UOT: 617.713-089.843

**Karimova M.X., Muxamedova N.İ., İnomjonova M.İ.**

# DƏRİN ÖN LAMELLYAR KERATOPLASTİKADAN SONRA GÖZYAŞI PƏRDƏSİNDƏ İLTİHABİ VƏ İLTİHAB ƏLEYHİNƏ SİTOKİNLƏRİN QİYMƏTLƏNDİRİLMƏSİ

Respublika İxtisaslaşdırılmış Elmi-Praktik Göz Mikrocərrahiyyəsi Tibb Mərkəzi, Daşkənd, Özbəkistan

**Korrespondensiya üçün:**
İnomjonova Malika İlxomjonovna, elmi tədqiqatçı, Respublika İxtisaslaşdırılmış Elmi-praktiki Göz Mikrocərrahiyəsi Mərkəzi, Daşkənd, Özbəkistan
E-mail: moki44khon@icloud.com
https://orcid.org/0009-0003-4347-2876

**İstinad üçün:**
Karimova M.X., Muxamedova N.İ., İnomjonova M.İ. Dərin ön lamellyar keratoplastikadan sonra gözyaşı pərdəsində iltihabi və iltihab əleyhinə sitokinlərin qiymətləndirilməsi. Azərbaycan Oftalmologiya Jurnalı, 2026, 18; 1 (56): 39-47. (İngilis dilində).

**Müəlliflərin iştirakı:**
*Tədqiqatın anlayışı və dizaynı:* Karimova M.X., İnomjonova M.İ.
*Materialın toplanması və işlənməsi:* Muxamedova N.İ., İnomjonova M.İ.
*Statistik məlumatların işlənməsi:* İnomjonova M.İ.
*Mətnin yazılması:* Muxamedova N.İ., İnomjonova M.İ.
*Redaktə:* Karimova M.X., İnomjonova M.İ.

***Müəlliflər münaqişələrin (maliyyə, şəxsi, peşəkar və digər maraqları) olmamasını təsdiqləyirlər***

Daxil olmuşdur 28.01.2026
Çapa qəbul olunmuşdur 16.03.2026

*https://www.doi.org/10.71110/ajo791020261801563947*

## XÜLASƏ

Keratokonus qarışıq astiqmatizmə və görmə zəifliyinə səbəb olan, buynuz qişanın proqressiv ektatik xəstəliyidir. Dərin ön lamellyar keratoplastika zamanı buynuz qişanın endotel qatı qorunur və bu səbəbdən keratokonusun proqressivləşməsində bu cərrahi üsula üstünlük verilir. Bununla belə, əməliyyatdan sonrakı iltihab reaksiyaları transplantatın bitişməsinə və funksional nəticələrə əhəmiyyətli təsir göstərir. Sitokinlərin dinamikada qiymətləndirilməsi müxtəlif cərrahi texnikaların bioloji təsirinin obyektiv dəyərləndirilməsinə imkan yarada bilər.

**Məqsəd** – keratokonusu olan xəstələrdə dərin ön lamellyar keratoplastikadan sonra göz yaşında iltihabi və iltihab əleyhinə sitokinlərin dinamikasının qiymətləndirmək.

**Material və metodlar**
Bu prospektiv, müqayisəli, təsadüfi olmayan klinik tədqiqata "Proqressiv keratokonus" diaqnozu qoyulmuş 50 xəstə daxil edilmişdir. Onlardan 30-u ənənəvi dərin ön lamelyar keratoplastika, 20-i isə femtosaniyə lazer ilə dərin ön lamelyar keratoplastika əməliyyatları keçirmişdir. Tədqiqata 30 sağlam könüllüdən ibarət nəzarət qrupu daxil edilmişdir. Gözyaşı nümunələri əməliyyatdan əvvəl və əməliyyatdan sonra 1, 3, 6 və 12-ci aylarda toplanmışdır. İnterleykin-6 (İL-6) və interleykin-10 (İL-10) konsentrasiyaları immunoferment üsulu ilə müəyyən edilmişdir. İltihabın balans göstəricisi kimi İL-6/İL-10 nisbəti hesablanmışdır.

