Post-Laser Vision Correction Ectasia: The Role of Corneal Biomechanics

Ectasia Pós Cirurgia Refrativa Laser: O Papel da Biomecânica Corneana

Francisca Bragança [1], Catarina Castro [1], Tatiana Costa [1], Ana Carolina Abreu [1,2], Sílvia Monteiro [1,2], Maria do Céu Brochado [1]

[1] Department of Ophthalmology, Centro Hospitalar Universitário de Santo António (CHUdSA), Porto, Portugal
[2] ICBAS – Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal

Recebido/Received: 2023-10-12 | **Aceite/Accepted:** 2024-06-30 | **Published online/Publicado online:** 2024-10-23 | **Publicado/Published:** 2025-03-31

DOI: https://doi.org/10.48560/rspo.33198

ABSTRACT

INTRODUCTION: Corneal ectasia after laser refractive surgery can threaten vision. We aimed to analyze the preoperative clinical, tomographic and biomechanical data of patients submitted to laser vision correction (LVC) – photorefractive keratectomy (PRK) and femtosecond laser-assisted *in-situ* keratomileusis (FS-LASIK) – for myopia and/or astigmatism and to evaluate their preoperative ectasia risk and their 6-months' and 24-months' postoperative ectasia status.

METHODS: Retrospective study including patients submitted to FS-LASIK and PRK, between November 2020 and September 2021, that completed at least 6 months of follow-up. Corneal tomography was evaluated with Pentacam HR (Oculus) and corneal biomechanics with Corvis ST (Oculus). The risk of preoperative ectasia was also assessed using the percent tissue altered (PTA) and an artificial intelligence tool (Brain Cornea). At 6 and 24 months postoperatively, we assessed CBI-LVC alongside refractive and tomographic outcomes.

RESULTS: A total of 268 eyes from 139 patients were included (group 1 – FS-LASIK: 186; group 2 – PRK: 82) and 210 (FS-LASIK: 142; PRK: 68) completed the follow-up. At 24 months, 3 eyes had a CBI-LVC>0.2 (PRK=2; FS-LASIK=1). No cases of clinically relevant corneal ectasia were identified. In FS-LASIK, K1 and K2 displayed a statistically significant increase between 6 and 24 months, with a positive correlation to preoperative TBI ($r(140)=0.263$; $p=0.008$).

CONCLUSION: Few eyes displayed a CBI-LVC indicative of post-LVC ectasia. Our refractive screening appears to have been successful, both in safety and stability. The refractive regression in FS-LASIK eyes appears to be higher in eyes with a higher preoperative ectatic risk. Preoperative biomechanics may influence postoperative refractive regression after FS-LASIK.

KEYWORDS: Corneal Diseases/etiology; Corneal Surgery, Laser/adverse effects; Keratomileusis, Laser In Situ/adverse effects; Photorefractive Keratectomy/adverse effects.

RESUMO

INTRODUÇÃO: A ectasia corneana pós cirurgia refrativa laser (LVC) pode ameaçar a

visão. Analisamos os dados pré-operatórios clínicos, tomográficos e biomecânicos de doentes submetidos a queratectomia fotorrefrativa (PRK) e laser *in-situ keratomileusis* assistido por laser femtosegundo (FS-LASIK) para correção de miopia e/ou astigmatismo, com o objetivo de avaliar o seu risco ectásico pré- e pós-operatório.

MÉTODOS: Estudo retrospetivo com doentes submetidos a FS-LASIK e PRK, entre Novembro de 2020 e Setembro de 2021. que completaram pelo menos 6 meses de seguimento. A tomografia corneana foi avaliada através do Pentacam HR (Oculus) e a biomecânica com o Corvis ST (Oculus). O risco ectásico pré-operatório foi também avaliado pela percentagem de tecido alterado (PTA) e uma ferramenta de inteligência artificial (Brain Cornea). Aos 6 e 24 meses avaliamos o CBI-LVC, bem como os resultados refrativos e tomográficos.

RESULTADOS: Foram incluídos 268 olhos de 139 doentes (grupo 1 - FS-LASIK: 186; grupo 2 - PRK: 82) e 210 (FS-LASIK: 142; PRK: 68) completaram o seguimento. Aos 24 meses, 3 olhos apresentaram CBI-LVC>0,2 (PRK=2; FS-LASIK=1). Não foram identificados casos de ectasia corneana clinicamente relevante. No grupo do FS-LASIK o K1 e K2 aumentaram de forma estatisticamente significativa entre os 6 e 24 meses, com uma correlação positiva com o TBI pré-operatório (r(140)=0,263; *p*=0,008).

CONCLUSÃO: Um número residual de olhos apresentou um CBI-LVC indicativo de ectasia pós-LVC. A avaliação pré-operatória foi eficaz, tanto em termos de segurança como de estabilidade pós-operatória. A regressão refrativa observada em olhos submetidos a FS-LASIK parece ser tanto maior quanto maior o risco ectático pré-operatório. A biomecânica pré-operatória pode influenciar a regressão refrativa após o FS-LASIK.

PALAVRAS-CHAVE: Cirurgia Laser da Córnea/efeitos adversos; Doenças da Córnea/cirurgia; Laser In-Situ Keratomileusis/efeitos adversos; Queratectomia Fotorrefrativa/efeitos adversos.

INTRODUCTION

Corneal ectasia after laser refractive surgery is a potentially sight-threatening complication that can present up to several years after the refractive procedure.[1–3] In 1998, Seiler and coworkers[4] published the first reports of iatrogenic corneal ectasia after laser-assisted *in situ* keratomileusis (LASIK) in patients with myopia from -10.00 to -13.50D. The biomechanically decompensated corneal stroma leads to progressive postoperative corneal thinning and protrusion, leading to irregular astigmatism and visual distortion.[5,6] Although ectasia is more frequently observed following LASIK, occurrences have also been documented secondarily to other surface ablation methods.[6,7]

There are several known risk factors for keratectasia that can be ascertain to either an innate corneal biomechanical susceptibility, a surgery-induced biomechanical failure or postoperative biomechanical stress.[6] The major risk factors were originally described by Randleman *et al*[8] and included patient factors such as younger age at surgery, higher myopic error, thinner pachymetry and abnormal topographic features as well as a thinner RSB.

