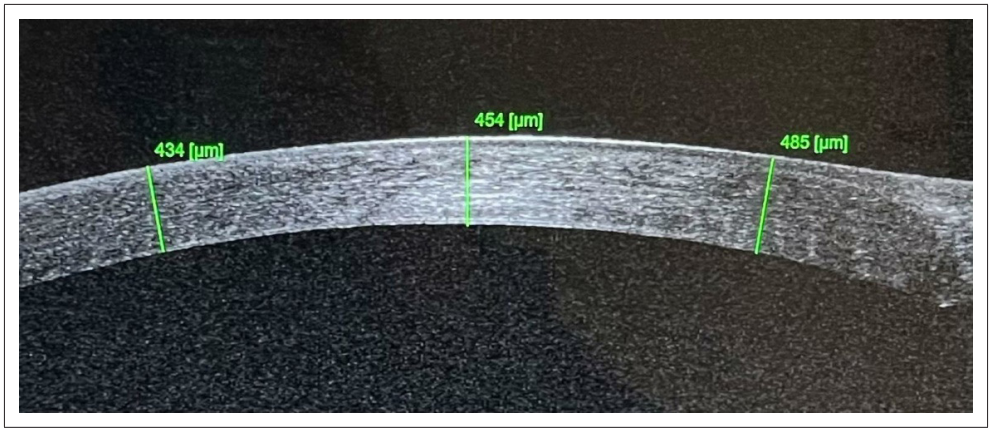

Fig. 2. Anterior segment optic coherence tomography image of a deep anterior lamellar keratoplasty with big bubble technique patient.

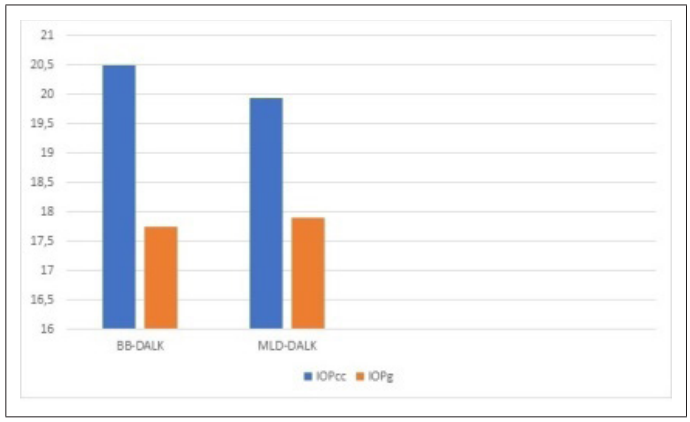

Fig. 3. Comparison of cornea-compensated intraocular pressure (IOP) and Goldmann-correlated IOP within the groups.

IOPcc of 20.50±6.47 and 19.93±4.29 mmHg, and IOPg of 17.74±6.59 and 17.9±4.5 mmHg in the BB-DALK and MLD-DALK eyes, respectively (p>0.05). The IOPcc values were higher than the IOPg values in both the BB-DALK and MLD-DALK groups (p<0.01) (Fig. 3). IOPcc, IOPg, CH, and CRF did not correlate with RSB in the MLD-DALK group (Fig. 4a-d). No significant correlations were observed between CCT and CH, CRF, IOPg, or IOPcc in eyes with BB-DALK and MLD-DALK.

Discussion

In recent years, DALK has become a suitable surgical method for treating keratoconus, where the endothelium and Descemet's membrane are intact.[11-15] The term of graft survival, complication rates, patient-reported outcomes, and corneal stability in this study provides a broader perspective on the efficacy of BB-DALK and MLD-DALK. The high graft survival rates in both groups align with previous reports of DALK's favorable long-term outcomes compared to penetrating keratoplasty, likely due to preserved endothelial integrity. Complication rates were low and similar between groups, suggesting that MLD-DALK remains a safe alternative when BB formation fails, despite its technically demanding nature. The stability of K max and CCT over time reinforces the biomechanical equivalence observed in CH and CRF measurements, suggesting that neither technique compromises long-term corneal integrity. These findings highlight the versatility of DALK and support its use in keratoconus management, particularly in cases where BB-DALK is not feasible.