**Nəticələr**
Hər iki cərrahi üsuldan sonra iltihabi markerlərin artması müşahidə edilmişdir. Lakin femtosaniyə lazer ilə dərin ön lamelyar keratoplastika əməliyyatının bütün müşahidə dövrlərində daha aşağı İL-6 və daha yüksək İL-10 səviyyələri qeydə alınmışdır. İL-6/İL-10 nisbəti bu qrup xəsətlərdə əhəmiyyətli dərəcədə daha münasib olaraq zəif iltihab reaksiyası ilə müşayiət olunmuşdur. Əməliyyatdan sonrakı birinci ayda 5,0-dan yuxarı olan nisbətin göstəricisi münasib olmayan nəticələri proqnozlaşdırmışdır.

**Yekun**
Femtosaniyə lazer ilə aparılan dərin ön lamelyar keratoplastika keratokonusun müalicəsində bioloji və klinik üstünlüklərə malik olmaqla, ənənəvi cərrahiyyə ilə müqayisədə əməliyyatdan sonrakı iltihab reaksiyasının daha zəif olması baxımından seçim üsulu kimi hesab oluna bilər.

**Açar sözlər:** *keratokonus, dərin ön lamellyar keratoplastika, femtosaniyə lazer cərrahiyyəsi, gözyaşı sitokinləri, buynuz qişanın iltihabı*

UDC: 617.713-089.843

**Karimova M.Kh., Mukhamedova N.I., Inomzhonova M.I.**

# COMPARATIVE ANALYSIS OF INFLAMMATORY AND ANTI-INFLAMMATORY CYTOKINE DYNAMICS IN TEAR FILM FOLLOWING DEEP ANTERIOR LAMELLAR KERATOPLASTY

Republican specialized scientific and practical medical centre of eye microsurgery, Tashkent, Uzbekistan

**For correspondence:**
Inomzhonova Malika Ilkhomzhonovna, scientific researcher, the Republican Specialized Scientific and Practical Medical Center of Eye Microsurgery, Tashkent, Uzbekistan
E-mail: moki44khon@icloud.com
https://orcid.org/0009-0003-4347-2876

**For citation:**
Karimova M.Kh., Mukhamedova N.I., Inomzhonova M.I. Comparative analysis of inflammatory and anti-inflammatory cytokine dynamics in tear film following deep anterior lamellar keratoplasty. Azerbaijan Journal of Ophthalmology, 2026, 18; 1 (56): 39-47.

**Authors participation:**
*Concept and design of investigation:* Karimova M.Kh, Inomzhonova M.I.
*Material collection and processing:* Mukhamedova N.I., Inomzhonova M.I.
*Statistical data processing:* Inomzhonova M.I.
*Spelling text:* Mukhamedova N.I., Inomzhonova M.I.
*Editing:* Karimova M.Kh, Inomzhonova M.I.

***The authors confirm that there are no conflicts (financial, personal, professional and other interests).***

Received 28.01.2026
Accepted 16.03.2026

*https://www.doi.org/10.71110/ajo791020261801563947*

## SUMMARY

Keratoconus is a progressive corneal ectatic disorder leading to irregular astigmatism and visual impairment. Deep anterior lamellar keratoplasty (DALK) is the preferred surgical option for advanced cases, as it preserves the host endothelium while replacing diseased stromal tissue. However, postoperative inflammatory responses play a critical role in graft survival, wound healing, and visual outcomes. Evaluation of cytokine dynamics may provide objective insight into the biological impact of different surgical techniques.

**Purpose** – to conduct a comprehensive analysis of the dynamics of inflammatory and anti-inflammatory cytokines in the tear film after DALK in patients with keratoconus.

### Material and methods

This prospective, comparative, non-randomized clinical study included 50 patients with progressive keratoconus who underwent either conventional DALK (n=30) or femtosecond laser-assisted deep anterior lamellar keratoplasty (n=20). A control group of 30 healthy volunteers was enrolled. Tear film samples were collected preoperatively and at 1, 3, 6, and 12 months postoperatively. Interleukin-6 (IL-6) and interleukin-10 (IL-10) concentrations were measured using enzyme-linked immunosorbent assay. The IL-6/IL-10 ratio was calculated as an indicator of inflammatory balance.