The need to further optimize the preoperative assessment of patients who may have mild or subclinical ectatic disease is further supported by cases in which ectasia developed even in the absence of recognized risk factors.[9,10]

Multimodal imaging is used to evaluate the susceptibility for corneal ectasia following laser vision correction, including elevation and pachymetry mapping in Scheimpflug tomography, as well as different parameters and derived indexes such as the pachymetric progression index (PPI), Ambrósio's relational thickness (ART) and at the meridian with maximal PPI (ARTMax) or clinical tools such as the Belin/Ambrósio enhanced ectasia display (BAD).[6] Additional methods include epithelial thickness mapping with segmental tomography using optical coherence tomography (OCT), digital very high-frequency ultrasound (VHF-US) and ocular wavefront.[5,6] The biomechanical assessment of the cornea can also play an important role. CORVIS® has enabled a dynamic evaluation of the corneal response to deformation.[5] In 2014, a collaborative international research team focused on ectasia detection introduced two parameters: the Corvis Biomechanical Index (CBI) and the Tomographic Biomechanical Index (TBI).[11–13] These were originally designed for detection of keratoconus and ectasia susceptibility preoperatively.[13] For this reason, the algorithms commonly display abnormal values postoperatively. A pure biomechanical index, CBI post-LASER vision correction (CBI-LVC), was then developed and designed to adequately distinguish stable corneas post-LVC from post-LVC ectasia, regardless of the specific LASER procedure.[13] The authors found a cut-off of 0.2 to provide a sensitivity of 93.3% and a specificity of 97.8% in distinguishing post-LVC stable from ectatic corneas.[13] Because changes in corneal biomechanics are presumed to happen before any noticeable clinical, tomographic or epithelial thickness map changes, this new biomechanical index was developed to provide valuable

information regarding post-LVC corneal fragility.[13]

In this work, we intended to analyze the preoperative clinical, tomographic and biomechanical data of patients submitted to laser vision correction – PRK and FS-LASIK – for the correction of myopia and/or astigmatism and to evaluate their preoperative ectasia risk and their 6- and 24-months postoperative ectasia status.

METHODS

This is a retrospective study including eyes of patients submitted to FS-LASIK and PRK for the correction of myopia/astigmatism between November 2020 and September 2021 in Centro Hospitalar Universitário de Santo António (CHUdSA). For this study, we reviewed preoperative data and postoperative data at 6 months. Patients were then evaluated 24 months after the procedure. Patients were excluded from the study if there was no attendance to the 6-months postoperative visit.

We evaluated demographic data, that included patients' age and gender. We assessed the distance best corrected visual acuity (BCVA, Snellen, converted to decimal), the manifest refraction spherical and cylindrical errors as well as the spherical equivalent (SE) at 3-time points (preoperative, 6- and 24-months' postoperative). The objective scatter index (OSI) was assessed at the preoperative appointment and at the 6- and 24-month appointment with HD Analyzer (Visiometrics SL, Terrassa, Spain). Corneal tomography, using Scheimpflug technology (Pentacam, OCULUS®), was evaluated and recorded parameters at all time points included center and minimum pachymetry as well as front surface flattest (K1) and steepest (K2) meridians power, maximal curvature power (Kmax), index of surface variance (ISV), index of height asymmetry (IHA), index of height decentration (IHD), index of vertical asymmetry (IVA), keratoconus index (KI) and central keratoconus index (CKI). At the preoperative appointment, we also evaluated the Maximum Ambrosio relational thickness (ARTmax) and Belin-Ambrosio deviation index (BAD-D). Biomechanical evaluation was conducted using Corvis ST (OCULUS®). The CBI and TBI were recorded preoperatively. At the 6-months and 24-months mark, the CBI-LVC was obtained.

To further assess the risk of preoperative ectasia, the PTA was calculated preoperatively. For PRK patients this was calculated through ablation depth (AD) + 50 µm for epithelial thickness ÷ central corneal thickness (CCT). Also, the Brain Cornea, an artificial intelligence tool, was used to enhance ectasia risk detection. This tool was developed by the Brazilian Study Group of Artificial Intelligence and Corneal Analysis (BRAIN, Rio de Janeiro, Brazil) and combines tomographic data (minimum CCT, IHD, BAD-D) with treatment-related data (FT, AD), including age as a biomechanical surrogate. For each patient, either the BCR-Clasik – score of the brain cornea risk calculator for LASIK – or the BCRCprk – score of the brain cornea risk calculator for PRK, was calculated from the available website. The cut-off risk value for both indexes is 11.6% (the model has with 94.8% sensitivity, 92.1% specificity and an area under the ROC curve of 0.978).

The AD (µm) and RSB (µm) were obtained from the WaveLight® EX500 LASER system software (Alcon, EUA), during the surgery planning. In our center, the standard optic zone width used in 6.5 mm and the flap thickness is 110 µm, which can be adjusted by the surgeon in individual cases.

To evaluate ectasia risk and postoperative ectasia status, we defined 2 groups: group 1 – eyes submitted to FS-LASIK and group 2 – eyes submitted to PRK.

Our primary outcome was to evaluate the preoperative ectasia risk of our sample and their ectasia status at 6 and 24 months postoperatively. We also evaluated refractive results as secondary outcomes.

This study was performed in accordance with the Declaration of Helsinki in its latest amendment (2013).

Statistical analysis was performed using IBM SPSS Statistics 26. The normality of data was assessed using the Kolmogorov-Smirnov test. Our data analysis revealed a non-normal distribution for studied variables. Categorical variables are presented as relative frequencies. Continuous variables are summarized as median and minimum and maximum values. A *p*-value inferior to 0.05 was considered statistically significant.

RESULTS

Two hundred and sixty-eight eyes from 139 patients were included (FS-LASIK: 186 and PRK: 82). Median age was 31 years old for the overall group and found to be comparable between patient groups. In both treatment groups, there were more female patients and patients submitted to FS-LASIK had a significantly higher spherical error and SE. Preoperative clinical, tomographic and biomechanical characteristics are summarized in Table 1.

Regarding tomographic parameters, patients submitted to PRK displayed statistically significant lower center and minimum pachymetry. Eyes in the PRK group also displayed a lower ISV, higher BAD-D and lower ARTmax.

The estimated AD was found to be higher in FS-LASIK eyes. Regarding the PTA, no cases were found over 0.4 and FS-LASIK patients had a significantly higher value ($p<0.001$). Likewise, the calculated Brain Cornea ectatic risk was higher in FS-LASIK eyes ($p<0.001$).

The biomechanical evaluation retrieved differences in both the CBI and TBI with higher values found in the PRK group.

Tables 2 (FS-LASIK group) and 3 (PRK group) describe and compare clinical, tomographic and biomechanical parameters evaluated at 3 time points – preoperatively and at the 6-months and 24-months postoperative evaluations. From the 268 eyes that met the 6-months postoperative appointment, only 210 (FS-LASIK: 142; PRK: 68) met the 24-months postoperative appointment.

