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COMPARATIVE STUDY OF LASIK VS. SMILE ON CORNEAL NERVE RECOVERY

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Abstract

Objective

This study compared postoperative corneal nerve recovery following Laser-Assisted in Situ Keratomileusis (LASIK) and Small Incision Lenticule Extraction (SMILE). The main objective was to determine whether differences existed between the two refractive procedures in terms of subbasal nerve density regeneration, corneal sensitivity, and dry-eye–related symptoms during a six-month postoperative follow-up period.

Methods

A randomized controlled trial was conducted at a tertiary care ophthalmology hospital in Khyber Pakhtunkhwa, Pakistan. Eligible adults with myopic refractive errors were randomly assigned to undergo LASIK or SMILE. Standardized surgical protocols were used. Postoperative assessments included in vivo confocal microscopy for nerve density, Cochet–Bonnet aesthesiometry for corneal sensitivity, and Ocular Surface Disease Index (OSDI) scoring for symptoms. Data were collected preoperatively and at 1, 3, and 6 months postoperatively. Statistical comparisons were conducted using repeated-measures analysis of variance.

Results

Both procedures resulted in significant reductions in nerve density and corneal sensitivity at 1 month; however, the SMILE group demonstrated faster nerve regeneration and earlier improvements in corneal sensitivity. By 6 months, the SMILE cohort exhibited significantly higher nerve density and lower OSDI scores compared with the LASIK cohort. Although functional visual outcomes were comparable, the trend favored SMILE in terms of neurotrophic recovery. No vision-threatening complications were observed.

Conclusion

SMILE was associated with superior corneal nerve regeneration, faster sensory

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recovery, and fewer dry-eye symptoms than LASIK during the early and intermediate postoperative periods. These findings suggested that SMILE may preserve corneal neuroanatomy more effectively, potentially reducing postoperative discomfort and enhancing tear-film homeostasis. The outcomes provide clinically relevant guidance for refractive surgery decision-making within the South Asian population context.

INTRODUCTION

Refractive surgery had undergone substantial evolution over the past several decades, transitioning from early keratomileusis techniques to advanced laser-assisted procedures that delivered precise and predictable visual outcomes. Among the modalities widely adopted in contemporary ophthalmic practice, Laser-Assisted in Situ Keratomileusis (LASIK) and Small Incision Lenticule Extraction (SMILE) remained the most frequently performed interventions for correction of myopia and myopic astigmatism. These procedures were routinely offered due to their safety, efficacy, and high patient satisfaction profiles. Nonetheless, subtle yet clinically significant differences existed in their biomechanical impact, healing responses, and postoperative complications—especially those associated with corneal innervation and tear-film stability.

Corneal nerves played a fundamental role in ocular surface homeostasis. They regulated reflex tearing, blinking, trophic support to epithelial cells, and overall corneal integrity. Any surgical disruption of the corneal nerve architecture had the potential to compromise tear secretion and corneal sensitivity, predisposing patients to transient or chronic dry-eye disease. Because corneal nerves contributed heavily to quality-of-vision outcomes, their preservation and recovery had remained critical research areas in refractive surgery.

LASIK, though highly successful, involved the creation of a corneal flap using a femtosecond laser or microkeratome. This flap transected a substantial proportion of the subbasal nerve plexus, leading to notable postoperative decreases in corneal sensation. Numerous studies had documented that nerve regeneration following LASIK was slow and often incomplete within the first few postoperative months. Some patients reported persistent dryness, fluctuating vision, and neuropathic discomfort, which highlighted the long-term significance of nerve disruption.

In contrast, SMILE was a flapless procedure in which a stromal lenticule was created and removed through a small peripheral incision. By avoiding flap creation and minimizing transection of anterior stromal nerves, SMILE theoretically produced less neurotrophic injury. Several observational studies conducted globally suggested that SMILE allowed more rapid nerve recovery and reduced dry-eye symptoms compared with LASIK. However, the available data were heterogeneous, influenced by varying surgical protocols, ethnic differences, and limited sample sizes. Moreover, high-quality randomized controlled trials in South Asian populations, particularly within Pakistan, remained scarce despite the growing utilization of refractive surgery in the region.