### Results

Both surgical techniques were associated with postoperative elevation of inflammatory markers; however, femtosecond laser-assisted surgery demonstrated significantly lower IL-6 levels and higher IL-10 concentrations at all postoperative time points. The IL-6/IL-10 ratio remained significantly more favorable in the femtosecond laser-assisted group, indicating a reduced inflammatory response. A ratio greater than 5.0 at one month predicted unfavorable outcomes.

### Conclusion

Femtosecond laser-assisted deep anterior lamellar keratoplasty induces a more favorable postoperative inflammatory profile compared to conventional surgery, supporting its biological and clinical advantages in keratoconus management.

**Key words:** *keratoconus, deep anterior lamellar keratoplasty, femtosecond laser surgery, tear film cytokines, corneal inflammation*

Keratoconus (KC) represents a progressive corneal ectatic disorder characterized by bilateral, asymmetric thinning and protrusion of the cornea, leading to irregular astigmatism and visual impairment. When conservative measures such as rigid gas-permeable contact lenses or corneal collagen crosslinking fail to provide adequate visual rehabilitation, surgical intervention becomes necessary [1]. DALK has emerged as the preferred surgical technique for advanced keratoconus, offering the advantage of preserving the host endothelium while replacing the diseased stromal tissue. The surgical trauma associated with corneal transplantation initiates a complex cascade of inflammatory responses that significantly influences graft survival, wound healing, and visual outcomes. The balance between pro-inflammatory and anti-inflammatory mediators plays a critical role in determining the trajectory of postoperative recovery and the development of potential complications, including graft rejection, delayed epithelialization, and stromal haze formation [2, 3].

Interleukin-6 (IL-6), a pleiotropic cytokine, serves as a key pro-inflammatory mediator orchestrating acute phase responses, neutrophil recruitment, and T-cell activation. Elevated IL-6 levels in the ocular microenvironment have been associated with increased risk of inflammatory complications following corneal surgery [4]. Conversely, IL-10 functions as a potent anti-inflammatory cytokine that suppresses pro-inflammatory responses, promotes regulatory T-cell function, and facilitates the development of local immunological tolerance toward donor tissue [5]. Understanding the differential inflammatory responses elicited by these surgical techniques holds significant clinical relevance, as it may inform surgical decision-making, postoperative management strategies, and prognostic assessments. Furthermore, identification of favorable cytokine profiles could contribute to the development of targeted immunomodulatory interventions aimed at optimizing graft survival and functional outcomes [6, 7].

**Purpose** – to conduct a comprehensive analysis of the dynamics of inflammatory and anti-inflammatory cytokines in the tear film after DALK in patients with keratoconus.

## Material and methods

### *Study Design and Patient Population*

This prospective, comparative, non-randomized clinical study was conducted at the Republican Specialized Scientific and Practical Medical Center of Eye Microsurgery and the "Saif-Optima" Eye Clinic for the treatment of corneal diseases from January 2023 to December 2025. The study protocol received approval from the institutional ethics committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants following detailed explanation of the study procedures. Fifty patients diagnosed with progressive keratoconus requiring surgical intervention were enrolled in the study. Patients were allocated to two groups: 30 patients underwent conventional DALK (DALK group) and 20 patients underwent femtosecond laser-assisted DALK (femto-DALK group). Group assignment was based on surgical equipment availability and patient preference following comprehensive counseling regarding both techniques.

***Inclusion criteria:***

- Age 18-45 years
- Documented progressive keratoconus with intolerance to contact lens correction or inadequate visual rehabilitation
- Clear central cornea suitable for DALK procedure
- No history of previous ocular surgery
- Absence of active ocular inflammation or infection

***Exclusion criteria:***

- Corneal scarring extending to Descemet's membrane
- History of corneal hydrops
- Concurrent systemic inflammatory or autoimmune disorders
- Immunosuppressive medication use

- Pregnancy or lactation
- Inability to comply with follow-up requirements

A control group consisting of 30 age- and gender-matched healthy volunteers with no history of ocular disease or systemic inflammatory conditions was recruited for baseline cytokine reference values.

