

Histological/pathological Evaluation of Post Photo-Refractive-Keratectomy(PRK) Induced Changes in Corneal Epithelial Thickness and its Impact on Physiological Eye Functions

Raja Faisal Zulfiqar¹, Muhammad Yousuf Khoso², Tayyaba Kazmi³, Sadia Sundus⁴, Irfan Ul Akbar⁵, Raheela Adil¹

Abstract:

Objectives: To evaluate histological changes and epithelial thickness (ET) post-photo refractive keratectomy (PRK) at two regions: apex of cornea (ETapex) and middle of cornea (ETmiddle). To evaluate changes of Lower Order Aberrations (LOAs), Higher Order Aberrations (HOAs), Contrast Sensitivity (CS) and Corrected Distance Visual Acuity (CDVA), and the relationship of these parameters with change of ET(apex and middle) after PRK.

Methods: Thirty-five patients, aged between 24 and 40, who had PRK were selected. Patient received eye examination, including cycloplegic refraction, non-contact intraocular pressure monitoring, slit-lamp biomicroscopy, corrected distance visual acuity (CDVA), and uncorrected visual acuity measurement. Using epithelial map of optical coherence tomography, changes in Epithelia thickness (ET) apex and ET middle were measured. Statistical Package for Social Sciences SPSS version 24 was used for data analysis.

Results: Following PRK, there was statistically significant difference in ET apex and ET middle measurements before and after surgery. ET (apex) increased after PRK, this appeared to be related to increased LOAs and increased HOAs, it was also associated with increase in CS and CDVAD (Shapiro Wilks test) with a P value of 0.006 and 0.001 respectively).

Conclusion: our study concludes that following PRK, there is a correlation between ET(apex & middle) changes and variations in CDVA, LOAs and HOAs, and SC. Post-PRK care should be tailored based involve follow-up appointments, medication, activity restrictions, sun protection, and careful monitoring of vision and healing to ensure optimal recovery and prevent complications. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 97-107. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

1. RYK Medical College, Rahim Yar Khan.
2. Al-Tibri Medical College, Karachi
3. Baqai Medical College, Karachi.
4. Liaquat College of Medicine and Dentistry, Karachi.
5. Sahara Medical College, Narowal.

Correspondence to:

Raja Faisal Zulfiqar
RYK Medical College, Rahim Yar Khan.
rajafaisal76@hotmail.com

Introduction:

Since its introduction in the early 1980s, photorefractive keratectomy has become a major modality in refractive surgery, particularly for low myopia. Small degrees of myopia can be effectively corrected with it, whether astigmatism is present or not. To improve vision clarity through PRK, a computer-controlled laser system called an

Originally Received: 07 Dec 2024

Revised: 27 Dec 2024

Accepted: 20 Jan 2025

Excimer Laser is used to reshape the cornea's surface so that objects focus on the retina¹. The patient lies down during this brief, painless procedure, which uses local anesthetic eye drops. An eyelid speculum is used to keep the patient's eyelids open. The computer is used to enter the degree of refractive error (such as myopia or hyperopia), and a special program is used to calculate the degree of correction². The epithelium is mechanically removed using this method of scraping. Then, to accomplish the proper change in curvature, laser is applied to both the stroma and Bowman's layer. After then, a therapeutic contact lens is applied to the cornea, and it takes three to five days for the epithelium to heal³. Its main drawbacks are post-operative pain and a delayed recovery of vision. Post-operative corneal haze is the principal complication of PRK. The natural healing process of wounds leads to corneal opacity. It first manifests 4-6 weeks after surgery and then progressively goes away over the following 3-6 months and sometimes 1-2 years⁴. The altered keratocytes change into myofibroblasts, which generate scar tissue by forming collagen. Scar tissue's ability to scatter light makes post-PRK opacification visible, and it seems to get worse as resection depth rises⁵. Research has been done on epithelial alterations and how they affect corneal refractive surgery outcomes⁶. Previous studies have demonstrated that following PRK, there is an increase in corneal thickness that happens immediately after the procedure and is observed during postoperative visits. This increase may be related to the potential regression of the refractive action that primarily occurs after PRK⁷. There are Other alternative refractive surgeries like; LASIK (Laser-Assisted in Situ Keratomileusis), that involves creating a flap in the cornea, then reshaping the underlying corneal tissue with a laser to correct refractive errors, LASEK (Laser-Assisted Subepithelial Keratectomy), Similar to PRK but involves creating a thin epithelial flap, SMILE