The ORA can measure two pressure-derived parameters: CH and CRF. While CH represents viscoelastic characteristics, CRF measures the total resistance of the cornea.[16,17] In

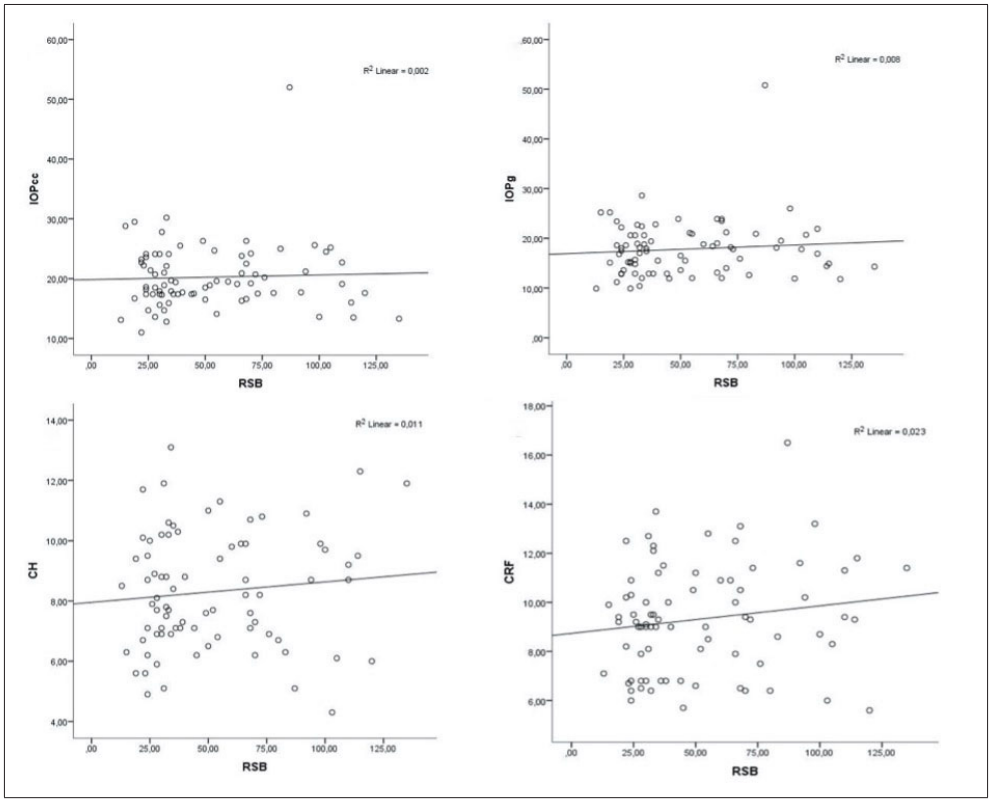

Fig. 4. Correlation between (a) residual stromal bed and cornea-compensated intraocular pressure (IOP), (b) Goldmann-correlated IOP, (c) corneal resistance factor, and (d) corneal hysteresis in the deep anterior lamellar keratoplasty with manual lamellar dissection technique group.

many studies conducted on keratoconic eyes, CH and CRF were found to be lower than those in normal eyes.[18,19] Hosny *et al.* [9] compared the biomechanical features of the cornea in eyes with previous PK and DALK using the ORA. They found that keratoconic eyes that underwent PK had significantly lower CH and CRF values than those that had undergone previous DALK. They also reported that post-DALK keratoconic eyes were similar to normal corneas in terms of corneal biomechanics. They concluded that an intact host Descemet's membrane acts as a strong barrier and maintains corneal rigidity.[9] In another study, Abdelkader found that corneal biomechanics were better in post-DALK eyes than in post-PK eyes at 3 months. However, these results have been reported to be comparable at 1 year.[20] In the BB-DALK technique, the thickness of the RSB cannot be quantified, which is indicative of the complete exposure of Descemet's membrane, as intended by the Anwar technique. In the present study, qualitative assessments using AS-OCT alongside intraoperative surgical records in patients who underwent BB-DALK confirmed the absence of residual stromal tissue, thereby validating the effective execution of the technique. These findings suggest that BB-DALK achieves a more uniform stromal clearance compared to MLD-DALK. Furthermore, the lack of correlation between the mean RSB thickness (75.8 µm) observed in MLD-DALK and post-operative biomechanical parameters CH, CRF, as well as BCVA, indicates that the absence of RSB in BB-DALK has minimal impact on these outcomes. This supports the notion that both techniques yield comparable results in terms of corneal biomechanics. Although we reported the mean RSB thickness, we did not perform subgroup analyses stratifying eyes into thinner versus thicker RSB categories. Similarly, correlation analyses exploring whether RSB thickness might subtly influence biomechanical behavior beyond the mean values were limited. Future studies with larger cohorts are warranted to better elucidate these potential associations.