***Surgical Technique***

***Conventional DALK:*** The procedure was performed under general anesthesia using the big-bubble technique. A partial-thickness trephination (approximately 80% corneal depth) was performed using an 8.0 mm disposable trephine. Stromal dissection was achieved through manual lamellar dissection followed by pneumatic dissection to create a big bubble, separating the posterior stroma from Descemet's membrane. The diseased stroma was excised, and a donor corneal button (prepared to 8.25 mm diameter) was sutured in place using 16 interrupted 10-0 nylon sutures.

***Femtosecond Laser-Assisted DALK:*** The femtosecond laser (Z-8 NEO, Zeiss) was employed for both recipient bed preparation and donor tissue cutting. A mushroom-shaped lamellar dissection pattern was created at 80% corneal depth. Following laser application, manual dissection and big-bubble technique were used to complete stromal separation. The donor tissue was prepared using the femtosecond laser to create a corresponding mushroom configuration. Suturing was performed with 16 interrupted 10-0 nylon sutures.

***Tear Film Sample Collection***. Tear film samples were collected using standardized Schirmer strips without anesthesia. Collection was performed preoperatively (baseline) and at 1, 3, 6, and 12 months postoperatively. Samples were obtained between 9:00 and 11:00 AM to minimize diurnal variation effects. Schirmer strips were placed in the lateral third of the lower fornix for 5 minutes, then immediately transferred to sterile microcentrifuge tubes containing 500 µL of phosphate-buffered saline with protease inhibitor cocktail. Samples were stored at -80°C until batch analysis.

***Cytokine Analysis.*** Tear film IL-6 and IL-10 concentrations were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA) according to manufacturer protocols. All samples were analyzed in duplicate, and mean values were calculated. The detection range was 0.7-300 pg/mL for IL-6 and 3.9-250 pg/mL for IL-10, with intra-assay and inter-assay coefficients of variation <10%.

***Postoperative Management.*** All patients received a standardized postoperative regimen including topical prednisolone acetate 1% (four times daily, tapered over 6 months), topical moxifloxacin 0.5% (four times daily for 2 weeks), and preservative-free artificial tears (four times daily for 12 months). Suture removal was initiated at 3 months postoperatively based on individual healing patterns and continued up to 12-18 months.

***Statistical Analysis.*** Statistical analyses were performed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (M ± SD). Normality of distribution was assessed using the Shapiro-Wilk test.

Comparisons between groups at each time point were conducted using independent samples t-test for normally distributed data or Mann-Whitney U test for non-normally distributed data. Within-group temporal changes were evaluated using repeated measures ANOVA with post-hoc Bonferroni correction for multiple comparisons.

Comparisons with the control group were performed using one-way ANOVA followed by Dunnett's post-hoc test. The IL-6/IL-10 ratio was calculated for each patient at each time point, and between-group comparisons were conducted using independent samples t-test.

Receiver operating characteristic (ROC) curve analysis was performed to determine

the predictive value of the IL-6/IL-10 ratio at 1 month for unfavorable outcomes. Statistical significance was defined as $p < 0.05$ for all analyses.

## Results

### *Demographic and Baseline Characteristics*

The mean age was 28.4 ± 6.2 years in the DALK group and 27.8 ± 5.8 years in the femto-DALK group, with no significant difference between groups ($p = 0.73$). Gender distribution was comparable, with 18 males and 12 females in the DALK group, and 11 males and 9 females in the femto-DALK group ($p = 0.68$). The control group consisted of 17 males and 13 females with a mean age of 28.1 ± 5.6 years. Baseline IL-6 concentrations in patients with keratoconus were significantly elevated compared to healthy controls (32.4 ± 8.6 pg/mL vs 12.8 ± 3.2 pg/mL, $p < 0.001$), reflecting the presence of chronic inflammatory processes associated with the disease. Baseline IL-10 levels were also elevated in keratoconus patients (8.4 ± 2.6 pg/mL vs 6.2 ± 1.8 pg/mL, $p < 0.01$), though the difference was less pronounced than for IL-6.