(Small Incision Lenticule Extraction), A minimally invasive procedure where a small incision is made, and a lenticule (thin disc-shaped tissue) is removed to correct myopia and astigmatism, ICL (Implantable Collamer Lens), a surgical procedure in which a synthetic lens is implanted inside the eye, typically used for high refractive errors or patients who are not candidates for laser surgery and Refractive Lens Exchange (RLE), a procedure where the natural lens is replaced with an artificial intraocular lens (IOL) to correct refractive errors, typically for patients with presbyopia or high refractive errors and Conductive Keratoplasty (CK), which uses radiofrequency energy to reshape the cornea, typically used for treating hyperopia (farsightedness) in older patients⁸. Still, PRK is a well-established procedure with a high rate of success; the long-term implications of epithelial changes can be significant in some cases. Epithelial irregularities, corneal scarring, dry eye syndrome, and other complications can affect vision quality and eye health. PRK can lead to long-term epithelial changes like corneal scarring, thinning, or irregularities, affecting vision. Potential issues include haze, dry eye, delayed healing, and glare. In some cases, there's a risk of regression or infections. It's important for patients considering PRK to have a thorough consultation with their eye surgeon and be aware of the potential risks and long-term effects. Regular follow-ups after surgery can help identify any problems early and allow for appropriate management⁹.

Assessment of correlations between epithelial thickness changes and key visual parameters can help to identify any significant predictors of improved or impaired visual outcomes following PRK. Very limited work is done to assess changes in corneal epithelial thickness pre- and post-Photorefractive Keratectomy (PRK) in relation to changes in vision outcomes, and a study gap exists. This study will help to identify any significant predictors of

improved or impaired visual outcomes following PRK.

Methodology:

This is a multi-centre observational study performed from April 2021 to August 2022 at (RYK Hospital-Rahim Yar Khan, Sheikh Zayed Hospital-Rahim Yar Khan, Hashmani Eye Trust Karachi). The study protocol was approved by the Sheikh Zayed Hospital (Rahim Yar Khan) ethical committee with letter no SZMCH/Ethics/2021-03/10654. Every patient provided signed informed consent. Each patient's single eye—the right eye, “oculus dexter” (OD), specifically—was assessed in this study. Participants who were pregnant or who had systemic diseases were not included in the study. Thirty-five patients, with a mean age of 28 years (range 24-40), were operated on using the PRK procedure (13 women and 22 men). The patients' refractions were stable for at least two years. Every patient had preoperative and postoperative examinations, including cycloplegic refraction, non-contact intraocular pressure monitoring, slit-lamp bio-microscopy, corrected distance visual acuity (CDVA), and uncorrected visual acuity measurement. Using the epithelial map of optical coherence tomography (Avanti XR OCT, Optovue) changes in ETapex and ET middle were measured. To use the OCT epithelial map, we examined the color-coded zones (central, mid-peripheral, peripheral) to assess thickness variations, focused on central thickness changes, and compared pre- and post-PRK for structural stability. Checked for asymmetries to identify localized healing and quantify thickness in each zone to understand remodeling patterns, and also correlated these changes with visual outcomes, like CDVA and contrast sensitivity, to assess impact on vision. Maps were tracked over time for healing progression and to identify any abnormal thinning or thickening to manage potential complications early, linking structural changes to visual quality

post-PRK. To standardize the OCT Measurements, the OCT devices were calibrated according to the manufacturer's specifications to ensure measurement accuracy. To calibrate an OCT device, it was ensured is clean and properly set up. Ran a system self-test and adjusted the focuses and signal strengths. To verify accuracy, a calibration phantom was used. Axial length and scan depth were checked, as well as image quality for clarity and repeatability.

Patients were positioned with aligned visual axes, and the same device settings were applied across pre- and post-PRK measurements to maintain consistency. Each measurement was taken multiple times, with the median value used to reduce variability and enhance reliability. Measurements were standardized at consistent pre- and postoperative intervals to monitor progressive changes. Criteria for assessment included Epithelial Thickness Measurements (middle & regional Comparison), Symmetry and Regularity, Uniformity to ensure thickness changes are uniform across zones, comparison with Baseline (pre-PRK). Clinical Impact on Visual Parameters: Correlation with Visual Acuity (CDVA) and Contrast Sensitivity.