In addition to CH and CRF measurements, ORA provides more accurate IOP results, as it is not significantly affected by CCT, corneal curvature, or axial length.[21] Feizi *et al.* [22] showed that after DALK, IOP values measured using ORA were significantly higher than those measured using Goldmann applanation tonometry (GAT). This study also observed that IOP_{CC}, which is less influenced by corneal properties than GAT, yielded the highest results.[22] Similar to Feizi's study, we found that IOPcc values were significantly higher than IOPg values in both the BB-DALK and MLD-DALK groups. In our study, IOPcc values were found to be significantly higher than IOPg values in both the BB-DALK and MLD-DALK groups ($p<0.01$). This observation aligns with previous findings by Feizi *et al*. [22] and suggests that changes in corneal properties following DALK may influence IOP measurements. Given that IOPcc, as measured by ORA, is less affected by parameters, such as CCT, corneal curvature, or axial length, this discrepancy likely reflects alterations in corneal biomechanics post-surgery. Specifically, the removal of diseased stroma and integration of donor tissue during DALK may modify the cornea's elastic properties and resistance, resulting in higher IOPcc readings compared to IOPg values obtained through GAT. This difference carries significant clinical implications. First, prolonged use of topical steroids, common in DALK patients, raises the risk of steroid-induced ocular hypertension or glaucoma. The finding that IOPcc exceeds IOPg suggests that traditional GAT measurements may underestimate true IOP in these patients, potentially leading to missed diagnoses of elevated IOP. Consequently, employing methods, such as ORA, which are less influenced by corneal biomechanics, could provide a more accurate assessment of IOP in the post-operative period. Second, the disparity between IOPcc and IOPg underscores the need for further investigation into how surgical modifications and healing processes affect corneal biomechanical parameters. Factors, such as donor stromal thickness, recipient bed characteristics, or suturing techniques may contribute to this difference and warrant exploration. Briefly, the elevated IOPcc relative to IOPg highlights the importance of a cautious approach to IOP monitoring in both BB and MLD DALK patients. Clinicians should consider incorporating ORA-derived IOPcc values into their diagnostic and management strategies, particularly for glaucoma screening or steroid therapy monitoring, to ensure more reliable outcomes. These findings emphasize the need for standardized IOP measurement protocols in the long-term follow-up of DALK patients and encourage future studies to further elucidate this phenomenon. Although Anwar's BB technique is considered to be the most successful approach for DALK, MLD is another viable option that could eliminate the need for PK.[4,23] In this study, we aimed to investigate and compare the effects of these two techniques on corneal biomechanics. We found that CH and CRF were similar between the MLD-DALK and BB-DALK techniques. This also suggests that the similarity of CF and CRF in the BB DALK and MLD DALK groups indicates that MLD DALK can be safely continued in patients where BB DALK cannot be performed. We emphasize that in the future, surgical procedures can be comfortably continued

with MLD DALK without encountering the complications associated with PKP due to similar CF and CRF values among subtypes of DALK surgery.

Akdemir *et al*.[10] studied the biomechanics of corneas that underwent DALK using the BB or MLD technique for keratoconus. Similar to our study, they concluded that the two methods used to perform successful DALK were not superior in terms of corneal biomechanical properties. In addition to their study, we evaluated the possible correlation between the RSB thickness and ORA findings in the MLD-DALK group. We concluded that an average of 75.8 µm RSB thickness did not affect the visual acuity or the effect of the RSB on corneal biomechanics.

