Original Article

Clinical Outcomes of Different Surgical Techniques in Limbal Stem Cell Deficiency

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Abstract

Objectives: This study aimed to evaluate the long-term outcomes of limbal stem cell deficiency (LSCD) treated with various limbal stem cell transplantation (LSCT) techniques.

Materials and Methods: This retrospective study included 32 eyes of 29 patients who underwent LSCT. Clinical evaluation was performed based on preoperative and postoperative best corrected visual acuity (BCVA, logarithm of the minimum angle of resolution [logMAR]), degree of corneal neovascularization, extent of corneal involvement, and clarity of the central visual axis. Human leukocyte antigen (HLA) compatibility in allograft recipients was assessed via HLA tissue typing. The Kruskal-Wallis and Wilcoxon tests were used to compare variables between groups.

Results: A total of 84.4% (n=27) of the eyes had LSCD secondary to chemical injury. Median preoperative and postoperative BCVA (logMAR) values were 2.1 and 1.8 (p=0.01) in the conjunctival limbal allograft (CLAL) group (n=22; 18 living-related, 4 deceased donors), 0.9 and 0.7 (p=0.11) in the conjunctival limbal autograft (CLAU) group (n=4), and 2.1 and 1.3 (p=0.04) in the simple limbal epithelial transplantation (SLET) group (n=6; 3 autografts, 3 allografts), respectively. There was no statistically significant difference in BCVA improvement between groups. Median clinical scores improved from 10 to 6 in the CLAL group (p<0.001), from 7 to 4 in the CLAU group (p=0.11), and from 10 to 3 in the SLET group (p=0.03). Preoperatively, a statistically significant difference in clinical scores was observed only between the CLAU and SLET groups (p=0.029); however, no significant difference was found between groups postoperatively. HLA compatibility was 75% in 15 eyes that received living-related CLAL, and 100% in all 3 eyes that underwent allogeneic SLET.

Conclusion: Different LSCT techniques may be applied in LSCD depending on the underlying etiology and extent of involvement. Favorable outcomes can also be achieved with allogeneic approaches when HLA compatibility is ensured.

Keywords: Limbal stem cell deficiency, limbal stem cell transplantation, simple limbal epithelial transplantation, conjunctival limbal allograft, conjunctival limbal autograft

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Introduction

Limbal stem cells (LSCs) are adult stem cells that differentiate into corneal epithelium, playing a critical role in maintaining the integrity and transparency of the corneal surface.[1] The Vogt palisades within the limbal region are densely populated with LSCs and provide the specialized microenvironment necessary for their survival and function. In addition, LSCs are located within limbal epithelial crypts and pits, contributing to the formation of a functional barrier between the cornea and conjunctiva.[2,3,4]

Direct damage to LSCs and/or disruption of their niche leads to limbal stem cell deficiency (LSCD). The loss of limbal barrier function allows conjunctival epithelial cells to migrate onto the corneal surface, resulting in ocular surface instability. Neovascularization within the corneal epithelium and stroma compromises corneal transparency, potentially causing significant visual impairment or blindness.[5,6] Moreover, LSCD is often associated with a deficiency of goblet cells, which further

contributes to ocular surface deterioration through impaired tear film function.

LSCD can be classified as either primary or secondary. Primary LSCD arises from genetic or congenital conditions such as *PAX6* mutations and aniridia,[7,8] congenital epidermal dysplasia,[9,10] dyskeratosis congenita,[11] and xeroderma pigmentosum.[12] In contrast, secondary LSCD is typically acquired and may result from chemical or thermal injuries,[13] cicatrizing disorders such as mucous membrane pemphigoid,[14] Stevens-Johnson syndrome,[15,16] or graft-versus-host disease.[17] Additional causes include ocular surgeries, radiation, cryotherapy, systemic chemotherapy,[18] and drug-induced toxicity, commonly associated with agents like mitomycin C, 5-fluorouracil, antiglaucoma medications, or sulfur mustard.[19,20] Iatrogenic factors such as ocular surgical interventions and contact lens wear also contribute to the development of secondary LSCD.[21]

The management of LSCD varies according to disease severity, stage, and underlying etiology, and may involve medical, surgical, or combined therapeutic approaches. Medical therapy is the first-line treatment, as optimizing the ocular surface supports residual stem cell function in partial LSCD and enhances graft survival in surgical cases. Surgical intervention focuses on restoring LSCs, typically via autologous or allogeneic limbal stem cell transplantation (LSCT). The choice of LSCT technique (e.g., keratolimbal or conjunctival limbal graft, simple limbal epithelial transplantation [SLET], and cultivated limbal epithelial transplantation [CLET]) depends on the extent of disease and donor availability.