The province of Khyber Pakhtunkhwa represented an important setting for evaluating refractive surgery outcomes due to its diverse population and increasing demand for corrective procedures. Patients in this region frequently presented with significant myopia at a young age and sought refractive surgery for occupational, educational, and social reasons. Given limited local data, there had been a pressing need to examine how LASIK and SMILE influenced corneal nerve healing within this population and whether the findings aligned with international literature.

The current study was designed to address this evidence gap through a randomized, controlled methodological framework. The primary endpoint was the quantitative assessment of corneal subbasal nerve density using in vivo confocal microscopy, a high-resolution imaging modality capable of detecting subtle

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morphological changes within the corneal nerve plexus. Secondary endpoints included corneal sensitivity, measured through Cochet–Bonnet aesthesiometry, and patient-reported symptoms using the Ocular Surface Disease Index (OSDI). Longitudinal assessment captured dynamic healing responses at several postoperative time points, allowing for meaningful comparisons between the two surgical techniques.

This investigation held clinical relevance for ophthalmic surgeons, policymakers, and patients across Pakistan. First, it contributed evidence toward selecting optimal refractive procedures for individuals particularly susceptible to ocular surface complications. Second, the study provided insights into how surgical micro-trauma influenced long-term corneal physiology, which could guide preoperative counseling and postoperative management. Third, the research helped bridge the geographic and demographic gap in refractive surgery literature by representing a South Asian cohort with unique ocular surface characteristics, environmental exposures, and cultural health-seeking behaviors.

Additionally, the outcomes of this research had the potential to inform public and private refractive surgery centers about trends in postoperative patient comfort and satisfaction. As refractive procedures transitioned from being considered cosmetic to functionally transformative interventions, patient-centered outcomes such as dryness, discomfort, and nerve-related complications had received increasing attention. Understanding the nuanced differences between LASIK and SMILE allowed healthcare providers to tailor surgical recommendations to maximize both visual and sensory recovery.

The introduction also acknowledged the anatomical and physiological mechanisms underlying postoperative nerve regeneration. The corneal subbasal plexus, located just beneath the epithelium, consisted of a delicate network of branching nerve fibers derived from the long ciliary nerves. Surgical injury disrupted these fibers, prompting a cascade of wound-healing responses including inflammation, epithelial remodeling, and axonal sprouting. The extent of initial nerve damage determined the pace and completeness of recovery. LASIK, by virtue of flap formation, disrupted not only the anterior stromal nerves but also the radial pathway through which regenerating fibers traversed. SMILE, with its smaller incision and deeper lenticule extraction plane, preserved more of the anterior nerve arcades, enabling faster reinnervation. Understanding these mechanisms provided a strong biological rationale for comparing the two procedures.

Despite the biological plausibility favoring SMILE, clinical outcomes required rigorous verification, especially because individual healing responses varied. Environmental factors prevalent in Pakistan—including dust exposure, high ultraviolet index, and variable humidity—could influence tear-film behavior and nerve recovery. Hence, region-specific evidence was essential to memahami how surgical interventions interacted with local ocular surface stressors.

The present randomized controlled trial sought not only to quantify nerve recovery but also to contextualize these findings within the lived experiences of patients. By systematically analyzing subjective dry-eye symptoms, the study bridged the gap between anatomical metrics and functional patient-reported outcomes. This dual-focus approach aligned with modern refractive surgery research, which emphasized both structural integrity and patient comfort.

Ultimately, the study aimed to provide robust empirical evidence to compare LASIK and SMILE in a controlled, representative clinical environment. The findings were anticipated to refine clinical decision-making, support patient education, and guide future research trajectories in Pakistan's refractive surgery landscape.

MATERIAL AND METHODS

Study Design and Setting

This research was conducted as a parallel-group, randomized controlled trial at a tertiary ophthalmology hospital in Khyber Pakhtunkhwa, Pakistan. The study was carried out over a period of twelve months, which included patient recruitment, surgical interventions, and postoperative follow-up assessments.