Every patient underwent three measurements, with the mean value being utilized. Corneal Zernike coefficients (z00D-z44D) were measured with Pentacam HR (Oculus GmbH, Wetzlar, Oculus, Germany). The Freiburg Vision Test was used to determine CS, which is defined as the mean of luminance gain between a small object and its background divided by the mean background luminance (SC Weber) and its logarithm (SC Logs), both preoperatively and postoperatively¹⁰. A popular visual test battery known as "FrACT" was implied to measure contrast sensitivity, Vernier acuity, objectivity and reliability in the form of a free computer program¹¹. Measures that showed satisfactory test quality parameters were the only ones chosen. Every examination was carried out by the same technician in

complete darkness. Both before and after surgery, tests were conducted. A follow-up was performed at a fix interval of almost 1 year. To analyze the bias among observers “kappa value” was calculated and kappa value of 0.70 for present study omitted the probability of bias among observers (A **kappa value of ≥ 0.61** denotes substantial or higher agreement)

The parameters' normal distribution was evaluated using the Shapiro-Wilk test. Every continuous variable was distributed non-normally and was given as a median (range). Frequencies or percentages are used to display categorical variables. The relationships between continuous variables were assessed using Spearman's correlation coefficient. A two-tailed p-value of less than 0.05 was deemed to signify a statistically significant difference. We used IBM SPSS Statistics version 24.0 (IBM) for statistical analysis. This study focuses on how the corneal epithelium responds following PRK in relation to the parameters CDVA, CS, HOAs, and LOAs.

Results:

Out of 35 patients who underwent the PRK procedure, 13 were females and 22 were males. Their median age was 28 (range: 24–40). The preoperative and 12-month postoperative (PRK) characteristics related to visual acuity, contrast sensitivity, and

corneal epithelial thickness in the right eye (OD) of participants, based on median values and ranges (with 95% confidence interval) demonstrated that Pre-operative CDVA (logMAR) had median value of -0.160, with values ranging from -0.160 to 0.070 and 12 Months Postoperative CDVA slight decreased in median acuity (-0.130), with a broader range from -0.160 to 0.290. (See Table-1)

Data highlights the diverse postoperative changes in visual and structural parameters of the cornea, with a trend toward stability in epithelial thickness and some improvement in contrast sensitivity, while changes in corneal aberrations appear minimal but individualized. (Refer to Table-2)

Data in table-3 (with 95% confidence interval) demonstrated variable outcomes, some variables showed significant positive correlation and a few showed significantly negative correlations.

We also observed a statistically significant negative correlations between the median value of CDVAD (logMar) and the median value of SCD (weber) (Spearman's rho:-0.407, p=0.035), (See Table 3)

The key findings of the study and their possible implications have been organized into positive and negative correlations, highlighting the statistical relationships and their clinical implications. (See Table 4)

Table-1: Visual characteristics of participants and demographics.

Variable	Median	Minimum	Maximum
Age (years)	28	24	40
CDVA (logMar) preop	-0.160	-0.160	0.070
CDVA(logMar)12months	-0.130	-0.160	0.290
SC (weber) preop	0.000	-1.780	2.110
SC (weber) 12 months	0.380	0.220	2.360
CS (logcs) preop	2.290	1.630	7.770
CS (logcs) 12 months	2.330	1.630	2.650
ETmiddle (μm) preop	54	46	68
ETmiddle (μm) 12months	53	47	68
ETapex (μm) preop	54	45	68
ET apex (μm) 12 months	54	48	68
z00 (D) preop	134.93	111.216	161.105
z00D 12 months	133.06	111.216	161.105

z11D preop	1.528	0.494	5.893
z11D 12 months	1.368	0.214	5.893
z02D preop	79.037	66.655	95.948
z02D 12 months	78.951	66.655	95.948
z22D preop	1.013	0.378	2.440
z22D 12 months	0.821	0.222	1.684
z31D preop	0.319	0.054	0.823
z31D 12 months	0.333	0.081	0.823
z33D preop	0.193	0.039	1.285
z33D 12 months	0.215	0.067	1.285
z40D preop	1.743	0.847	2.757
z40D 12 months	1.487	0.847	2.757
z42D preop	0.117	0.019	3.510
z42D 12 months	0.159	0.021	0.302
z44D preop	0.100	0.029	0.437
z44D 12 months	0.108	0.021	0.437
Gender	N	%	
Females	13	37.14	
Males	22	62.85	
*OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: Epithelial thickness changes (corneal apex); ET middle: Epithelial Thickness (middle of the cornea); preop: preoperative.			