In 1989, Kenyon and Tseng[22] reported the successful transplantation of conjunctival limbal autografts (CLAU) from the healthy contralateral eye in patients with unilateral LSCD. However, the relatively large grafts (typically harvested in two segments spanning 2-3 clock hours) pose a risk of iatrogenic LSCD in the donor eye. As an alternative, excellent long-term clinical outcomes have been reported with the *ex vivo* expansion of LSCs harvested from a small biopsy of the healthy or a donor eye that is cultured on various substrates and subsequently transplanted onto the affected eye.[23,24] Another surgical option is SLET, which uses a 2x2 mm limbal tissue sample divided into 6-10 small fragments and placed on an amniotic membrane-covered cornea with fibrin glue. This approach enables *in vivo* expansion of cells without the need for *ex vivo* laboratory culturing.[25] Due to the minimal tissue requirement, the risk to the donor site is negligible. SLET can be performed using either autologous or allogeneic grafts.

In cases of bilateral total LSCD, allogeneic tissue is required for LSCT. The donor is typically either deceased or a living relative of the patient.[26,27] However, allografts require long-term systemic immunosuppression, and the survival rate of transplanted cells is generally inferior to that of autologous grafts.[28] An alternative approach in such cases is the transplantation of cultivated autologous oral mucosal epithelial cells. While this technique has shown success in stabilizing the ocular surface, the degree of visual improvement achieved is often suboptimal.[29,30]

This study aimed to evaluate the long-term clinical outcomes of LSCD cases managed with various LSCT techniques.

Materials and Methods

This retrospective study evaluated 32 eyes of 29 patients with LSCD of various etiologies who underwent LSCT between January 2010 and January 2023 at the Department of Ophthalmology, Eskisehir Osmangazi University Faculty of Medicine. The study was approved by the Clinical Research Ethics Board of Eskişehir Osmangazi University (number: E-25403353-050.99-2400074876, subject: 2024-102, decision number: 47, decision date: 19.03.2024) and adhered to the ethical principles of the Declaration of Helsinki.

Data collected included patients' demographic characteristics, LSCD etiology and severity, biomicroscopic and fundus examination findings, best corrected visual acuity (BCVA), age at the time of surgery, surgical technique, and any additional procedures. For cases involving allogeneic transplantation, human leukocyte antigen (HLA) typing results were also analyzed. BCVA was recorded in logarithm of the minimum angle of resolution (logMAR) units.

Pre- and postoperative corneal evaluations included assessment of the damaged corneal area, degree of neovascularization, and clarity of the central visual axis using the clinical grading system described by Aravena et al.[31] (Figure 1 and 2A). For area of damage, the cornea was divided into four quadrants perpendicular to the axis with the largest involvement and graded from 1 to 4 based on the extent of involvement. Corneal neovascularization was scored by dividing the cornea into four areas and assigning a grade of 1 to 4 according to the number of areas involved. For central optical axis clarity, a score of 2 was given if the axis was opaque, and 0 if it was clear. The total score was calculated as the clinical severity score. In cases of LSCD secondary to chemical burns, we also applied the Roper-Hall classification for corneal

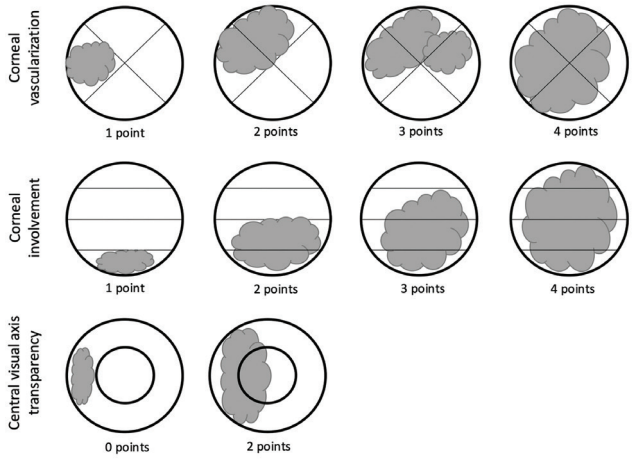

Figure 1. Representative diagram of the clinical grading system used in limbal stem cell deficiency. The diagram illustrates the evaluation criteria for limbal involvement by clock hours (top panel), corneal surface area involvement (middle panel), and central visual axis involvement (bottom panel)[31]

haze and limbal ischemia, as well as the Dua classification, which provides a more detailed assessment based on extent of limbal involvement (in clock hours) and percentage of conjunctival involvement (Figure 2B, C).[32,33] A postoperative improvement of at least 0.2 logMAR units in BCVA was considered a successful outcome. In patients who underwent allogeneic LSCT, HLA matching was evaluated between the recipient and related donors for HLA-A, B, C, DR, and DQ loci.