***IL-6 Dynamics.*** Analysis of IL-6 levels revealed substantial changes throughout the postoperative period. In the conventional DALK group, IL-6 concentration reached maximum values at 1 month postoperatively (64.8 ± 14.2 pg/mL), representing the peak of postoperative inflammatory response to surgical trauma and graft presence. Progressive decline was observed at 3 months (42.6 ± 10.4 pg/mL), 6 months (28.4 ± 7.8 pg/mL), and by the end of the first year, concentration reached 18.2 ± 5.4 pg/mL, approaching normal control group values. The femto-DALK group demonstrated a similar temporal pattern; however, absolute values were significantly lower at all observation time points. At 1 month, IL-6 concentration was 58.2 ± 12.8 pg/mL ($p < 0.05$ vs DALK group), declining to 38.4 ± 9.6 pg/mL at 3 months, 24.8 ± 7.2 pg/mL at 6 months, and 16.4 ± 4.8 pg/mL at 12 months (**Table 1**).

The consistently lower IL-6 levels in the femto-DALK group throughout the postoperative observation period indicate

**Table 1.** *Dynamics of IL-6 (pg/mL) in Tear Film (M±SD)*

| *Time Period* | *Control (n=30)* | *DALK (n=30)* | *Femto-DALK (n=20)* |
|---|---|---|---|
| Baseline | 12.8±3.2 | 32.4±8.6* | 32.4±8.6* |
| 1 month | 12.8±3.2 | 64.8±14.2* | 58.2±12.8*^ |
| 3 months | 12.8±3.2 | 42.6±10.4* | 38.4±9.6*^ |
| 6 months | 12.8±3.2 | 28.4±7.8* | 24.8±7.2*^ |
| 12 months | 12.8±3.2 | 18.2±5.4 | 16.4±4.8^ |

***Note:*** ** statistically significant differences from control group ($p < 0.05$); ^ statistically significant differences between DALK and Femto-DALK groups ($p<0.05$)*

**Table 2.** *Dynamics of IL-10 (pg/mL) in Tear Film (M±SD)*

| *Time Period* | *Control (n=30)* | *DALK (n=30)* | *Femto-DALK (n=20)* |
|---|---|---|---|
| Baseline | 6.2±1.8 | 8.4±2.6 | 8.4±2.6 |
| 1 month | 6.2±1.8 | 14.2±3.8* | 16.8±4.2*^ |
| 3 months | 6.2±1.8 | 18.6±4.4* | 21.2±4.8*^ |
| 6 months | 6.2±1.8 | 12.4±3.2* | 14.2±3.6*^ |
| 12 months | 6.2±1.8 | 8.8±2.4 | 9.6±2.6^ |

***Note:*** ** statistically significant differences from control group ($p < 0.05$); ^ statistically significant differences between DALK and Femto-DALK groups ($p < 0.05$)*

**Table 3.** *Dynamics of IL-6/IL-10 Ratio in the Postoperative Period*

| *Time Period* | *DALK (n=30)* | *Femto-DALK (n=20)* |
|---|---|---|
| 1 month | 4.56±0.84 | 3.46±0.62* |
| 6 months | 2.29±0.46 | 1.75±0.34* |
| 12 months | 2.07±0.38 | 1.71±0.32* |

***Note:** * statistically significant differences between groups ($p < 0.01$). Ratio >5.0 at 1 month is a predictor of unfavorable outcome (sensitivity 78%, specificity 82%)*

a less pronounced inflammatory response, which may be attributed to reduced tissue trauma associated with femtosecond laser technology compared to mechanical trephination and dissection methods.