In our study, the MLD-DALK technique was employed in cases where the BB-DALK technique failed to achieve a successful BB, such as due to difficulties in separating the stroma from Descemet's membrane. This approach may introduce a selection bias, as patients in the MLD-DALK group could represent more challenging cases with potentially thinner peripheral corneas or greater disease severity. To address this potential bias and enhance the reliability of our findings, we compared DALK types. Although the MLD DALK group appeared to have a thinner mean corneal thickness, higher mean K values, and higher mean disease stage, no statistically significant difference was found between the two groups. This finding suggests that the impact of selection bias may be reduced, rendering CH comparable between the groups.

The first limitation of our study is the exclusion of patients who underwent PKP. The primary reason for this is our longstanding shift away from performing PKP, particularly in patients with keratoconus. The second limitation of our study is the relatively small sample size, retrospective and non-randomized nature. Although the necessary numbers were obtained in the G power analysis, studies with larger samples would yield better results. Another important limitation is that the biomechanical evaluation was based solely on ORA. Although ORA provides clinically useful data, its relatively low repeatability and interobserver variability must be acknowledged. Moreover, more advanced devices, such as the Corvis ST could have provided dynamic and more reproducible biomechanical parameters. The lack of such complementary tools limits the comprehensiveness of our biomechanical assessment. The inclusion of such a device could offer a more comprehensive biomechanical profile of the cornea following BB-DALK and MLD-DALK, potentially revealing subtle differences not captured by the ORA. Future studies are encouraged to incorporate the Corvis ST or similar technologies to validate and expand upon our findings, particularly in assessing the long-term impact of RSB thickness and surgical technique on corneal stability and rigidity. On the other hand, since MLD was specifically performed in cases where BB formation failed, the retrospective and non-randomized nature of the study inevitably introduces a selection bias. These patients may inherently represent more complex keratoconus cases, and this factor should be considered when interpreting our findings.

This study compared the effects of BB and MLD techniques in DALK on corneal biomechanics and visual outcomes in patients with keratoconus. At 18 months post-operatively, CH and CRF values were similar between the BB-DALK and MLD-DALK groups ($p>0.05$). Similarly, no significant difference was observed in BCVA between the two techniques ($p>0.05$). In the MLD-DALK group, the mean RSB thickness was measured as 75.8±27.7 µm, yet no significant correlation was found between RSB thickness and BCVA, CH, CRF, or IOP parameters. Notably, IOPcc values were significantly higher than IOPg values in both groups ($p<0.01$), underscoring the importance of using IOP measurement methods less influenced by corneal biomechanics (e.g., ORA-derived IOPcc) following DALK. In conclusion, the MLD-DALK technique yields comparable outcomes to BB-DALK in terms of visual acuity and corneal biomechanics. In cases where the BB technique is not feasible, MLD-DALK serves as a safe and effective alternative, potentially eliminating the need for penetrating keratoplasty. Ophthalmologists should keep in mind that a cautious approach to IOPcc monitoring is essential, as IOPcc is higher than IOPg in both subtypes of the DALK surgical technique. Larger-scale studies are needed to evaluate the long-term outcomes.

Conclusion

The MLD-DALK technique yields comparable outcomes to BB-DALK in terms of visual acuity and corneal biomechanics. In cases where the BB technique is not feasible, MLDDALK serves as a safe and effective alternative, potentially eliminating the need for penetrating keratoplasty. Ophthalmologists should keep in mind that a cautious approach to IOPcc monitoring is essential, as IOPcc is higher than IOPg in both subtypes of the DALK surgical technique.

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Ethics Committee Approval: This study was approved by The Ankara Bilkent City Hospital Ethic Committee (approval number: E-22-3135).

Informed Consent: Written informed consents were obtained from patient and his family.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.E.K., Y.A., O.E.K.; Design: E.E.K., O.E.K.; Supervision: O.E.K.; Resource: E.E.K.; Materials: Y.A., G.C., A.B.G.; Data Collection and/or Processing: Y.A., G.Ç., A.B.G.; Analysis and/or Interpretation: E.E.K., Y.A., G.C., A.B.G., O.E.K.; Literature Search: E.E.K., Y.A., G.C.; Writing: E.E.K., G.Ç.; Critical Reviews: E.E.K., O.E.K.

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