Three surgical techniques were employed for LSCT: conjunctival limbal allograft (CLAL), CLAU, and SLET. All procedures were performed by the same surgeon (N.Y.).

Conjunctival Limbal Allograft and Autograft Surgery

For donor tissue preparation, conjunctival limbal grafts were harvested from the 12 and 6 o'clock positions, each spanning approximately 2 clock hours, ensuring that the total graft size did not exceed 6 clock hours. The incision began from the conjunctival side and extended 1 mm into the cornea from the limbus to include stem cells. The tissue was dissected and transferred into balanced salt solution (BSS). After harvesting from both areas, the donor sites were partially closed using two 10-0 nylon sutures without excessive tension. In the recipient eye, a 360-degree conjunctival peritomy was performed, and any symblepharon was lysed. Abnormal corneal epithelium and fibrovascular pannus were carefully removed without damaging the underlying stroma. The graft segments were sutured to the area of LSCD using 10-0 nylon sutures.

Simple Limbal Epithelial Transplantation

For autologous or allogeneic SLET, a 2-mm limbal tissue was obtained from the superior limbus. The incision extended from the conjunctiva 1 mm into the cornea to include stem cells. The tissue was then placed in BSS. The recipient site was prepared similarly with a 360-degree peritomy and symblepharon release, if present. Abnormal corneal epithelium and pannus were removed without stromal damage. A human amniotic membrane (basement membrane side facing upward) was placed over the cornea and adjacent bare sclera and secured using fibrin glue. The membrane was gently flattened with a spatula to avoid folds. The limbal tissue was cut into 6-10 small pieces using Vannas scissors and placed in a circular pattern over the mid-peripheral cornea (epithelial side up). The correct orientation of the small graft fragments can be determined by the pigmentation and/or smooth surface of the epithelial side, as well as the presence of whitish fibrous strands on the stromal side. Care was taken to ensure that no tissue fragments were placed over the pupillary area or the limbus. Each tissue fragment was fixed with a drop of fibrin glue, and after polymerization, a large-diameter bandage contact lens was applied.

A threshold of logMAR 2.0 (≈ counting fingers at 1 meter) was defined as the lower limit of functional visual acuity, and keratoplasty was indicated when visual acuity remained worse than this level due to persistent stromal opacity.

Preoperative and Postoperative Management

All patients received topical 0.1% dexamethasone sodium phosphate (Dexa-Sine SE, Liba Laboratories, İstanbul, Türkiye) and/or 0.05% cyclosporine A (Restasis, Allergan, Irvine, CA, USA), together with artificial tears containing polyvinyl alcohol-povidone (Refresh single dose, Allergan, Irvine, CA, USA) and/or sodium hyaluronate (Eyestil, SIFI S.p.A., Catania, Italy) and/or carbomer (Thilo-Tears SE, Alcon/Thilo Pharma, Freiburg, Germany), prior to surgery. In selected cases, vitamin A ointment (VitA-POS, Ursapharm GmbH, Saarbrücken, Germany) was also applied preoperatively. In patients with acquired LSCD, LSCT was performed at least one year after the causative event. Postoperatively, all patients received a standardized topical regimen consisting of an antibiotic, a corticosteroid, and cyclosporine. Preservative-free topical antibiotics (netilmicin [Netira, SIFI S.p.A., Catania, Italy] or moxifloxacin [Vigamox, Alcon Laboratories, Fort Worth, TX, USA]) were administered four times daily for one month. Topical 0.1% dexamethasone sodium phosphate, initiated at a frequency of 6-8 times daily, was progressively tapered and discontinued within 6-12 months. Topical 0.05% cyclosporine A, prescribed at a dosage of 2-4 times daily, was maintained for a minimum duration of one year. In addition, patients undergoing allogeneic transplantation received systemic cyclosporine (Sandimmun Neoral, Novartis Pharma AG, Basel, Switzerland) at a dose of 3-5 mg/kg/day, targeting blood levels of 100-200 ng/mL, which was continued for at least one year.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM, Inc., Armonk, NY, USA). Normality testing with the Shapiro-Wilk and Kolmogorov-Smirnov tests indicated that the variables were not normally distributed. Descriptive statistics for numerical variables were expressed as