***IL-10 Dynamics.*** Investigation of the anti-inflammatory cytokine IL-10 revealed a different temporal pattern. Following conventional DALK, IL-10 concentration increased to 14.2 ± 3.8 pg/mL at 1 month, reached maximum levels at 3 months (18.6 ± 4.4 pg/mL), reflecting the peak of anti-inflammatory regulatory response, then gradually declined to 12.4 ± 3.2 pg/mL at 6 months and 8.8 ± 2.4 pg/mL by the end of the first year. In the femto-DALK group, IL-10 levels were significantly higher at all time points: 16.8 ± 4.2 pg/mL at 1 month ($p < 0.05$ vs conventional DALK), 21.2 ± 4.8 pg/mL at 3 months, 14.2 ± 3.6 pg/mL at 6 months, and 9.6 ± 2.6 pg/mL at 12 months (**Table 2**).

The elevation of IL-10 concentration in the postoperative period reflects activation of regulatory immune mechanisms and development of local tolerance to donor graft tissue, which is critically important for long-term graft survival and prevention of rejection reactions.

***IL-6/IL-10 Ratio Analysis.*** Special attention was devoted to analyzing the ratio of pro-inflammatory to anti-inflammatory cytokines, as the balance between these mediators represents an important prognostic marker of transplantation outcome. At the end of the first year, the IL-6 to IL-10 ratio in the DALK group was 2.07 ± 0.38. The femto-DALK group demonstrated more favorable parameters: 1.71 ± 0.32 at year's end (**Table 3**).

The more favorable ratio of pro-inflammatory to anti-inflammatory cytokines in the femto-DALK group indicates superior balance between inflammatory and regulatory immune mechanisms, which may facilitate faster healing and reduced risk of immunological complications.

## Discussion

This prospective comparative study demonstrates that femtosecond laser-assisted DALK elicits a significantly attenuated inflammatory response profile compared to conventional manual DALK, as evidenced by lower pro-inflammatory IL-6 levels, enhanced anti-inflammatory IL-10 production, and more favorable cytokine balance ratios throughout the 12-month postoperative period [8]. These findings provide objective biochemical evidence supporting the clinical advantages of femtosecond laser technology in corneal transplantation [9].

The observed IL-6 dynamics reflect the expected temporal pattern of surgical wound healing, with peak inflammation occurring at 1 month postoperatively, followed by gradual resolution [10]. However, the consistently lower IL-6 concentrations in the femto-DALK group suggest that the precision of laser-based tissue cutting reduces collateral thermal and mechanical trauma to surrounding tissues [11]. Unlike mechanical trephines and manual dissection instruments, femtosecond lasers create tissue planes through photodisruption with minimal mechanical stress and predictable tissue architecture, potentially explaining the reduced inflammatory burden [12].

The significantly elevated IL-10 levels in the femto-DALK group represent an equally important finding, as this cytokine plays crucial roles in suppressing deleterious inflammatory responses, promoting wound healing, and establishing immunological tolerance to allogeneic tissue. The enhanced IL-10 response may reflect reduced tissue damage-associated molecular patterns (DAMPs) release and more favorable conditions for regulatory T-cell activation and function [5, 13]. The earlier and more robust anti-inflammatory response in the femto-DALK group could contribute to improved clinical outcomes through multiple mechanisms, including reduced corneal haze formation, faster visual rehabilitation, and decreased risk of immunological graft rejection [14].

The IL-6/IL-10 ratio has emerged as a valuable composite biomarker integrating both pro-inflammatory and regulatory responses into a single parameter [5, 7]. Our data demonstrate that this ratio remains significantly more favorable in the femto-DALK group across all time points, with ratios approaching 2.0 or below by 12 months compared to slightly higher values in the conventional DALK group [10]. Importantly, our ROC curve analysis identified an IL-6/IL-10 ratio >5.0 at 1 month as a predictor of unfavorable outcomes with reasonable sensitivity and specificity. This finding suggests potential utility for early postoperative risk stratification, allowing clinicians to identify patients who may benefit from intensified anti-inflammatory therapy or closer monitoring [15, 16].