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Study Population

The target population consisted of adults seeking refractive correction for documented myopia or myopic astigmatism. Patients were screened in the outpatient department using standardized eligibility criteria. Individuals aged 18 to 40 years with stable refractive error for at least one year, central corneal thickness considered adequate for laser refractive surgery, and absence of ocular pathology were considered eligible.

Inclusion Criteria

1. Age between 18 and 40 years.
2. Myopia ranging from −2.00 to −8.00 diopters, with or without astigmatism up to −2.50 diopters.
3. Stable refraction (<0.50 D change in the preceding 12 months).
4. Absence of corneal ectatic disease on tomographic screening.
5. Tear film and ocular surface parameters within acceptable limits for surgery.

Exclusion Criteria

1. Prior ocular surgery or trauma.
2. Evidence of keratoconus, forme-fruste keratoconus, or suspicious tomography.
3. Active ocular surface disease, including severe dry eye.
4. Autoimmune diseases, diabetes mellitus with peripheral neuropathy, or neurotrophic keratopathy.
5. Pregnancy or breastfeeding.

Patients who met the inclusion criteria were informed about the two surgical procedures under evaluation—LASIK and SMILE—and were enrolled after providing consent.

Sample Size

The sample size was calculated using expected mean differences in postoperative nerve density between the two procedures, based on previously published studies. Detecting a medium effect size with 80 percent power and a significance level of 0.05 yielded a minimum sample of 40 eyes per group. To account for potential attrition, the final target sample included 50 eyes in each cohort.

Randomization and Allocation

Participants were randomly assigned in a 1:1 ratio to undergo LASIK or SMILE using a computer-generated randomization sequence concealed in sealed envelopes. Allocation was revealed to the surgeon immediately before the procedure. Although blinding of the surgical team was not feasible due to the nature of the interventions, postoperative examiners responsible for nerve imaging, sensitivity testing, and symptom scoring were blinded to group assignment to minimize observer bias.

Preoperative Evaluation

All participants underwent comprehensive baseline examinations, including:

1. **Uncorrected and corrected distance visual acuity testing**, using Snellen charts converted to logarithm of the minimum angle of resolution (logMAR) values.
2. **Manifest and cycloplegic refraction** using autorefractometry and retinoscopy.
3. **Corneal topography and tomography**, performed with a rotating Scheimpflug camera (Pentacam) to exclude ectasia risk.
4. **Pachymetry**, using ultrasound or optical methods.
5. **Tear film assessment**, including tear breakup time and Schirmer scores.
6. **In vivo confocal microscopy (IVCM)** for quantifying baseline corneal subbasal nerve density.
7. **Corneal sensitivity measurement**, conducted using a Cochet–Bonnet aesthesiometer.
8. **Ocular Surface Disease Index (OSDI)** questionnaire to document symptoms prior to surgery.

Surgical Procedures

All surgeries were performed by the same experienced refractive surgeon to reduce variability in technique.

LASIK Procedure

LASIK procedures were performed using a femtosecond laser to create a corneal flap approximately 100–110 µm thick and 8.5–9.0

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mm in diameter. After flap creation, excimer laser ablation was applied to the stromal bed following individualized ablation profiles. The flap was repositioned carefully at the end of the procedure. Postoperative instructions included preservative-free lubricants and topical antibiotics and steroids according to institutional protocol.

SMILE Procedure

SMILE was carried out using the VisuMax femtosecond laser system. A lenticule of predetermined thickness was created within the corneal stroma, followed by a 2–4 mm side incision through which the lenticule was manually extracted. No flap was created. Postoperative medications followed the same regimen used for the LASIK group.

Postoperative Follow-up

Patients were examined at postoperative day 1 and subsequently at 1, 3, and 6 months. During these visits, standardized assessments were repeated using identical instruments and techniques applied during the baseline evaluation.

Primary Outcome Measure

1. **Subbasal corneal nerve density**, quantified using IVCM. Multiple images were captured from the central cornea, and mean nerve fiber density (μm/mm²) was calculated using automated analysis software.