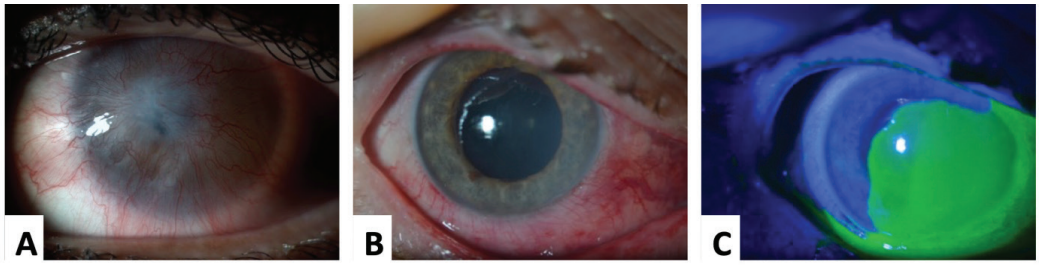

Figure 2. A) An eye that developed limbal stem cell deficiency following chemical injury, with a score of 12 according to the Aravena classification.[31] B, C) An eye in the acute stage of chemical injury, classified as stage III according to the Roper-Hall classification and grade IV according to the Dua classification

median (range). The Kruskal-Wallis test was used to compare numerical variables between groups, and the Wilcoxon test was used for pre- and postoperative comparisons within groups. A p value <0.05 was considered statistically significant.

Results

The median age of patients was 35.5 years (2-62 years), and 75% were male. The majority of eyes (n=27; 84.4%) developed LSCD secondary to chemical injuries. Three eyes had hereditary dyskeratosis, one had long-standing bullous keratopathy, and one had a history of corneal infection. CLAL was performed in 22 eyes, CLAU in 4 eyes, and SLET in 6 eyes (3 autografts and 3 allografts). Overall, 8 of 32 eyes (25%) required keratoplasty for visually significant stromal opacity: 2 eyes underwent simultaneous penetrating keratoplasty (PK) at the time of LSCT, 5 eyes underwent PK at a mean of 4.8 years post-LSCT (range: 4 months to 15 years), and 1 eye received deep anterior lamellar keratoplasty 12 years after CLAL. The median follow-up period was 60 months (12-108 months). Pre- and postoperative images of three eyes that underwent CLAL or SLET are shown in Figure 3.

Among eyes with LSCD secondary to chemical burns, 7 were classified as Stage 3 and 20 as Stage 4 according to the Roper-Hall classification. Based on the Dua classification, 3 eyes were grade IV, 5 were grade V, and 19 were grade VI. In the CLAL group (n=17), Roper-Hall classification identified 5 eyes as stage 3 and 12 as Stage 4, whereas Dua classification identified 1 eye as grade IV, 4 as grade V, and 12 as grade VI. In the CLAU group (n=4), 2 eyes were stage 3 and 2 were stage 4 by Roper-Hall; according to Dua classification, 2 were grade IV, 1 was grade V, and 1 was grade VI. In the SLET group (n=6), all eyes were stage 4 based on Roper-Hall, and all were grade VI based on Dua classification (Table 1).

Preoperative and postoperative median BCVA values were 2.1 (0.52-2.8) and 1.8 (0.22-2.8) logMAR for the CLAL group, 0.9 (0.7-2.8) and 0.7 (0.52-2.3) logMAR for the CLAU group, and 2.1 (1.8-2.3) and 1.3 (0.52-2.3) logMAR for the SLET group, respectively (Figure 4). There was no statistically significant difference in preoperative and postoperative BCVA between the groups. However, a significant improvement in visual acuity was observed within the CLAL group (p=0.01) and the SLET group (p=0.04). Although the CLAU group showed an improvement