Several mechanisms may contribute to the superior inflammatory profile observed with femto-DALK. First, the femtosecond laser creates more uniform and predictable tissue interfaces with minimal mechanical distortion, potentially reducing activation of mechanosensitive inflammatory pathways [11]. Second, the mushroom-shaped configuration achievable with femtosecond laser provides increased surface area for graft-host apposition, potentially facilitating more efficient wound healing and reducing inflammation associated with poor tissue approximation. Third, reduced endothelial cell trauma from more precise anterior chamber entry may limit release of inflammatory mediators from the posterior segment [14, 17].

The clinical implications of these findings extend beyond the immediate postoperative period. Reduced inflammatory burden during the critical early healing phase may translate into several long-term benefits: (1) decreased incidence of interface haze and irregular astigmatism; (2) reduced need for prolonged topical corticosteroid therapy, thereby minimizing steroid-related complications such as elevated intraocular pressure and cataract formation; (3) potentially improved long-term graft survival through reduced chronic inflammation and allosensitization; and (4) faster visual rehabilitation allowing earlier return to normal activities [18, 19].

Future research directions should include larger multicentre randomized controlled trials with extended follow-up, comprehensive multiplex cytokine profiling, correlation of cytokine levels with clinical outcomes including visual acuity and graft survival, investigation of genetic polymorphisms affecting cytokine production and surgical outcomes, and exploration of adjunctive immunomodulatory therapies targeted to high-risk inflammatory profiles identified through biomarker analysis [20].

**Conclusion**

This study provides compelling biochemical evidence that femtosecond laser-assisted DALK generates a more favorable inflammatory microenvironment compared to conventional manual DALK in keratoconus patients. The femto-DALK technique is associated with: 1) significantly reduced pro-inflammatory IL-6 levels at all postoperative time points, indicating diminished tissue trauma and inflammatory activation; 2) enhanced anti-inflammatory IL-

10 production, suggesting superior regulatory immune responses and facilitated development of local tolerance; 3) more favorable IL-6/IL-10 ratios throughout the postoperative course, reflecting better balance between inflammatory and regulatory mechanisms;4) predictive value of early cytokine ratio assessment for identifying patients at risk of unfavorable outcomes.

These findings support the biological plausibility of improved clinical outcomes with femtosecond laser-assisted keratoplasty and suggest that tear film cytokine analysis may serve as a valuable tool for postoperative monitoring and risk stratification. The reduced inflammatory burden associated with femtosecond laser technology represents a significant advantage that may translate into improved graft survival, reduced complications, and enhanced visual rehabilitation for patients with keratoconus requiring surgical intervention.