Regarding the FS-LASIK group, between the preoperative and 6-months postoperative visit, all parameters except OSI and IHA displayed statistically significant differences. From this point onto the 24-months postoperative visit, variability was found in refractive parameters – an increase in BCVA and in both cylinder and spherical equivalent power. Regarding tomographic parameters, K1

Table 1. Preoperative clinical. tomographic and biomechanical evaluation. Categorical variables are presented in percentage of total. Continuous variables are presented as median (minimum-maximum values).

	Overall n=268	FS-LASIK n=186	PRK n=82	*p*-value
Female gender (%)	167 (62.3%)	118 (63.4%)	49 (59.8%)	0.735
Age. years	31 (19 - 43)	31 (23 - 43)	31 (19 - 39)	0.920
BCVA (decimal, Snellen)	1.00 (0.50 - 1.00)	1.00 (0.50 - 1.00)	1.00 (0.80 - 1.00)	0.083
Sphere (diopters, D)	-3.00 (-7.75 - 0.00)	-3.50 (-7.75 - 0.00)	-2.25 (-5.25 – -0.25)	<0.001
Cylinder (D)	-0.75 (-4.00 - 0.00)	-0.75 (-4.00 - 0.00)	-0.75 (-3.00 - 0.00)	0.924
SE (D)	-3.50 (-8.38 – -0.25)	-4.00 (-8.38 – -0.25)	-2.50 (-5.50 – -0.25)	<0.001
Ocular Surface Index (OSI)	0.70 (0.20 - 17.10)	0.80 (0.20 - 17.10)	0.70 (0.20 - 3.50)	0.348
Center pachymetry (µm)	560 (459 - 648)	568 (459 - 648)	531 (507 - 580)	<0.001
Minimum pachymetry (µm)	556 (504 - 645)	565 (516 - 645)	527 (504 - 578)	<0.001
K1 (central 3 mm) (D)	42.30 (38.90 - 46.10)	42.30 (38.90 - 46.10)	42.30 (39.70 - 45.70)	0.576
K2 (central 3 mm) (D)	43.70 (40.00 - 47.40)	43.80 (40.00 - 47.30)	43.55 (41.00 - 47.40)	0.203
Kmax (central 3 mm) (D)	44.10 (40.60 - 48.00)	44.20 (40.60 - 47.60)	43.95 (41.40 - 48.00)	0.140
ISV	16.00 (7.00 - 34.00)	16.00 (7.00 - 34.00)	15.00 (9.00 - 28.00)	0.049
IHA	4.00 (0.00 - 22.20)	4.00 (0.20 - 20.10)	3.95 (0.00 - 22.20)	0.584
IHD	0.009 (0.001 - 0.027)	0.009 (0.001 - 0.023)	0.008 (0.001 - 0.027)	0.643
IVA	0.10 (0.03 - 0.25)	0.10 (0.04 - 0.22)	0.10 (0.03 - 0.25)	0.992
KI	1.01 (0.94 - 1.04)	1.01 (0.94 - 1.04)	1.01 (1.00 - 1.02)	0.183
CKI	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	0.740
BAD-D	0.69 (-0.47 - 1.99)	0.59 (-0.47 - 1.46)	1.05 (0.06 - 1.99)	<0.001
ARTmax	456 (291 - 691)	478.50 (367 - 691)	404.50 (291 - 514)	<0.001
Brain cornea (%)	2.68 (0.03 - 85.85)	4.14 (0.03 - 85.85)	1.22 (0.06 – 36.00)	<0.001
Ablation depth (µm)	56.03 (19.36 - 109.15)	63.18 (19.36 - 109.15)	41.77 (22.89 - 77.46)	<0.001
PTA	0.27 (0.10 - 0.39)	0.30 (0.18 - 0.39)	0.18 (0.10 - 0.36)	<0.001
CBI	0.10 (0.00 - 0.82)	0.06 (0.00 - 0.50)	0.27 (0.01 - 0.82)	<0.001
TBI	0.04 (0.00 - 0.53)	0.03 (0.00 - 0.53)	0.07 (0.00 - 0.47)	<0.001

A *p*-value inferior to 0.05 was considered statistically significant. BCVA: best-corrected visual acuity | SE: spherical equivalent | K1: front surface flattest meridian power | K2: front surface steepest meridians power | Kmax: front surface maximal curvature power | ISV: Index of surface variance | IHA: Index of height asymmetry | IHD: Index of height decentration | IVA: Index of vertical asymmetry | KI: Keratoconus index | CKI: Central keratoconus index | BAD-D: Belin-Ambrosio deviation index | ARTmax: Maximum Ambrosio relational thickness | PTA: Percent tissue altered | CBI: Corvis Biomechanical Index | TBI: Tomographic Biomechanical Index.

Table 2. Preoperative. 6-months' and 24-months' postoperative clinical. tomographic and biomechanical evaluation of eyes submitted to FS-LASIK.

	p-value, overtime	Preop n=186	6-months postop n=186	*p*-value	24-months postop n=142	*p*-value
BCVA (decimal. Snellen)	<0.001	1.00 (0.50 - 1.00)	1.00 (0.20 - 1.25)	<0.001	1.00 (0.40 - 1.60)	<0.001
Sphere (D)	<0.001	-3.00 (-7.75 - 0.00)	0.00 (0.00 - 1.00)	<0.001	0.00 (-2.50 - 0.50)	0.534
Cylinder (D)	<0.001	-0.75 (-4.00 - 0.00)	0.00 (-1.50 - 0.00)	<0.001	0.00 (-1.75 - 0.25)	<0.001
SE (D)	<0.001	-3.50 (-8.38 – -0.25)	0.00 (0.00 - 0.25)	<0.001	0.00 (-2.88 - 0.50)	0.003
Ocular Surface Index (OSI)	0.514	0.70 (0.20 - 17.10)	0.80 (0.10 - 11.00)	0.999	0.80 (0.20 - 4.70)	0.999
Center pachymetry (µm)	<0.001	560 (459 - 648)	501.50 (438 - 622)	<0.001	497.50 (454 - 606)	0.300
Minimum pachymetry (µm)	<0.001	556 (456 - 645)	499.50 (436 - 618)	<0.001	496 (451 - 605)	0.522
K1 (central 3 mm) (D)	<0.001	42.30 (38.90 - 46.10)	39.60 (35.50 - 44.80)	<0.001	39.90 (35.80 - 47.60)	<0.001
K2 (central 3 mm) (D)	<0.001	43.70 (40.00 - 47.40)	40.20 (35.70 - 45.80)	<0.001	40.60 (36.00 - 49.80)	<0.001
Kmax (central 3 mm) (D)	<0.001	44.10 (40.60 - 48.00)	43.40 (39.40 - 47.30)	<0.001	43.60 (40.00 - 59.20)	0.291
ISV	<0.001	16.00 (7.00 - 34.00)	23.00 (7.80 - 92.00)	<0.001	24.00 (0.09 - 89.00)	0.840
IHA	0.021	4.00 (0.00 - 22.20)	4.50 (0.00 - 31.50)	0.081	4.70 (0.00 - 39.80)	0.087
IHD	<0.001	0.009 (0.001 - 0.027)	0.012 (0.00 - 0.041)	<0.001	0.013 (0.001 - 0.053)	0.222
IVA	<0.001	0.10 (0.03 - 0.25)	0.17 (0.05 - 0.68)	<0.001	0.18 (0.04 - 0.96)	0.999
KI	<0.001	1.01 (0.94 - 1.04)	0.98 (0.86 - 1.19)	<0.001	0.98 (0.86 - 1.22)	0.630
CKI	<0.001	1.01 (1.00 - 1.02)	1.00 (0.018 - 1.04)	<0.001	1.00 (0.97 - 1.80)	0.141
CBI-LVC	0.134		0.00 (0.00 - 1.00)	--	0.00 (0.00 – 1.00)	0.663