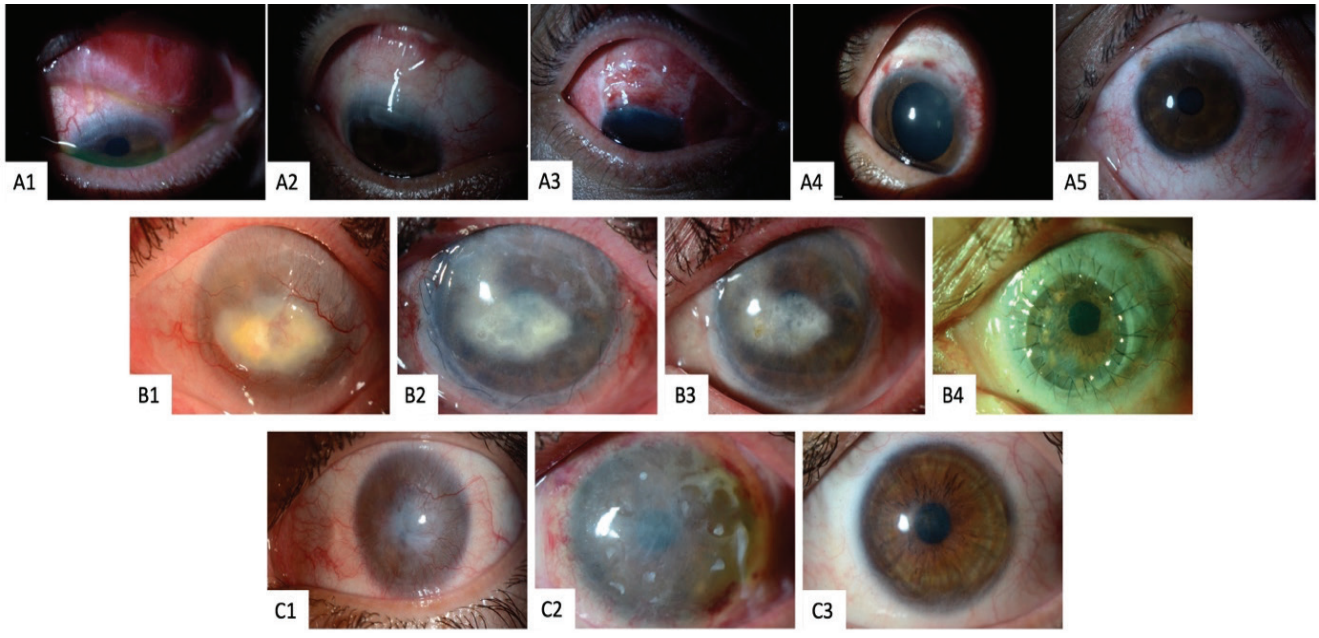

Figure 3. A1-5) A patient with a history of chemical injury and associated symblepharon. Symblepharon release and conjunctival limbal allograft (CLAL) were performed. Clear cornea achieved one year after bilateral living-related CLAL. B1-4) A patient with a history of chemical injury who underwent CLAL. Twelve years later, deep anterior lamellar keratoplasty was performed. C1-3) A patient who underwent simple limbal epithelial transplantation. Postoperatively, corneal haze decreased, neovascularization regressed, and the visual axis was cleared

Table 1. Preoperative severity distribution in patients with limbal stem cell deficiency secondary to chemical injury

Group (eyes)	Roper-Hall classification		Dua classification			Clinical score[31] median (range)
	Stage 3	Stage 4	Grade IV	Grade V	Grade VI	
CLAL (n=17)	5	12	1	4	12	10 (6-10)
CLAU (n=4)	2	2	2	1	1	7 (4-10)
SLET (n=6)	0	6	0	0	6	10 (10-10)

CLAL: Conjunctival limbal allograft, CLAU: Conjunctival limbal autograft, SLET: Simple limbal epithelial transplantation

in visual acuity, the change did not reach statistical significance (p=0.11). The overall success rate, defined as improvement in visual acuity, was 31.3%. By group, success rates were 36.4% for CLAL and 33.3% for SLET, whereas no improvement in visual acuity was observed in the CLAU group (0%).

The median clinical scores improved from 10 (6-10) to 6 (1-10) in the CLAL group, from 7 (4-10) to 4 (3-4) in the CLAU group, and from 10 (10-10) to 3 (1-7) in the SLET group (Figure 5). Although all groups demonstrated postoperative clinical improvement, the change was statistically significant in the CLAL (p<0.001) and SLET (p=0.03) groups, while it did not reach statistical significance in the CLAU group (p=0.11). A statistically significant difference in preoperative clinical scores was observed only between the CLAU and SLET groups (p=0.029), whereas no significant difference was found among the groups postoperatively (p>0.05).

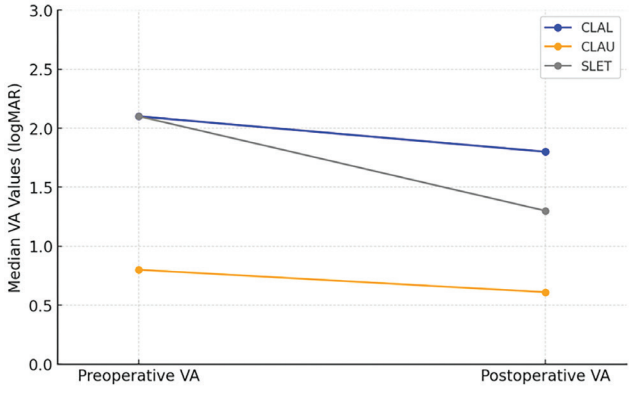

Figure 4. Changes in preoperative and postoperative median visual acuity (VA) in the conjunctival limbal allograft (CLAL), conjunctival limbal autograft (CLAU), and simple limbal epithelial transplantation (SLET) groups
logMAR: Logarithm of the minimum angle of resolution