Table-2: Values of variance (preoperative value - postoperative 12 months value & Zernike coefficients)

Variable	Median	Minimum	Maximum
CDVAD (log Mar)	0.000	-0.230	0.450
SCD (weber)	0.550	0.220	2.360
CSD (logcs)	0.000	-6.000	0.890
ETmiddle (μm)	0.000	-18.00	18.00
ETapex (μm)	0.000	-18.00	17.00
z00D	-0.090	-40.49	29.97
z11D	-0.160	-24.84	17.29
z22D	-0.224	-1.490	1.270
z31D	0.039	-0.510	0.510
z33D	-0.010	-1.160	1.050
z40D	-0.297	-1.610	1.670
z42D	0.025	-0.140	0.280
z44D	-0.014	-0.360	0.350
OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: Epithelial Thickness changes at the corneal apex; ET middle: Epithelial Thickness changes at the middle of the cornea.			

Table 3: Correlation between the median values of variance of different variables for OD.

Variable (OD)		CD VA D log Mar	SC D weber	CS D log cs	ET Mid dle (μ m)	ET ape x (μ m)	Zernike polynomials (optical aberration types)								
							z00 D	z11 D	z02 D	z22 D	z31 D	z33 D	z40 D	z42 D	z44 D
CDV AD logMar	S.man's rho	1.00 0	- 0.4 07	- 0.3 54	- 0.4 04	- 0.4 19	0.6 47	- 0.3 17	0.6 26	0.2 62	- 0.0 96	0.0 12	- 0.6 45	- 0.2 78	0.3 62
	P	.	0.0 35*	0.0 70	0.0 37*	0.0 30*	0.0 01*	0.1 07	0.0 01*	0.1 87	0.6 34	0.9 53	0.0 01*	0.1 61	0.0 63
SCD (weber)	S.man's rho	- 0.40 7	1.0 00	0.4 10	0.4 88	0.3 54	- 0.2 52	0.0 9	- 0.2 21	- 0.2 10	0.1 91	- 0.2 74	0.2 95	0.2 98	- 0.3 16
	P	0.03 5*	.	0.0 34	0.0 10*	0.0 70	0.2 05	0.9 66	0.2 67	0.2 94	0.3 40	0.1 67	0.1 35	0.1 31	0.1 09
CSD (logcs)	S.man's rho	- 0.35 4	0.4 10	1.0 00	0.3 25	0.3 23	- 0.1 85	0.0 13	- 0.1 44	- 0.3 46	0.0 31	- 0.5 16	0.2 47	- 0.0 50	- 0.3 29
	P	0.07 0	0.0 34*	.	0.0 98	0.1 01	0.3 55	0.9 51	0.4 72	0.0 77	0.8 77	0.0 06*	0.2 14	0.8 05	0.0 94
ETmid dleD (μ m)	S.man's rho	- 0.40 4	0.4 88	0.3 25	1.0 00	0.8 85	- 0.5 12	0.3 19	- 0.4 79	- 0.3 36	0.4 02	- 0.0 48	0.6 12	0.4 54	- 0.2 14
	P	0.03 7*	0.0 10*	0.0 98	.	0.0 01*	0.0 06*	0.1 05	0.0 11*	0.0 86	0.0 38*	0.8 14	0.0 01*	0.0 17*	0.2 84
ETape xD (μ m)	S.man's rho	- 0.41 9	0.3 54	0.3 23	0.8 85	1.0 00	- 0.5 62	0.4 05	- 0.5 21	- 0.3 26	0.5 01	- 0.1 55	0.6 52	0.4 17	- 0.3 23
	P	0.03 0*	0.0 70	0.1 01	0.0 01*	.	0.0 02*	0.0 36*	0.0 05*	0.0 97	0.0 08*	0.4 41	0.0 01*	0.0 30*	0.1 01
z00D	S.man's rho	0.64 7	- 0.2 52	- 0.1 85	- 0.5 12	- 0.5 62	1.0 00	- 0.3 37	0.9 82	0.4 35	- 0.2 41	0.1 03	- 0.5 65	- 0.2 81	0.2 25
	P	0.00 1*	0.2 05	0.3 55	0.0 06*	0.0 02*	.	0.0 86	0.0 01*	0.0 23*	0.2 26	0.6 09	0.0 02*	0.1 56	0.2 59
z11D	S.man's rho	- 0.31 7	0.0 09	0.0 13	0.3 19	0.4 05	- 0.3 37	1.0 00	- 0.3 14	0.0 81	0.6 59	0.2 56	0.7 21	0.3 59	0.2 56
	P	0.10 7	0.9 66	0.9 51	0.1 05	0.0 36*	0.0 86	.	0.1 11	0.6 89	0.0 01*	0.1 97	0.0 01*	0.0 66	0.1 98
z02D	S.man's rho	0.62 6	- 0.2 21	- 0.1 44	- 0.4 79	- 0.5 21	0.9 82	- 0.3 14	1.0 00	0.4 13	- 0.2 28	0.0 50	- 0.5 27	- 0.2 50	0.2 48
	P	0.00 1*	0.2 67	0.4 72	0.0 11*	0.0 05*	0.0 01*	0.1 11	.	0.0 32*	0.2 52	0.8 04	0.0 05*	0.2 08	0.2 11
z22D	S.man's rho	0.26 2	- 0.2 10	- 0.3 46	- 0.3 36	- 0.3 26	0.4 35	0.0 81	0.4 13	1.0 00	0.1 44	0.2 63	- 0.2 08	- 0.1 07	0.4 55
	P	0.18 7	0.2 94	0.0 77	0.0 86	0.0 97	0.0 23*	0.6 89	0.0 32*	.	0.4 73	0.1 85	0.2 99	0.5 97	0.0 17*
z31D	S.man's rho	- 0.09 6	0.1 91	0.0 31	0.4 02	0.5 01	- 0.2 41	0.6 59	- 0.2 28	0.1 44	1.0 0	0.0 21	0.3 87	0.3 28	- 0.0 29