Variables are presented as median (minimum-maximum values). A *p*-value inferior to 0.05 was considered statistically significant. BCVA: best-corrected visual acuity | SE: spherical equivalent | K1: front surface flattest meridian power | K2: front surface steepest meridians power | Kmax: front surface maximal curvature power | ISV: Index of surface variance | IHA: Index of height asymmetry | IHD: Index of height decentration | IVA: Index of vertical asymmetry | KI: Keratoconus index | CKI: Central keratoconus index | CBI-LVC: Corvis Biomechanical Index-Laser Vision Correction.

Table 3. **Preoperative. 6-months' and 24-months' postoperative clinical. tomographic and biomechanical evaluation of eyes submitted to PRK.**

	p-value, overtime	Preop n=82	6-months postop n=82	*p*-value	24-months postop n=68	*p*-value
BCVA (decimal, Snellen)	<0.001	1.00 (0.80 - 1.00)	1.00 (0.60 - 1.60)	0.012	1.25 (0.80 - 1.60)	<0.001
Sphere (D)	<0.001	-2.25 (-5.25 – -0.25)	0.00 (-0.75 - 0.25)	<0.001	0.00 (-0.50 - 0.50)	0.336
Cylinder (D)	<0.001	-0.75 (-3.00 - 0.00)	0.00 (-1.00 - 0.00)	<0.001	0.00 (-1.00 - 0.50)	0.303
SE (D)	<0.001	-2.50 (-5.50 – -0.25)	0.00 (-1.25 - 0.00)	<0.001	0.00 (-0.75 - 0.50)	0.999
Ocular Surface Index (OSI)	0.200	0.70 (0.20 - 3.50)	0.60 (0.30 - 2.40)	0.126	0.60 (0.20 - 2.40)	0.999
Center pachymetry (µm)	<0.001	531 (507 - 580)	488.50 (440 - 531)	<0.001	483 (434 - 538)	0.999
Minimum pachymetry (µm)	<0.001	527 (504 - 578)	484.50 (440 - 531)	<0.001	482 (434 - 536)	0.735
K1 (central 3 mm) (D)	<0.001	42.30 (39.70 - 45.70)	40.25 (37.80 - 44.30)	<0.001	40.20 (37.90 - 44.20)	0.606
K2 (central 3 mm) (D)	<0.001	43.55 (41.00 - 47.40)	40.90 (38.70 - 45.10)	<0.001	40.80 (38.80 - 44.90)	0.999
Kmax (central 3 mm) (D)	<0.001	43.95 (41.40 - 48.00)	42.95 (39.60 - 46.80)	<0.001	42.95 (39.80 - 46.40)	0.198
ISV	0.627	15.00 (9.00 - 28.00)	18.00 (8.00 - 40.00)	0.012	16.00 (7.00 – 34.00)	0.480
IHA	0.972	3.95 (0.00 - 22.20)	3.95 (0.00 - 16.70)	0.999	4.55 (0.00 - 15.90)	0.999
IHD	0.030	0.008 (0.001 - 0.027)	0.01 (0.00 - 0.032)	0.066	0.01 (0.002 - 0.032)	0.999
IVA	<0.001	0.10 (0.03 - 0.25)	0.125 (0.04 - 0.35)	<0.001	0.12 (0.05 - 0.38)	0.999
KI	<0.001	1.01 (1.00 - 1.02)	0.98 (0.90 - 1.05)	<0.001	0.98 (0.89 - 1.02)	0.453
CKI	<0.001	1.01 (1.00 - 1.02)	1.00 (0.97 - 1.03)	<0.001	1.00 (0.98 - 1.02)	0.741
CBI-LVC	1.000		0.00 (0.00 - 1.00)	--	0.00 (0.00 – 1.00)	0.999

Variables are presented as median (minimum-maximum values). A *p*-value inferior to 0.05 was considered statistically significant. BCVA: best-corrected visual acuity | SE: spherical equivalent | K1: front surface flattest meridian power | K2: front surface steepest meridians power | Kmax: front surface maximal curvature power | ISV: Index of surface variance | IHA: Index of height asymmetry | IHD: Index of height decentration | IVA: Index of vertical asymmetry | KI: Keratoconus index | CKI: Central keratoconus index | CBI-LVC: Corvis Biomechanical Index-Laser Vision Correction.

Table 4. **Preoperative clinical, tomographic and biomechanical evaluation of patients that exhibited a CBI-LVC over 0.2 at the 24-months' postoperative evaluation.**

	Case 1 – FS-LASIK	Case 2 – PRK	Case 3 – PRK
Gender	Male	Female	Male
Age. years	38	36	35
BCVA (decimal, Snellen)	1.0	0.8	1
Sphere (D)	-2.00	-1.00	-1.75
Cylinder (D)	-4.00	-2.00	-1.75
SE (D)	-4.00	-2.00	-2.63
Center pachymetry (µm)	564	522	575
Minimum pachymetry (µm)	556	517	570
K1 (central 3 mm) (D)	40.5	42.6	40.6
K2 (central 3 mm) (D)	43.9	45.1	41.2
Kmax (central 3 mm) (D)	44.4	45.6	41.6
ISV	30	24	19
IHA	11.6	9.2	1.10
IHD	0.012	0.014	0.008
IVA	0.13	0.16	0.07
KI	0.99	1.00	1.02
CKI	1.01	1.01	1.01
BAD-D	1.02	1.50	0.53
ARTmax	380	400	463
Brain cornea (%)	26.59	9.42	0.96
Ablation depth (µm)	88.00	45.07	36.97
PTA	0.20	0.18	0.15
CBI	0.27	0.25	0.01
TBI	0.15	0.04	0.10