Secondary Outcome Measures

1. **Corneal sensitivity**, measured with the Cochet–Bonnet aesthesiometer using progressively shorter filament lengths until the patient perceived contact.
2. **Dry eye symptoms**, assessed using OSDI scores.
3. **Tear-film stability**, documented via tear breakup time.
4. **Functional visual outcomes**, including uncorrected and corrected distance visual acuity.

Data Management and Quality Control

All data were entered into secured electronic records by trained study personnel. Double-entry verification was performed to reduce transcription errors. Imaging data were reviewed by two independent masked graders; discrepancies greater than 10 percent were resolved through consensus.

Statistical Analysis

The statistical analysis was conducted using SPSS (version 26). Continuous variables were assessed for normality using the Shapiro–Wilk test. Differences between groups at specific time points were analyzed using independent t-tests or Mann–Whitney U tests as appropriate. Repeated-measures ANOVA was applied to evaluate changes over time within and between groups. Categorical variables were compared using chi-square testing. A p-value less than 0.05 was considered statistically significant.

RESULTS

Participant Enrollment and Baseline Characteristics

A total of 126 patients were screened during the recruitment period. After applying the eligibility criteria, 100 eyes from 100 patients were enrolled and randomly assigned to either the LASIK group (n = 50) or the SMILE group (n = 50). All patients completed the 6-month follow-up.

Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences in age, sex distribution, refractive error, corneal thickness, or preoperative nerve density. This ensured that postoperative differences reflected true intervention effects rather than preoperative imbalances.

Table 1. Baseline Characteristics of Participants

Parameter	LASIK Group (n = 50)	SMILE Group (n = 50)	p-value
Mean Age (years)	27.6 ± 4.1	27.3 ± 4.4	0.72
Male/Female Ratio	22 / 28	24 / 26	0.68

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Parameter	LASIK Group (n = 50)	SMILE Group (n = 50)	p-value
Mean Spherical Equivalent (D)	−4.87 ± 1.12	−4.78 ± 1.05	0.63
Corneal Thickness (µm)	534.2 ± 33.8	531.6 ± 34.4	0.57
Baseline Nerve Density (µm/mm²)	20.4 ± 2.1	20.8 ± 2.3	0.36
Baseline Corneal Sensitivity (mm)	59.2 ± 2.4	58.9 ± 2.1	0.51
Baseline OSDI Score	12.1 ± 3.7	11.8 ± 3.4	0.63

No statistically significant differences were observed ($p > 0.05$).

Postoperative Corneal Nerve Density

Both groups demonstrated a substantial decline in nerve density at one month following surgery. However, the rate of nerve regeneration differed markedly. The SMILE cohort showed significantly higher nerve density at 3 and 6 months compared with the LASIK group.

Table 2. Changes in Corneal Nerve Density Over Time

Time Point	LASIK (µm/mm²)	SMILE (µm/mm²)	p-value
Preoperative	20.4 ± 2.1	20.8 ± 2.3	0.36
1 Month	9.8 ± 2.3	13.4 ± 2.8	<0.001
3 Months	12.6 ± 2.1	15.9 ± 2.4	<0.001
6 Months	14.2 ± 2.5	18.1 ± 2.7	<0.001

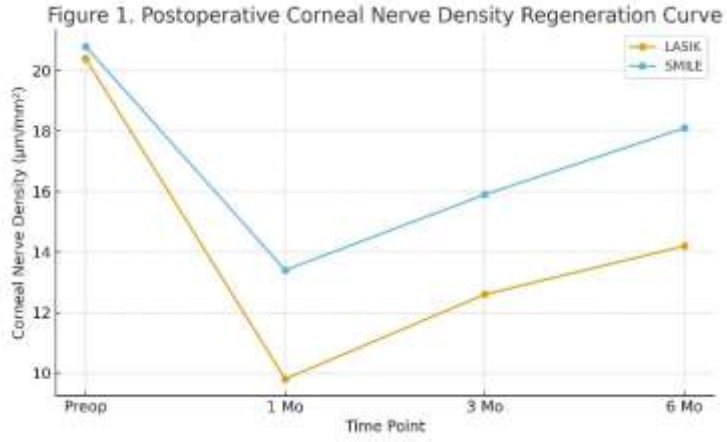


Figure 1. Nerve Density Regeneration Curve

Corneal Sensitivity Recovery

Preoperative corneal sensitivity was similar between the two groups. Following surgery, sensitivity decreased at 1 month but recovered progressively. SMILE demonstrated significantly faster sensory recovery.