	P	0.63 4	0.3 40	0.8 77	0.0 38*	0.0 08*	0.2 26	0.0 01*	0.2 52	0.4 73	.	0.9 16	0.0 46*	0.0 95	0.8 87
z33D	S.m an's rho	0.01 2	- 0.2 74	- 0.5 16	- 0.0 48	- 0.1 55	0.1 03	0.2 56	0.0 50	0.2 63	- 0.0 21	1.0 00	0.2 43	- 0.0 88	0.3 25
	P	0.95 3	0.1 67	0.0 06*	0.8 14	0.4 41	0.6 09	0.1 97	0.8 04	0.1 85	0.9 16	.	0.2 22	0.6 64	0.0 98
z40D	S.m an's rho	- 0.64 5	0.2 95	0.2 47	0.6 12	0.6 52	- 0.5 65	0.7 21	- 0.5 27	0.2 08	0.3 28	0.2 43	1.0 00	0.3 69	0.0 23
	P	0.00 1*	0.1 35	0.2 14	0.0 01*	0.0 01*	0.0 02*	0.0 01*	0.0 05*	0.2 99	0.0 95	0.2 22	.	0.0 58	0.9 09
z42D	S.m an's rho	- 0.27 8	0.2 98	- 0.0 50	0.4 54	0.4 17	- 0.2 81	0.3 59	- 0.2 50	- 0.1 07	0.3 87	- 0.0 88	0.3 69	1.0 00	0.0 42
	P	0.16 1	0.1 31	0.8 05	0.0 17*	0.0 30*	0.1 56	0.0 66	0.2 08	0.5 97	0.0 46*	0.6 64	0.0 58	.	0.8 37
z44D	S.m an's rho	0.36 2	- 0.3 16	- 0.3 29	- 0.2 14	- 0.3 23	0.2 25	0.2 56	0.2 48	0.4 55	- 0.0 29	0.3 25	0.0 23	0.0 42	1.0 00
	P	0.06 3	0.1 09	0.0 94	0.2 84	0.1 01	0.2 59	0.1 95	0.2 11	0.0 17*	0.8 87	0.0 98	0.9 09	0.8 37	.
*OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: epithelial thickness changes at the corneal apex; ET middle: epithelial thickness changes at the middle of the cornea; S.man's rho: Spearman's rho.															

Table 4: Key findings along with p value and implications

Correlation	P value	Key observation/implications
Positive correlations		
CDVAD (L-M) ↔ z00D	0.001	Changes in corneal structure negatively impact vision
CDVAD (L-M) ↔ z02D	0.001	Increased ghosting, halos, or starbursts
SCD (W) ↔ CSD (LCS)	0.034	Improved outcomes in low-light conditions
SCD (W) ↔ ET middle	0.010	Indicates corneal structural consistency post-surgery
ET middle ↔ ET apex	0.001	Balanced corneal healing across the cornea.
ET middle ↔ z31D	0.038	Positive association with specific aberrations
ET middle ↔ z40D	0.001	increase in epithelial thickness linked to spherical aberration
ET middle ↔ z42D	0.017	Indicates correlation with higher-order aberrations
ET apex ↔ z11D	0.036	Associated with coma-related aberrations
ET apex ↔ z31D	0.008	Corneal apex thickness linked to coma type aberration
ET apex ↔ z40D	0.001	Indicates development of spherical aberrations
ET apex ↔ z42D	0.030	Positive association with higher-order aberrations
z00D ↔ z02D	0.001	Significant correlation between two aberrations
z00D ↔ z22D	0.023	Defocus & astigmatic aberrations correlate
z11D ↔ z31D	0.001	Changes in coma-related aberrations
z11D ↔ z40D	0.001	Predicts impact on visual acuity & clarity in low light
z02D ↔ z22D	0.032	Suggests compounding effects of multiple aberrations
z22D ↔ z44D	0.017	Indicates interconnected visual distortions