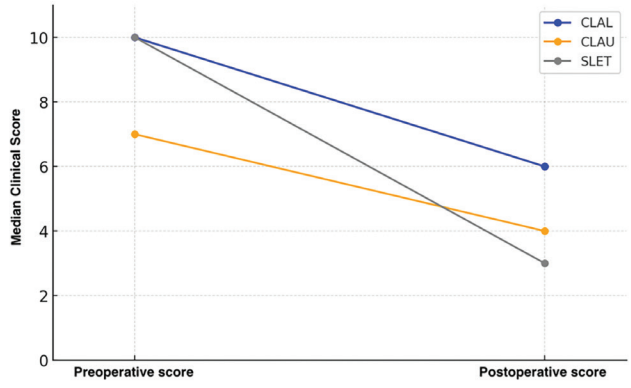

Figure 5. Changes in median preoperative and postoperative clinical scores in the conjunctival limbal allograft (CLAL), conjunctival limbal autograft (CLAU), and simple limbal epithelial transplantation (SLET) groups

Postoperative complications were observed in several cases. LSC graft failure developed in two eyes, which subsequently presented with persistent epithelial defects that were managed with autologous serum therapy. Conjunctivalization occurred in two eyes. Keratitis developed in two eyes: one following autologous serum application and the other presenting as crystalline keratopathy. In addition, glaucoma developed in two eyes, both of which were treated with Ahmed glaucoma valve implantation. None of the donors developed conjunctivalization or iatrogenic LSCD. A localized subconjunctival hemorrhage following biopsy occurred in 22 of 28 living donor eyes (78.6%) and resolved spontaneously in all cases. The wound site exhibited complete healing within one week, with no evidence of refractive changes in the donor.

HLA tissue typing data were available for 15 eyes that underwent CLAL, with a mean compatibility rate of 75% (range: 50%-100%). In contrast, all 3 eyes that underwent allogeneic SLET had 100% HLA compatibility. Figure 6 shows the distribution of compatibility percentages across HLA subgroups. Using the median value of 67% as the cut-off, HLA compatibility above 67% was defined as high (n=7, median 100%, range 71%-100%) and 67% or below as low (n=8, median 62%, range 50%-67%) in the CLAL group. In the high-compatibility group, significant improvement was observed in both visual acuity (1.2 to 0.52, p=0.03) and clinical scores (8 to 5, p=0.04), whereas in the low-compatibility group, improvement was limited to clinical scores only (9.5 to 7, p=0.03), with no significant improvement in visual acuity (2 to 2, p=0.5).

Discussion

The long-term outcomes of CLAL, CLAU, and SLET (both autograft and allograft) surgical techniques were evaluated in patients with LSCD of various etiologies. A significant improvement in both visual acuity and clinical scores was observed in patients who underwent CLAL and SLET.

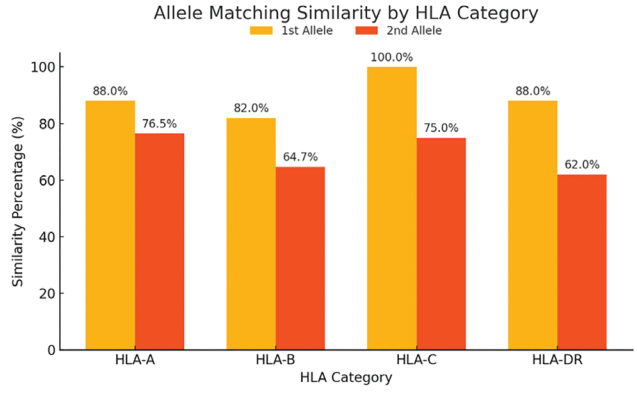

Figure 6. Human leukocyte antigen (HLA) compatibility percentages by HLA subgroups

Although the CLAU group demonstrated a slight postoperative improvement in visual acuity and clinical condition, these changes were not statistically significant. A significant difference in clinical scores was observed only between the CLAU and SLET groups preoperatively, whereas no significant differences were detected among the other groups preoperatively or among all groups postoperatively.

Severe trauma or inflammation of the limbus may result in LSCD, clinically characterized by progressive corneal neovascularization, conjunctivalization, and scarring of the corneal surface, ultimately leading to epithelial dysfunction and corneal blindness.[34] In such cases, treatment is directed toward promoting regeneration of the corneal epithelium and restoring corneal transparency. Early-stage LSCD secondary to limbal niche dysfunction may be managed medically without the need for surgical intervention.[35] However, LSCT is the mainstay of treatment in advanced LSCD.