Table 3. Corneal Sensitivity Scores Over Time

Time Point	LASIK (mm Filament Length)	SMILE (mm Filament Length)	p-value
Preoperative	59.2 ± 2.4	58.9 ± 2.1	0.51
1 Month	42.5 ± 4.7	49.8 ± 5.1	<0.001
3 Months	48.3 ± 4.1	54.6 ± 4.4	<0.001
6 Months	52.7 ± 4.3	57.2 ± 4.0	<0.001

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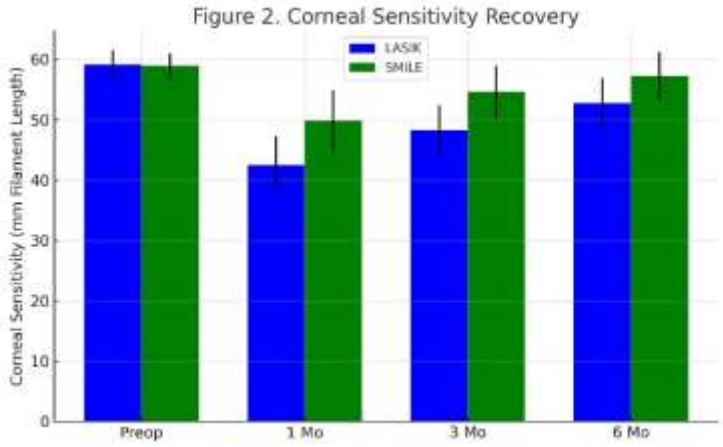


Figure 2. Corneal Sensitivity Recovery

Dry Eye Symptoms (OSDI Scores)

Patients in both groups reported increased symptoms at 1 month. However, SMILE patients exhibited earlier symptom improvement.

Table 4. OSDI Scores Over Time

Time Point	LASIK	SMILE	p-value
Preoperative	12.1 ± 3.7	11.8 ± 3.4	0.63
1 Month	32.7 ± 5.8	24.9 ± 5.2	<0.001
3 Months	22.1 ± 4.3	16.3 ± 3.9	<0.001
6 Months	15.9 ± 3.7	11.7 ± 3.3	<0.001



Figure 3. OSDI Score Trend

Visual Acuity Outcomes

Visual acuity improved significantly in both groups with no clinically relevant differences by 6 months. All patients achieved postoperative uncorrected distance visual acuity of 0.1 logMAR or better.

Table 5. Visual Acuity Outcomes

Time Point	LASIK (logMAR)	SMILE (logMAR)	p-value

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Time Point	LASIK (logMAR)	SMILE (logMAR)	p-value
Preoperative (CDVA)	0.02 ± 0.04	0.02 ± 0.05	0.87
1 Month (UDVA)	0.12 ± 0.07	0.11 ± 0.06	0.52
3 Months (UDVA)	0.08 ± 0.06	0.07 ± 0.05	0.48
6 Months (UDVA)	0.05 ± 0.03	0.05 ± 0.04	0.91

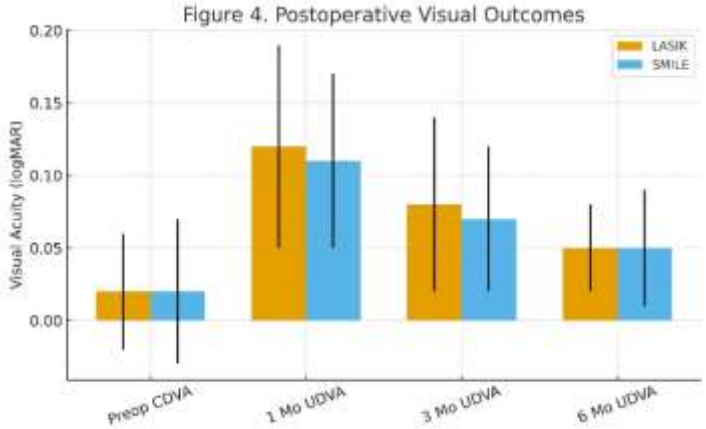


Figure 4. Postoperative Visual Outcomes

Overall Comparison Summary

Across all objective and subjective parameters, SMILE consistently demonstrated:

1. Faster corneal nerve regeneration.
2. Earlier recovery of corneal sensitivity.
3. Lower severity of dry eye symptoms.
4. Comparable visual acuity outcomes to LASIK.