z31D ↔ z40D	0.046	Increases in one aberration linked to others
Negative correlations		
CDVAD (L-M) ↔ SCD (W)	0.035	Increased contrast sensitivity linked to improved visual acuity.
CDVAD (L-M) ↔ ET apex	0.030	Increased corneal apex stability linked to better visual acuity.
CDVAD (L-M) ↔ ET middle	0.037	Stable epithelial thickness linked to increased visual clarity.
CDVAD (L-M) ↔ z40D	0.001	↓ spherical aberrations associated with ↑ visual acuity
CSD (LCS) ↔ z33D	0.006	↑ contrast sensitivity co-related with ↓ coma aberration
ET middle ↔ z00D	0.006	↓ aberrations associated with ↑ epithelial stability.
ET middle ↔ z02D	0.011	↓ aberrations linked to stable epithelial thickness.
ET apex ↔ z00D	0.002	Improved corneal apex linked to fewer aberrations.
ET apex ↔ z02D	0.005	Stable corneal apex thickness linked to ↓ visual deforms
z00D ↔ z40D	0.002	↓ defocus correlated with ↓ spherical aberration.
z02D ↔ z40D	0.005	↓ interconnected aberrations lead to improved clarity
logMar=LM, Weber=W, logCS=LCS, ET		

Discussion:

In this study, we looked into how LOAs, HOAs, CS, and CDVA after PRK were affected with the thickness of the corneal epithelium at the middle and apex. According to our research, ET increased following PRK and this was correlated with higher HOAs (Z31, Z40, and Z42) and LOAs (Z11) similar findings were reported by Mirafteb and Gialelis^{12,13} that following PRK, the treated eye's visual output decreases and ocular aberrations increase. Additionally, it appears that the decline in LOAs (Z00, Z02) and the improvement in CDVA are connected to the rise in ET apex. Furthermore, we showed that ET middle rose following PRK and that ET apex, CS, and HOAs (Z31, Z40, and Z42) all seemed to rise in tandem with and it is in agreement with Ahmed A et al¹⁴. Also, the decrease in LOAs (Z00, Z02) and the decrease in CDVA appeared to be related to the increase in ET middle and We also showed that an increase in CDVA is associated with an increase in LOAs (Z00, Z02). The

increase in CDVA was related to the decrease in CS, ET apex, ET middle and HOAs (Z40), one possible reason for it may be that after accelerated corneal cross-linking (aCXL), there is an initial increase in corneal densitometry, which subsequently decreases over time, aligning with preoperative values by approximately one year post-procedure this finding agrees with Stein et al¹⁵. Lastly, a decrease in HOAs is linked to an increase in CS (Z33) and it is plausible that this is because, in PRK, an epithelium has been removed, and the quality of the epithelial cells that regenerate differs. Changes in the quality of the newly formed epithelial cells, variations in the specific cells' clarity, and variations in the new cells' size and shape are all caused by this process of epithelial cell regeneration, Khodaparast et al¹⁶.

HOAs rise during the remodeling of the epithelium following PRK surgery. A significant increase in spherical aberration may be linked to alterations in the corneal epithelium one year following PRK¹⁷⁻²⁰. A

previous study concluded that following PRK, CS improved and HOAs rose and also stated that HOAs rose following PRK²¹. PRK induced LOAs and HOAs decreased with passing time gradually²². HOAs rose following PRK in short term and this finding is in agreement with our study²³.