The CLAU technique, first introduced in 1989, requires a healthy fellow eye. Using an autograft eliminates the risk of graft rejection and the need for systemic immunosuppression but also introduces the risk of iatrogenic LSCD in the donor eye.[36] The CLAL technique, while requiring larger graft tissue and systemic immunosuppressive therapy, remains one of the most commonly preferred approaches in the management of bilateral LSCD. Tran et al.[37] reported significant improvement in visual acuity by postoperative month 12 compared with baseline, particularly in traumatic and toxic cases undergoing allogeneic LSCT. However, their study did not address HLA matching. HLA matching between donor and recipient in CLAL procedures has been shown to improve surgical success rates.[38] In this study, the significant clinical improvement observed in the CLAL group may be attributable to the high degree of HLA compatibility (mean match rate of 75%). In the CLAL group, higher HLA compatibility (above 67%) was associated with significant improvements in both visual acuity and clinical scores, whereas lower compatibility (≤67%) led to improvement only in clinical scores, without a corresponding gain in visual acuity. These findings suggest that the degree of HLA compatibility may play a critical role in determining functional outcomes after allogeneic LSCT, particularly with regard to visual recovery.

In 1997, Pellegrini et al.[23] introduced the CLET technique, which involves *ex vivo* expansion of limbal tissue from a healthy eye to generate a transplantable epithelial sheet. Although clinically effective in restoring the ocular surface, CLET is associated with high costs and necessitates access to a clinical-grade laboratory. In 2012, Sangwan et al.[25] introduced the SLET technique, which combines the advantages of both CLAU and CLET while avoiding many of their limitations. SLET requires minimal donor tissue (under 1 clock hour), obviates the need for cell culture, and does not necessitate systemic immunosuppression. These advantages have contributed to its widespread adoption in the management of LSCD. Additionally, SLET incorporates amniotic membrane transplantation, which supports stem cell proliferation via its growth factors.[39] In this study, amniotic membrane transplantation was performed in all SLET patients.

Although SLET is widely employed as a single-stage treatment for unilateral LSCD, successful outcomes have also been reported in bilateral cases using allogeneic grafts.[40,41] However, systemic immunosuppression is necessary to maintain graft viability. In this cohort, three of six eyes treated with SLET had bilateral LSCD and consequently received allogeneic grafts. To minimize the risk of graft rejection, donor-recipient HLA compatibility was assessed preoperatively, and only donors with 100% HLA match were selected. SLET is known to have a relatively short learning curve and is easily reproducible.[42] However, it may be insufficient as a standalone procedure in cases of severe symblepharon, in which additional conjunctival grafting is often required. While Arora et al.[43] reported no significant difference in symblepharon scores between SLET and CLAU at six months, other studies have identified preoperative symblepharon as a risk factor for SLET failure.[42,44]

A review comparing different LSCT techniques reported comparable anatomical success rates among SLET, CLET, CLAL, and keratolimbal allograft (KLAL) procedures, whereas another review evaluating three different techniques suggested that postoperative clinical outcomes were superior in SLET and CLAU compared to CLET.[45,46] Although KLAL and CLET were not performed in this study, the clinical outcomes of three different surgical approaches were evaluated. Postoperative clinical scores were comparable across the three groups. Significant improvements in visual acuity and clinical scores were observed in eyes treated with CLAL and SLET, whereas the CLAU group showed only mild improvements that did not reach statistical significance. This may be attributed to the smaller sample size in the CLAU group and the relatively better baseline condition of eyes in this group. The median preoperative clinical score was 7 in the CLAU group, compared with 10 in the CLAL group and 10 in the SLET group.

In a study investigating the treatment of chemical burns, the most common cause of LSCD, patients with low-grade injuries benefited significantly from medical therapy, amniotic membrane transplantation, limbal grafting, and subsequent keratoplasty, whereas those with severe injuries were more prone to failure despite all available treatment modalities.[47] For advanced LSCD, surgical restoration of LSCs is required, and the choice of LSCT technique is of critical importance, depending on factors such as disease laterality, availability of donor tissue, and the need for systemic immunosuppression. In cases of unilateral LSCD, the most effective treatment method is SLET, which can also be applied in bilateral cases using grafts from HLA-compatible first-degree relatives. SLET is advantageous due to its minimal tissue requirements and the absence of the need for immunosuppression in autologous cases. In unilateral cases, CLAU can also be performed without the need for immunosuppression, although it carries the risk of iatrogenic LSCD in the donor eye. However, CLAL grafts are more easily obtainable, either from living or deceased donors. Nevertheless,

both necessitate lifelong systemic immunosuppression, and harvesting from a living donor also carries the risk of iatrogenic LSCD. CLET provides an alternative by expanding a small limbal biopsy *ex vivo* to generate an epithelial sheet, thereby reducing donor-site morbidity. However, it requires specialized laboratory facilities, is costly, and outcomes may vary due to differences in culture methods and potential loss of limbal niche cells.