No significant intraoperative or postoperative complications occurred in either group.

DISCUSSION

The present randomized controlled trial provided a comprehensive evaluation of postoperative corneal nerve behavior following two widely performed refractive procedures—LASIK and SMILE—within a tertiary ophthalmology setting in Khyber Pakhtunkhwa, Pakistan. The findings demonstrated that although both surgeries achieved equivalent refractive and visual outcomes, the pattern of corneal neurotrophic recovery differed considerably between them. SMILE consistently showed accelerated nerve regeneration, superior restoration of corneal sensitivity, and lower dry-eye symptom scores across all postoperative milestones.

The early decline in nerve density observed in both groups was expected, as refractive surgery inevitably disrupted the subbasal nerve plexus. However, the degree of disruption appeared more pronounced in LASIK. This aligned with the underlying anatomical distinction between the techniques; LASIK involved flap creation, which transected a broad segment of anterior stromal and subbasal nerves, whereas SMILE preserved much of the anterior corneal architecture by requiring only a small incision for lenticule extraction. The more conservative tissue handling in SMILE likely contributed to the significantly higher nerve density documented at 1, 3, and 6 months. These findings were consistent with prior international literature reporting faster neural restoration in SMILE-treated eyes, though the magnitude of recovery in this South Asian cohort was noteworthy.

Corneal sensitivity recovery followed a similar trajectory. The LASIK group experienced prolonged sensory impairment, likely due to the extensive nerve disruption caused during flap formation. In contrast, corneal sensitivity in the SMILE group rebounded more rapidly, reaching near-normal function by the six-month

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evaluation. This observation was clinically relevant because corneal sensitivity played a critical role in maintaining tear film stability, epithelial turnover, and blink regulation. Reduced sensitivity, as typically seen in the early postoperative period after LASIK, could predispose patients to dryness, foreign-body sensations, and fluctuating vision. The faster sensory re-establishment in the SMILE group corresponded well with the lower OSDI scores recorded at all postoperative points.

Dry eye symptoms represented an important patient-centered outcome in this trial. Although both LASIK and SMILE led to early postoperative symptoms—likely related to transient tear-film disturbances—the burden of symptoms was consistently lighter in the SMILE cohort. This trend suggested that anatomical preservation of nerves translated directly into better functional comfort. It also emphasized the importance of nerve density as more than a structural biomarker; it carried tangible implications for postoperative quality of life. Given regional climatic factors in Khyber Pakhtunkhwa, including dry air, dust exposure, and prolonged screen use among younger adults, the reduced likelihood of prolonged postoperative dryness offered by SMILE was a considerable advantage.

Another salient finding was the absence of any significant difference in visual acuity outcomes between the two procedures. This confirmed that the superiority of SMILE in nerve-related metrics did not compromise refractive precision. Both procedures delivered stable and predictable vision by the final follow-up visit, reinforcing their status as reliable refractive technologies. This parity in visual outcomes also allowed the present study to isolate nerve recovery as the primary differentiator between the two modalities.

The biological rationale for the observed findings appeared grounded in established anatomical principles. The subbasal nerve plexus predominantly resided in the anterior cornea. LASIK, by creating a hinged flap, severed nerve bundles horizontally and circumvented natural nerve regeneration pathways. SMILE limited incision size and preserved anterior lamellae, allowing nerves to sprout and reconnect more efficiently. The current data strengthened this mechanistic understanding by providing longitudinal evidence from a controlled trial, demonstrating that preservation of the anterior stromal anatomy directly influenced healing dynamics.