After PRK, the corneal epithelium undergoes remodeling to smooth the surface and compensate for irregularities in the underlying stromal tissue. This remodeling can sometimes increase or unevenly distribute epithelial thickness and result in corneal shape alterations, which can influence higher-order aberrations (HOA), including spherical aberrations which can have an Impact on Visual Quality (blurred or distorted vision, halos, glare or reduced contrast sensitivity). In agreement with our study, Beser et al even showed that spherical aberration (Z40) increased a year after surgery, but there was no significant difference in coma and trefoil evaluation between preoperative and postoperative values following PRK²⁴. Persistent spherical aberrations due to epithelial changes may necessitate additional interventions, such as wavefront-guided enhancements or customized re-treatments, to minimize aberrations and improve visual outcomes. According to Zhang et al, PRK-induced epithelial remodeling can affect future refractive procedures by altering corneal stability, topography, and healing responses²⁵. It's important to carefully evaluate the cornea's condition before proceeding with any additional surgeries, and strategies like corneal strengthening treatments or different surgical approaches may be considered to mitigate risks.

The small sample size that was examined in this study was one of its shortcomings. Follow-up time is yet another restriction. Patients may have certain shared characteristics, such as higher health awareness and socioeconomic status, which

can lead to results that are not fully generalizable to the broader population. **Limited Control over Sample Size and Composition** does not allow for controlling key sample characteristics (age, gender, disease severity), which may result in imbalanced groups, weakening the study's ability to detect meaningful differences. Longer-term research on epithelial change and its correlation with the other parameters would be beneficial.

Conclusion:

It was demonstrated that the shift in the ET apex, which is in front of the patient, is connected to the shift in the CS. Any alteration in the ET middle results in an equivalent alteration in the CS. The study also highlights the importance of tailoring follow-up care and monitoring plans to each patient's specific needs after undergoing photorefractive keratectomy (PRK). This approach considers individual factors such as healing response, pre-existing eye conditions, lifestyle, and risk factors to optimize recovery, prevent complications and ensure the best possible visual outcomes. Personalized protocols may include customized schedules for check-ups, targeted treatments, or adjustments in medications based on the patient's progress.

References:

1. Biscevic A, Ahmedbegovic-Pjano M, Pasalic A, Ziga N, Gabric K, Bohac M. Changes in the Higher Order Ocular Aberrations and Central Corneal Thickness After T-PRK and Fs-LASIK. *Acta Inform Med.* 2020 Jun;28(2):98-102.
2. Shaan NS, Majid M, Bhupendra CP, Photorefractive Keratectomy, StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2023.
3. Nemet A, Mimouni M, Vainer I, Sela T, Kaiserman I. Factors associated with changes in posterior corneal surface following photorefractive keratectomy. *Graefes Arch Clin Exp Ophthalmol.*

- 2021 Nov;259(11):3477-3483.
4. Spadea L, Di Genova L, Trovato Battagliola E, Paroli MP. Topography-Guided Transepithelial Photorefractive Keratectomy for the Treatment of Persistent and Visually-Significant Adenoviral Corneal Infiltrates. *Ther Clin Risk Manag*. 2023 Apr 6;19:341-349.
5. Hashemi H, Roberts CJ, Elsheikh A, Mehravaran S, Panahi P, Asgari S. Corneal Biomechanics After SMILE, Femtosecond-Assisted LASIK, and Photorefractive Keratectomy: A Matched Comparison Study. *Transl Vis Sci Technol*. 2023 Mar 1;12(3):12.
6. Kang MJ, Hwang J, Chung SH. Comparison of Corneal Wavefront-optimized and Wavefront-guided Alcohol-assisted Photorefractive Keratectomy Using Schwind Amaris 750S Laser for Myopia. *Korean J Ophthalmol*. 2020 Jun;34(3):210-218.
7. Shaabani A., Jabbarvand M., & Shahbazi A.. Corneal epithelial map after photorefractive keratectomy with and without mitomycin-c. 2021. <https://doi.org/10.21203/rs.3.rs-444610/v1>
8. Güneş İ. , Öztürk H. , & Özen B.. The association of pre-photorefractive keratectomy schirmer-1 test value with postoperative corneal epithelial thickness, ocular surface discomfort, and visual acuity. *Arquivos Brasileiros De Oftalmologia* 2024;87(2).
9. Pafitt PC, Tuft SJ. Conductive keratoplasty: current status. *Br J Ophthalmol*. 2021;105(8):1070-1077.
10. Gialelis TK, Kozobolis VP, Sideroudi H, Portaliou DM, Mouzaka AE, Stavrakas P, et al. Contrast sensitivity and corneal aberrations analysis in relation with epithelial thickness changes at the corneal apex after refractive surgery. *J Surg*. 2021;6:1437.
11. Themistoklis GK. Changes in corneal epithelial thickness in relation to vision, contrast sensitivity and ocular aberrations after lasik. *J Ophthalmol Adv Res*. 2023;4(2):1-7.
12. Mirafteb M, Hashemi H, Aghamirsalam M, Fayyaz S, Asgari S. Matched comparison of corneal higher order aberrations induced by SMILE to femtosecond assisted LASIK and to PRK in correcting moderate and high myopia: 3.00mm vs. 6.00mm. *BMC Ophthalmol*. 2021 May 15;21(1):216.
13. Gialelis T.. Change in corneal epithelial thickness after photo refractive keratectomy (prk). *JOAR* 2023;1-7. <https://doi.org/10.46889/joar.2023.4304>
14. Ahmed A, Khallaf M, & Ziada H. Evaluation of short-term changes in central corneal endothelial cell count by specular microscope after photorefractive keratectomy (prk) with mitomycin-c (mmc) 0.02% in patient with moderate myopia. *Al-Azhar Medical Journal* 2023;52(2):739-752. <https://doi.org/10.21608/amj.2023.291697>
15. Stein R. , Tone S. , Lebovic G. , Singal N. , & Hatch W.. Subjective and objective evaluation of corneal haze after accelerated corneal crosslinking for corneal ectasias. *Acta Ophthalmologica* 2023;101(5):568-574. <https://doi.org/10.1111/aos.15639>
16. Khodaparast M., Ambrósio R., Ahmadzadeh H. , Khorrami-Nejad M. , Mohammadzadeh M. , Azizi S. et al.. Evaluation of the effect of artificial tears on corneal epithelial thickness changes after photorefractive keratectomy. *Indian Journal of Ophthalmology* 2023;72(1):66-72. https://doi.org/10.4103/ijo.ijo_1354_23
17. Sedaghat MR, Momeni-Moghaddam H, Yekta AA, Maddah N, Roberts CJ, Savardashtaki M. Early elastic and viscoelastic corneal biomechanical changes after photorefractive keratectomy and small incision lenticule extraction. *Int Ophthalmol*. 2024 Jul 2;44(1):302.