BCVA: best-corrected visual acuity | SE: spherical equivalent | K1: front surface flattest meridian power | K2: front surface steepest meridians power | Kmax: front surface maximal curvature power | ISV: Index of surface variance | IHA: Index of height asymmetry | IHD: Index of height decentration | IVA: Index of vertical asymmetry | KI: Keratoconus index | CKI: Central keratoconus index | BAD-D: Belin-Ambrosio deviation index | ARTmax: Maximum Ambrosio relational thickness | PTA: Percent tissue altered | CBI: Corvis Biomechanical Index | TBI: Tomographic Biomechanical Index.

and K2 displayed a statistically significant increase, while all other indices remained stable through follow-up. We subsequently evaluated possible correlations between the mean keratometry variation in this group with several preoperative parameters. There was no correlation with age, pachymetry, ablation depth, BAD-D, ART-max or CBI. A positive correlation was found with preoperative TBI ($r(140)=0.263$; $p=0.008$). In the biomechanical evaluation, no difference was found between CBI-LVC at different time points. Using the defined cut-off value of 0.2, only 2 eyes (CBI-LVC=0.43 and CBI-LVC=1.00) presented values above this at the 6-months visit – 1 was lost to follow-up and the other had a CBI-LVC=0 at the end visit. Only 1 eye treated with FS-LASIK indeed developed a value of 1.00 at the end of follow-up (with CBI-LVC=0 at 6-months).

Regarding the PRK group, between the preoperative and 6-months postoperative visit, all parameters except OSI, IHA and IHD displayed statistically significant differences. From this point onto the 24-months postoperative visit, variability was found only in BCVA, which suffered an improvement. Regarding all tomographic and biomechanical parameters, no statistically significant differences were found from the 6-months visit to the end of follow-up. For a CBI-LVC cut-off value of 0.2, 3 eyes presented above this value (CBI-LVC=0.37; CBI-LVC=0.52 and CBI-LVC=1) at the 6-months visit – from these, only 1 exhibited a CBI-

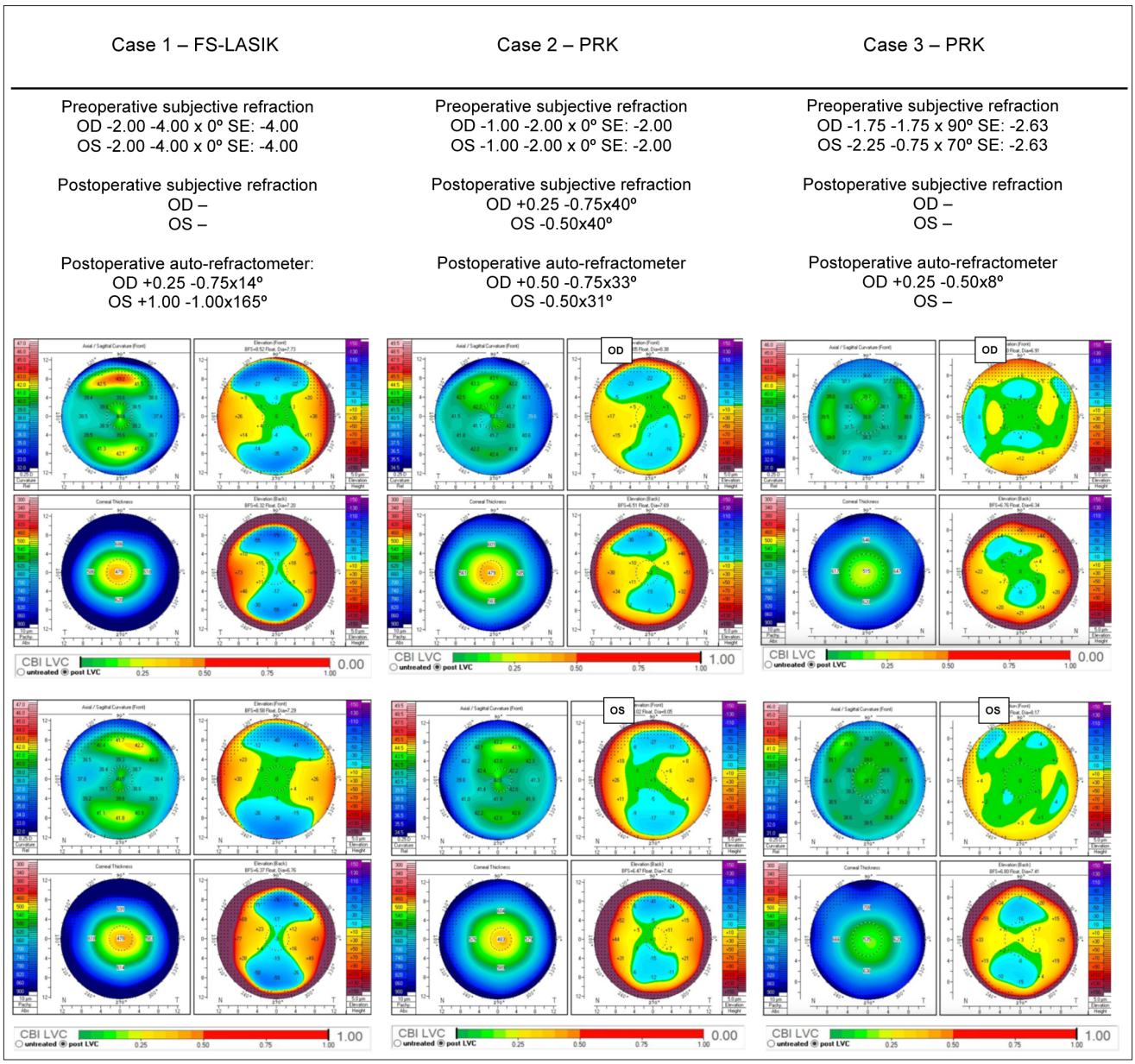

Figure 1. 24-month postoperative Pentacam 4-map refractive report of the right and left eyes of patients exhibiting a value of CBI-LVC over 0.2 in one eye. The four maps. Clockwise, from the top left include the sagittal power, anterior (front) elevation, and posterior (back) elevation. and pachymetry. At the bottom of each display, the 24-month postoperative CBI-LVC is presented.

LVC>0.2 at the end of follow-up. Additionally, 1 eye revealed CBI-LVC>0.2 (CBI-LVC=1.0) at the end of follow-up despite a value of 0 at the 6-months appointment.

A preoperative characterization of the 3 eyes exhibiting biomechanical ectasia features as measured through CBI-LVC is displayed in Table 4. None of the eyes involved had values suggesting higher ectasia risk for parameters evaluated preoperatively. In Fig. 1. we present the 4-map refractive display (Pentacam) of the 3 patients who exhibited a CBI-LVC>0.2 in one eye at the end of follow-up. The contralateral eye is included for comparison and the preoperative and postoperative refraction is displayed.