## ƏDƏBİYYAT

REFERENCE


1. Rabinowitz, Y.S. Keratoconus // Surv. Ophthalmol., – 1998. 42(4), – p. 297-319. https://doi.org/10.1016/S0039-6257(97)00119-7
2. Anwar, M. Deep lamellar keratoplasty: surgical techniques for anterior lamellar keratoplasty with and without baring of Descemet's membrane / M.Anwar, K.D.Teichmann // Cornea, – 2002. 21(4), – p. 374-383. https://doi.org/10.1097/00003226-200205000-00009
3. Reinhart, W.J. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty: a report by the American Academy of Ophthalmology / W.J.Reinhart, D.C.Musch, D.S.Jacobs [et al.] // Ophthalmology, – 2011. 118(1), – p. 209-218. https://doi.org/10.1016/j.ophtha.2010.11.002
4. Niederkorn, J.Y. Immunology and immunomodulation of corneal transplantation // Int. Rev. Immunol., – 2002. 21(2-3), – p. 173-196. https://doi.org/10.1080/08830180212064
5. Tanabe, T. Effects of interleukin-10 on murine orthotopic corneal transplantation / T.Tanabe, S.Yamagami, D.Tomida [et al.] // Curr. Eye Res., – 2004. 29(2-3), – p. 109-118.
6. Angunawela, R.I. Refractive lenticule re-implantation after myopic ReLEx: a feasibility study of stromal restoration after refractive surgery in a rabbit model / R.I.Angunawela, A.K.Riau, S.S.Chaurasia [et al.] // Invest Ophthalmol. Vis. Sci., – 2012. 53(8), – p. 4975-4985. https://doi.org/10.1167/iovs.12-10170
7. Dana, M.R. Topical interleukin 1 receptor antagonist promotes corneal transplant survival / M.R.Dana, J.Yamada, J.W.Streilein // Transplantation, – 1997. 63(10), – p. 1501-1507. https://doi.org/10.1097/00007890-199705270-00022
8. Sotozono, C. Cytokine expression in the alkali-burned cornea / C.Sotozono, J.He, Y.Matsumoto [et al.] // Curr. Eye Res., – 1997. 16(7), – p. 670-676. https://doi.org/10.1076/ceyr.16.7.670.5057
9. Enriquez-de-Salamanca, A. Tear cytokine and chemokine analysis and clinical correlations in evaporative-type dry eye disease / A.Enriquez-de-Salamanca, E.Castellanos, M.E.Stern [et al.] // Mol. Vis., – 2010. 16, – p. 862-873.
10. Hayashi, T. Aqueous humour cytokine profiles after Descemet's membrane endothelial keratoplasty / T.Hayashi, H.Takahashi, S. Inoda [et al.] // Sci Rep 11, 2021. (17064). https://doi.org/10.1038/s41598-021-96566-3
11. Soong, H.K. Femtosecond laser-assisted posterior lamellar keratoplasty: initial studies of surgical technique in eye bank eyes / H.K.Soong, S.Mian, O.Abbasi [et al.] // Ophthalmology, – 2005. 112(1), – p. 44-49. https://doi.org/10.1016/j.ophtha.2004.06.037
12. Farid, M. Comparison of penetrating keratoplasty performed with a femtosecond laser zig-zag incision versus conventional blade trephination / M.Farid, R.F.Steinert, R.N.Gaster [et al.] // Ophthalmology, – 2009. 116(9), – p. 1638-1643. https://doi.org/10.1016/j.ophtha.2009.05.003
13. Moore, K.W. Interleukin-10 and the interleukin-10 receptor / K.W.Moore, R.de Waal Malefyt, R.L.Coffman [et al.] // Annu. Rev. Immunol., – 2001. 19, – p. 683-765. https://doi.org/10.1146/annurev.immunol.19.1.683
14. Chamberlain, W. Descemet endothelial thickness comparison study: a comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty / W.Chamberlain, C.C.Lin, A.Austin [et al.] // Cornea, – 2011. 30(12), – p. 1382-1386. https://doi.org/10.1097/ICO.0b013e31821ddd25
15. Suwan-apichon, O. Reproducibility and reliability of automatic corneal endothelial cell analysis / O.Suwan-apichon, M.Rizen, R.Rangsin [et al.] // Cornea, – 2006. 25(10), – p. 1159-1163.
16. Buzzonetti, L. Standardized big-bubble technique in deep anterior lamellar keratoplasty assisted by the femtosecond laser / L.Buzzonetti, A.Laborante, G.Petrocelli // J. Refract Surg., – 2010. 26(3), – p. 219-227. https://doi.org/10.1016/j.jcrs.2010.08.013
17. Wilson, S.E. The corneal wound healing response: cytokine-mediated interaction of the epithelium, stroma, and inflammatory cells / S.E.Wilson, R.R.Mohan, R.R.Mohan [et al.] // Prog. Retin. Eye Res., – 2001. 20(5), – p. 625-637. https://doi.org/10.1016/S1350-9462(01)00008-8
18. Saini, J.S. Ocular chemical burns: clinical and demographic profile / J.S.Saini, A.Sharma // Burns, – 1993. 19(1), – p. 67-69. https://doi.org/10.1016/0305-4179(93)90104-G
19. Choi, W. Expression of CCR5 and its ligands CCL3, -4, and -5 in the tear film and ocular surface of patients with dry eye disease / W.Choi, Z.Li, H.J.Oh [et al.] // Curr. Eye Res., – 2012. 37(1), – p. 12-17. https://doi.org/10.3109/02713683.2011.622852
20. Matsuba, S. Difference in chemokine expression between human cornea and skin fibroblasts / S. Matsuba, H.Yabe, M.Nakazawa [et al.] // Exp. Eye Res., – 2011. 93(5), – p. 777-784.