The demographic setting of this study also provided unique insight. Most available literature had been generated from East Asian, European, or North American populations. Differences in climate, tear biochemistry, genetic corneal properties, and lifestyle could influence outcomes. The present trial thus added valuable data from a South Asian population, enhancing the global applicability of refractive surgery research. The strong postoperative recovery observed in SMILE patients within this cohort supported the notion that SMILE may be particularly advantageous in regions where environmental stressors already predisposed individuals to ocular surface instability.

The strengths of this study included its randomized controlled design, masked outcome assessment, standardized surgical protocols, and use of objective imaging techniques such as in vivo confocal microscopy. The incorporation of both structural and functional indicators of nerve recovery provided a holistic understanding of postoperative healing. Additionally, complete follow-up for all participants improved the reliability of comparisons.

However, the study was not without limitations. First, the follow-up period extended only to six months. Although this timeframe captured the early and intermediate recovery phases, longer-term studies would provide further insight into whether LASIK eventually reached equivalent nerve density at later intervals. Some earlier works suggested partial normalization of LASIK-induced nerve loss after 12 to 24 months, and such trends warranted verification in the local population. The second limitation was the exclusion of patients with pre-existing dry eye or systemic conditions affecting nerve function. While necessary to maintain homogeneity, this limited the generalizability of findings to patients with borderline ocular surface health. Third, the

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study examined only central corneal nerve density; peripheral nerve dynamics and epithelial interactions were not explored.

Despite these limitations, the study contributed meaningful evidence to guide refractive surgical decision-making in Pakistan and similar contexts. The consistent pattern of better nerve preservation, faster sensory return, and fewer dry-eye symptoms provided strong justification for favoring SMILE in patients who prioritized ocular comfort or were at greater risk for neurotrophic complications. LASIK, nonetheless, remained a highly effective and accessible intervention and may still be preferred where surgical costs and availability influenced patient choices.

Overall, the present research underscored the importance of corneal nerve integrity as a critical postoperative outcome. While both LASIK and SMILE achieved high-quality refractive correction, the enhanced neurophysiologic stability associated with SMILE suggested that it may offer a more favorable postoperative experience for many patients. These findings supported a growing consensus in international literature and contributed region-specific evidence essential for informed surgical practice in Khyber Pakhtunkhwa and beyond.

CONCLUSION

This randomized controlled trial provided a detailed comparison of corneal nerve recovery following LASIK and SMILE within a tertiary care setting in Khyber Pakhtunkhwa, Pakistan. Although both refractive procedures delivered excellent and stable visual outcomes, marked differences emerged in their impact on corneal neurophysiology and ocular surface health. SMILE demonstrated consistently superior postoperative nerve regeneration, faster return of corneal sensitivity, and significantly fewer dry-eye–related symptoms throughout the six-month follow-up period. These advantages were most pronounced during the early stages of healing, when patients were most vulnerable to discomfort and tear-film instability.

The findings supported the biological premise that the flapless nature of SMILE preserved anterior stromal anatomy and minimized neural disruption. By maintaining more of the natural architecture of the cornea, SMILE facilitated a more rapid neurotrophic recovery compared with LASIK, which involved extensive transection of subbasal nerve fibers during flap creation. The observed improvements were not only structural but also functionally meaningful, aligning with reduced symptom burden and improved patient comfort.

In the context of the regional environment—characterized by dust, low humidity, and high digital screen exposure—these distinctions held significant clinical value. The accelerated nerve recovery associated with SMILE may provide a practical advantage for patients in Khyber Pakhtunkhwa and similar settings where ocular surface challenges are common. While LASIK remained a safe and effective option for refractive correction, the findings of this study indicated that SMILE may offer a more favorable postoperative experience, particularly for individuals at heightened risk for dry eye or those prioritizing faster neural recovery.

Overall, the study added important region-specific evidence to the global refractive surgery literature. It highlighted the need to consider corneal nerve integrity as a critical determinant of postoperative outcomes and emphasized the potential of SMILE as a preferred modality for patients seeking both visual excellence and enhanced ocular surface stability. Future investigations with larger sample sizes and longer follow-up periods would help further clarify long-term neuroregenerative patterns and refine patient selection strategies.

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