Complications associated with various LSCT procedures share common features such as conjunctivalization and persistent epithelial defects, but also differ in certain aspects, particularly with respect to the adverse effects of systemic immunosuppression in allografts.[48] Due to the large graft size required, CLAU carries the risk of iatrogenic LSCD in the donor eye, which has been clinically documented.[49] Attempts to reduce graft size have been made to minimize this risk, but these smaller grafts have been associated with lower success rates and higher complication rates.[50] Delayed epithelial healing and persistent epithelial defects are among the most common complications after CLAU, often necessitating management such as amniotic membrane transplantation; in severe cases, corneal melting and perforation may still occur.[36,51] Donor site safety remains a concern, as long-term follow-up has revealed corneal ectasia and vascularization in some cases following CLAU.[52] In bilateral ocular surface damage, limbal allograft transplantation is indicated, but carries an inevitable risk of immunological failure and graft rejection.[53] Postoperative glaucoma has been reported in 26-32% of cases, and bacterial keratitis rates range between 8% and 14%.[54,55] By contrast, donor site complications after SLET appear to be minimal. Subconjunctival hemorrhage is relatively frequent but resolves spontaneously. The most prevalent complication in recipients is focal recurrence of pannus, which can be observed without intervention if stable, or effectively managed with repeat SLET, with or without conjunctival autografting.[44,56] Other reported issues include progressive conjunctivalization, symblepharon, and graft loss or detachment, which may contribute to recurrence and failure.[57,58] Rare complications such as epithelial hyperplasia, recurrent corneal neovascularization, and persistent epithelial defects have also been described.[58,59] In this cohort, postoperative complications included persistent epithelial defects, conjunctivalization, keratitis, and glaucoma requiring Ahmed valve implantation. Donor eyes remained largely safe, with no cases of conjunctivalization or iatrogenic LSCD. Localized subconjunctival hemorrhage occurred in 78.6% and resolved spontaneously, and all wounds healed within one week without refractive changes.

Study Limitations

One of the main limitations of this study is the small sample size and the unequal distribution of patients among the LSCT groups. Additional sources of heterogeneity include differences in mean age across groups, varying etiologies of LSCD, and discrepancies in preoperative clinical scores. These factors may limit both the generalizability and the objectivity of comparisons between surgical techniques. In particular, differences in LSCD severity prior to surgery may hinder accurate assessment of the relative efficacy of each technique. Postoperative clinical scores were similar between the CLAU and SLET groups. However, the lower preoperative scores and the smaller number of patients in the CLAU group may explain why a significant improvement was observed in the SLET group but not in the CLAU group. Nonetheless, application of the CLAU technique in a larger number of patients with more severe preoperative disease may still yield meaningful clinical benefits comparable to other techniques. Postoperative outcomes of LSCT may also vary depending on the underlying etiology and stage of LSCD, particularly in terms of inflammation and epithelialization rates.[60] Thus, comparisons between surgical techniques are likely to be more reliable and objective in cases with similar etiologies and baseline clinical scores. Another important limitation of this study is that some patients underwent keratoplasty either concurrently with or following LSCT. In such cases, the contribution of keratoplasty to clinical improvement cannot be excluded, potentially confounding the interpretation of outcomes attributed solely to LSCT.

Conclusion

Different LSCT techniques may be applied in the management of LSCD depending on the underlying etiology and whether the condition is unilateral or bilateral. Favorable outcomes have also been reported with allogeneic techniques, particularly when HLA compatibility is achieved. Among the available methods, the SLET technique appears to offer certain advantages over others due to its minimal tissue requirement, technical simplicity, and reproducibility.

Ethics

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Board of Eskişehir Osmangazi University (number: E-25403353-050.99-2400074876, subject: 2024-102, decision number: 47, decision date: 19.03.2024) and adhered to the ethical principles of the Declaration of Helsinki.

Informed Consent: Since it was a retrospective study, informed consent was not obtained.

Declarations

Authorship Contributions

Surgical and Medical Practices: N.Y., Concept: N.Y., S.M.İ., O.Ö., Design: N.Y., S.M.İ., O.Ö., Data Collection or Processing: N.Y., S.M.İ., O.Ö., Analysis or Interpretation: N.Y., S.M.İ., O.Ö., Literature Search: N.Y., S.M.İ., O.Ö., Writing: N.Y., S.M.İ., O.Ö.

Conflict of Interest: Nilgün Yıldırım, MD, is an Associate Editor of the Turkish Journal of Ophthalmology. She was not involved in the peer review of this article and had no access to information regarding its peer review. The other author has no disclosures.

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