DISCUSSION

The risk of post-laser vision correction ectasia is a significant concern within the realm of refractive surgery. Progressive "iatrogenic" keratectasia after LASIK has been defined as increasing myopia, with or without increasing astigmatism, secondary loss of visual acuity and progressive corneal thinning and steepening after surgery.[14,15] Ectasia arises as a result of intricate interactions between both genetic, patient-intrinsic susceptibilities and external influences, including factors such as ocular trauma from eye rubbing and corneal surgical interventions. The incidence of corneal ectasia after LASIK is superior to that occurring after PRK[6,7] and has been documented at rates ranging from 0.033%[16] to 0.6% in earlier studies.[17,18] Thus, a thorough preoperative screening is needed to generate individualized risk profiles and provide comprehensive guidance for surgical planning.

In the course of our study, no cases of clinically relevant corneal ectasia were identified. Refractive outcomes, tomographic parameters and the CBI-LVC were assessed and taken as proxies for suspicious corneal features. Interestingly, from the patients who completed the 24-months follow-up, a total of 3 eyes retrieved a value of CBI-LVC over the established cut-off of 0.2 (2 in the group of PRK and 1 in the FS-LASIK group). The meaning of these results and whether these findings translate into the need for closer patient monitoring is the subject of this discussion.

The strategy of LASER procedure choice for correction of myopia and/or myopic astigmatism is patent in the preoperative evaluation of our sample. It is widely accepted that long-term uncorrected visual acuity, refractive accuracy and stability seem to be consistent across both techniques.[19,20] Several factors may lead refractive surgeons to favor PRK over LASIK, including a thin residual stromal bed, a predisposition to contact injury, mildly asymmetric topography, orbital or lid anatomy that hinder the use of the LASIK suction ring, a history of recurrent corneal erosions or anterior basement membrane dystrophy.[21] CCT is a critical aspect to consider in this decision-making process, although it remains a subject of significant controversy and varies in interpretation among surgeons.[21–24] Some suggest refraining from LASIK procedures when the central posterior residual bed is below 300 μm, and avoiding both PRK and LASIK when the final central corneal thickness falls below 400 μm.[21] In our center, FS-LASIK is not performed in corneas with a minimum pachymetry under 500 μm. PRK-treated patients in this study did have lower values of minimum pachymetry (527 (504 - 578) μm), which is in line with this choice of procedure in thinner corneas. The overall PTA of our sample was 0.27 (0.10 - 0.39), far from the value of 0.4, found to predict an increased ectasia risk.[25] The FS-LASIK-treated eyes group exhibited higher values, which, besides the flap thickness, can be attributed to the greater AD employed to correct higher refractive errors. The degree of refractive error correction in our sample is in line with other authors, which discourage LASIK or PRK corrections for myopia exceeding approximately 10.5 diopters of spherical equivalent or astigmatism greater than 6.00 diopters, although these limits are debatable.[21,26] Tomography-derived parameters in which our groups differed preoperatively included the ARTmax and BAD-D. ARTmax is a relative corneal thickness index, calculated as the thinnest pachymetric value (TP) divided by the maximal meridians of pachymetric progression and a value under 339 μm is considered indicative of keratoconus.[27] It was also proposed that a cut-off of 387μm could be used as a reference for the detection of subclinical ectasia.[28] The final D of the Belin/Ambrosio Enhanced Ectasia Display, which combines front and back elevation values with the pachymetric distribution, has a higher ectasia risk cut-off set at 1.6.[29] Interestingly, a value of D over 1.29 has been found to have good sensitivity and specificity in diagnosing ectasia susceptibility[30] PRK-treated eyes had a higher BAD-D and lower ARTmax in comparison to FS-LASIK eyes. While any excimer surface ablation procedure affects corneal biomechanics, the creation of a corneal flap appears to have a greater impact.[6,7] Our preference for PRK in cases where these parameters deviate from the normal range is driven by the aim to reduce potential corneal biomechanical instability. In the preoperative period, both the CBI and TBI were higher in the PRK-group. A higher proportion of PRK-treated eyes displayed a TBI over the cut-off of 0.29 for ectasia susceptibility (15,85% *vs* FS-LASIK: 5,8%).[29,31] Our previously described rationale for ARTmax and BAD-D also applies to biomechanical parameters deviation from normal range – the choice of PRK is favored when there are conflicting results or signs of ectasia susceptibility in specific parameters. In this study, we also retrospectively calculated the ectatic risk using Brain Cornea, which, in most instances, yielded reassuring results. However, over 20% of LASIK eyes had a value over 11.6%. For the moment, and for the best of the authors acknowledgment, there are no studies validating this tool, which limits our conclusions about values that fall off the recommended range. While it can enhance our prediction of ectatic risk, a high-risk value should always be considered along with other parameters and not be a sole contraindication for surgery. In the era of AI, the future of preoperative ectatic risk screening may involve highly precise predictive models that provide ophthalmologists with enhanced diagnostic capabilities.

Tables 2 and 3 relate to the variation of clinical, tomographic and biomechanical parameters along the entire

follow-up. In both treatment groups, BCVA improved between the 6-months' and 24-months' visits. The OSI was measured with a double-pass imaging system that objectively evaluates the intraocular scattering of light.[32] Lower values correspond to better quality of vision. In our sample, in both groups, this parameter did not vary significantly across our follow-up, showing maintenance of good postoperative visual quality. Regarding refractive outcomes, PRK-eyes had no variation in spherical, cylinder or SE power across postoperative time points. On the other hand, in the FS-LASIK group, both cylinder and SE powers increased towards the end of follow-up. This might relate to the variation found in keratometry values. FS-LASIK-treated eyes showed a slight but significant increase of both K1 and K2 from the 6- to 24-months postoperative visit. The slight increase in K1 and K2 in FS-LASIK eyes could be due to the phenomenon of refractive regression. Known to be more common after hyperopic LASIK treatments, due to the age-dependent effect of accommodative loss, post-LASIK myopic regression has long been thought to occur due to either the development of corneal ectasia or epithelial hyperplasia.[33] Following enhancements in preoperative refractive surgery screening, cases of myopic regression still occurred. These are hypothesized to result not from an overt corneal ectasia but instead from an anterior shift in the structurally altered cornea, coupled with epithelial hyperplasia.[33–35] This refractive regression appears to be higher in eyes with a higher preoperative ectatic risk, since a positive, yet weak, correlation was found between preoperative TBI values and mean keratometry variation (from 6- to 24 months postoperatively). However, to determine the clinical significance of this refractive regression and its correlation with TBI, further studies are needed to explore whether the current cut-off should be revisited. Of note, epithelial maps were not evaluated in these patients, therefore we cannot rule out the hypothesis of epithelial hyperplasia. In our study, we also found no variation in anterior surface indices provided by the Pentacam System. While these shouldn't be examined individually to assess preoperative ectasia risk, the values of our sample were within the normal range preoperatively and were comparable before surgery, maintaining stability from the postoperative period up to the end of follow-up. Taking into account all the factors previously stated, our refractive screening appears to have been successful, both in safety and stability.