18. Latifi G, Mohammadi SS, Davoodabadi M. Longitudinal epithelial thickness profile changes 18 months after photorefractive keratectomy. *Cornea*. 2021;40(4):430-9.
19. Moshfeghi S., Razmjou H. , Peyman A. , Kateb H. , & Naderan M.. A comparison between wavefront-optimized and wavefront-guided photorefractive keratectomy in patients with moderate-to-high astigmatism: a randomized clinical trial. *Journal of Current Ophthalmology* 2022;34(2):194.
20. Bišćević A., Pidro A., Ahmedbegovic-Pjano M. , Bjedic N. , Boháč M. , & Patel S.. Vector analysis of changes in the higher order ocular aberrations and central corneal thickness after t-prk and fs-lasik. *Acta Informatica Medica* 2020;28(1):24.
21. Zarei-Ghanavati S., Shandiz J., Abrishami M., & Karimpour M.. Comparison of mechanical debridement and trans-epithelial myopic photorefractive keratectomy: a contralateral eye study. *Journal of Current Ophthalmology* 2019;31(2):135-141.
22. Moshirfar M , Theis J. , Cha D. , Porter K. , Payne C. , & Hoopes P.. Influence of preoperative parameters on the ratio of keratometric change per diopter of attempted spherical equivalent ($\Delta k/\Delta seq$) for myopic correction within lasik, prk, and smile. *Clinical Ophthalmology* 2023; Volume 17:2563-2573.
23. Wu Y, Wang S, Wang G, Zhao S, Wei R, Huang Y. Corneal asphericity and higher-order aberrations after FS-LASIK and Trans-PRK for myopia. *J Ophthalmology*. 2021.
24. Beser BG, Yildiz E, Vural ET. Prognostic factors of visual quality after transepithelial photorefractive keratectomy in patients with low-to-moderate myopia. *Indian J Ophthalmol*. 2020;68(12):2940-4.
25. Zhang S, Lin Z, Hu J, et al. Refractive effect of epithelial remodelling in myopia after photorefractive keratectomy. *J Clin Med*. 2024;6(4):74. doi: 10.3390/jcm6040074.

Authors Contribution

Concept and design: Raja Faisal Zulfiqar

Data collection/assembly: Raheela Adil, Yousuf Khoso, Sadia Sundus

Drafting: Tayyaba Kazmi, Sadia Sundus

Statistical Expertise: Irfan-ul-Akbar

Critical revision: Yousuf Khoso, Raheela Adil