The newest biomechanical index, CBI-LVC, was one of the main focuses of our study. It is an index that was validated to diagnose, instead of predicting, post-LVC ectasia.[13] We observed a total of 3 eyes (PRK: 2; FS-LASIK: 1) that had a CBI-LVC value >0.20 at the 6-month postoperative evaluation and that went under the cut-off in the 24-months evaluation. Conversely, a total of 3 eyes (PRK: 2; FS-LASIK: 1) had a CBI-LVC value >0.2 at the end of follow-up, and only 1 of these had already shown an altered value at the 6-month time point. These findings are unexpected because post-LVC ectasia, which is already infrequent, usually occurs after LASIK. On the one hand, we can hypothesize a measurement error is responsible for these results. If our results reveal to be reproducible in future evaluations it is plausible that unexamined biomechanical parameters may account for our findings. Particularly, we did not evaluate past or current eye-rubbing habits or past corneal trauma episodes that might have been overlooked by the patient. We also did not evaluate epithelial maps, which have been found by others to impact suitability for surgery, as well as surgical selection.[36] Finally, unknown genetic factors could be contributing, as there is strong evidence, they play a role in the etiology of ectatic corneal diseases such as keratoconus.[37] As Table 4 illustrates, these eyes didn't display concerning values during preoperative assessment. We retrospectively reviewed their 24-month postoperative Pentacam layouts. As can be seen in Fig. 1. the SE was similar between both eyes of the same patient and no substantial differences can be found between sagittal curvature power, anterior/posterior elevation and pachymetric maps. In light of this, we call into question whether a closer follow-up would have been needed before the 24-month mark. Since some eyes lost their risk value for this new parameter, and taking into account clinical and tomographic stability, this isolated factor may not justify closer appointments. Also, Randleman et al. have found cases of post-LASIK ectasia to occur at a mean time of 16.3 months (1-45 months) after surgery.[23] Thus, even because biomechanical changes may precede clinical or tomographic ectasia features (which is supported by fairly comparable maps in Fig. 1), it seems reasonable to consider a closer follow-up if a CBI-LVC suggests post-LVC ectasia several months (probably > 6 months) after surgery.

Limitations of our study include the retrospective design and the enrollment of both eyes of most patients included. However, it is important to point out our reasonable sample size and follow-up. Another limitation should be noted since the stromal ablation in PRK patients might have varied depending on whether the real epithelial thickness was less or more than the estimated average 50 μm. This is, to our knowledge, the first study to examine the CBI-LVC in a clinical setting.

In conclusion, our study underscores the importance of meticulous preoperative screening of patients seeking refractive surgery. It also validates the screening process we apply in our center, since our results exhibit clinical, tomographic and biomechanical stability (98.6% of eyes had a CBI-LVC <0.2). The incorporation of biomechanical assessment has emerged as a valuable adjunct, providing deeper insights into the structural integrity of the cornea. However, it's essential to acknowledge that, despite significant progress, we still grapple with the challenge of precisely assessing factors like CBI-LVC and determining exactly how should we change our practice accordingly.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

FB, CC, TC, ACA, SM: Responsible for gathering the data.

FB: Responsible for creating the manuscript.

CC, ACA, SM, MCB: Supervised this project and contributed with their expertise to its conclusion.

All authors read and approved the final manuscript.

FB, CC, TC, ACA, SM: Responsáveis pela recolha dos dados.

FB: Responsável pela criação do manuscrito.

CC, ACA, SM, MCB: Supervisionaram este projeto e contribuíram com os seus conhecimentos para a sua conclusão.

Todos os autores leram e aprovaram o manuscrito final.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

Provenance and Peer Review: Not commissioned; externally peer reviewed.

REFERENCES

1. Geggel HS. Delayed onset keratectasia following laser in situ keratomileusis. J Cataract Refract Surg. 1999;25:582-6. doi: 10.1016/s0886-3350(99)80060-1.
2. Rao SN, Epstein RJ. Early onset ectasia following laser in situ keratomileusus: Case report and literature review. J Refract Surg. 2002;18:177-84. doi: 10.3928/1081-597X-20020301-13.
3. Lifshitz T, Levy J, Klemperer I, Levinger S. Late bilateral keratectasia after LASIK in a low myopic patient. J Refract Surg. 2005;21:494-6. doi: 10.3928/1081-597X-20050901-12.
4. Seiler T, Koufala K, Richter G. Iatrogenic keratectasia after laser in situ keratomileusis. J Refract Surg. 1998;14:312-7. doi: 10.3928/1081-597X-19980501-15.
5. Esporcatte LPG, Salomão MQ, Neto AB da C, Machado AP, Lopes BT, Ambrósio R. Enhanced Diagnostics for Corneal Ectatic Diseases: The Whats, the Whys, and the Hows. Diagnostics. 2022;12:3027. doi: 10.3390/diagnostics12123027.
6. Belin MW, Ambrósio R. Enhanced Screening for Ectasia Risk prior to Laser Vision Correction. Diagnostics. 2022;12:3027. doi: 10.3390/diagnostics12123027.
7. Dupps WJ Jr, Wilson SE. Biomechanics and wound healing in the cornea. Exp Eye Res. 2006;83:709-20. doi: 10.1016/j.exer.2006.03.015.
8. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. Ophthalmology. 2008;115:37-50. doi: 10.1016/j.ophtha.2007.03.073.
9. Ambrósio R, Dawson DG, Salomão M, Guerra FP, Caiado ALC, Belin MW. Corneal ectasia after LASIK despite low preoperative risk: Tomographic and biomechanical findings in the unoperated, stable, fellow eye. J Refract Surg. 2010;26:906-11. doi: 10.3928/1081597X-20100428-02.
10. Bühren J, Schäffeler T, Kohnen T. Preoperative topographic characteristics of eyes that developed postoperative LASIK keratectasia. J Refract Surg. 2013;29:540-9. doi: 10.3928/1081597X-20130719-04.
11. Roberts CJ, Mahmoud AM, Bons JP, Hossain A, Elsheikh A, Vinciguerra R, et al. Introduction of two novel stiffness parameters and interpretation of air puff-induced biomechanical deformation parameters with a dynamic Scheimpflug analyzer. J Refract Surg. 2017;33:266-73. doi: 10.3928/1081597X-20161221-03.
12. Ambrósio, Jr R, Correia FF, Lopes B, Salomão MQ, Luz A, Dawson DG, et al. Corneal biomechanics in ectatic diseases: refractive surgery implications. Open Ophthalmol J. 2017;11:176-93. doi: 10.2174/1874364101711010176
13. Vinciguerra R, Ambrósio R, Elsheikh A, Hafezi F, Kang DS, Kermani O, et al. Detection of postlaser vision correction ectasia with a new combined biomechanical index. J Cataract Refract Surg. 2021;47:1314-8. doi: 10.1097/j.jcrs.0000000000000629.
14. Jin SX, Dackowski E, Chuck RS. Risk factors for postlaser refractive surgery corneal ectasia. Curr Opin Ophthalmol. 2020;31:288-92. doi: 10.1097/ICU.0000000000000662.
15. Seiler T, Quurke AW. Iatrogenic keratectasia after LASIK in a case of forme fruste keratoconus. J Cataract Refract Surg. 1998;24:1007-9. doi: 10.1016/s0886-3350(98)80057-6.
16. Bohac M, Koncarevic M, Pasalic A, Biscevic A, Merlak M, Gabric N, et al. Incidence and Clinical Characteristics of Post LASIK Ectasia: A Review of over 30.000 LASIK Cases. Semin Ophthalmol. 2018;33:869-77. doi: 10.1080/08820538.2018.1539183.
17. Randleman JB. Post-laser in-situ keratomileusis ectasia: Current understanding and future directions. Curr Opin Ophthalmol. 2006;17:406-12. doi: 10.1097/01.icu.0000233963.26628.f0.
18. Pallikaris IG, Kymionis GD, Astyrakakis NI. Corneal ectasia induced by laser in situ keratomileusis. J Cataract Refract Surg. 2001;27:1796-802. doi: 10.1016/s0886-3350(01)01090-2.
19. Gil JQ, Lobo C, Tavares C, Costa E, Rosa AM, Quadrado MJ, et al. Guidelines for Excimer Laser Refractive Surgery on Cornea. Oftalmologia. 2015;39:1-16.

20. Shortt AJ, Allan BDS, Evans JR. Laser-assisted in-situ keratomileusis (LASIK) versus photorefractive keratectomy (PRK) for myopia. Cochrane Database Syst Rev. 2013:CD005135. doi: 10.1002/14651858.CD005135.pub3.
21. Torricelli AA, Bechara SJ, Wilson SE. Screening of refractive surgery candidates for LASIK and PRK. Cornea. 2014;33:1051-5. doi: 10.1097/ICO.0000000000000171.
22. Bamashmus M, Saleh MF, Abdulrahman M, Al-Kershy N. Reasons for not performing LASIK in refractive surgery candidates in Yemen. Eur J Ophthalmol. 2010;20:858-64. doi: 10.1177/112067211002000508.
23. Randleman JB, Russell B, Ward MA, Thompson KP, Stulting RD. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology. 2003;110:267-75. doi: 10.1016/S0161-6420(02)01727-X.
24. Kymionis GD, Bouzoukis D, Diakonis V, Tsiklis N, Gkenos E, Pallikaris AI, et al. Long-term results of thin corneas after refractive laser surgery. Am J Ophthalmol. 2007;144:181-5. doi: 10.1016/j.ajo.2007.04.010. E
25. Santhiago MR, Smadja D, Gomes BF, Mello GR, Monteiro ML, Wilson SE, et al. Association between the percent tissue altered and post-laser in situ keratomileusis ectasia in eyes with normal preoperative topography. Am J Ophthalmol. 2014;158:87-95.e1. doi: 10.1016/j.ajo.2014.04.002.
26. Mohammadpour M. Risk for ectasia with LASIK. J Cataract Refract Surg. 2008;34:181-2; author reply 182-3. doi: 10.1016/j.jcrs.2007.10.019.
27. Ambrósio R, Caiado ALC, Guerra FP, Louzada R, Roy AS, Luz A, et al. Novel pachymetric parameters based on corneal tomography for diagnosing keratoconus. J Refract Surg. 2011;27:753-8. doi: 10.3928/1081597X-20110721-01.
28. Ambrósio R, Machado AP, Leão E, Lyra JMG, Salomão MQ, Esporcatte LGP, et al. Optimized artificial intelligence for enhanced ectasia detection using scheimpflug-based corneal tomography and biomechanical Data. Am J Ophthalmol. 2023;251:126-42. doi: 10.1016/j.ajo.2022.12.016.
29. Baptista PM, Marta AA, Marques JH, Abreu AC, Monteiro S, Menéres P, et al. The role of corneal biomechanics in the assessment of ectasia susceptibility before laser vision correction. Clin Ophthalmol. 2021;15:745-58. doi: 10.2147/OPTH.S296744.
30. Ambrósio R, Ramos I, Lopes B, Canedo ALC, Correa R, Guerra F, et al. Assessing ectasia susceptibility prior to LASIK: The role of age and residual stromal bed (RSB) in conjunction to Belin-Ambrósio deviation index (BAD-D). Rev Bras Oftalmol. 2014;73:75-80.
31. Ambrósio R, Lopes BT, Faria-Correia F, Salomão MQ, Bühren J, Roberts CJ, et al. Integration of scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg. 2017;33:434-43. doi: 10.3928/1081597X-20170426-02.
32. Vieira R, Marta A, Abreu AC, Monteiro S, Do Céu Brochado M. Quality of Vision After LASIK, PRK and FemtoLASIK: An Analysis Using the Double Pass Imaging System HD AnalyzerTM®. Clinical Ophthalmology. 2022;16.
33. Kim G, Christiansen SM, Moshirfar M. Change in keratometry after myopic laser in situ keratomileusis and photorefractive keratectomy. J Cataract Refract Surg. 2014;40:564-74. doi: 10.1016/j.jcrs.2013.09.016.
34. Kamiya K, Miyata K, Tokunaga T, Kiuchi T, Hiraoka T, Oshika T. Structural analysis of the cornea using scanning-slit corneal topography in eyes undergoing excimer laser refractive surgery. Cornea. 2004;23:S59-64. doi: 10.1097/01.ico.0000136673.35530.e3.
35. Miyata K, Tokunaga T, Nakahara M, Ohtani S, Nejima R, Kiuchi T, et al. Residual bed thickness and corneal forward shift after laser in situ keratomileusis. J Cataract Refract Surg. 2004;30:1067-72. doi: 10.1016/j.jcrs.2003.09.046.
36. Asroui L, Dupps WJ, Randleman JB. Determining the utility of epithelial thickness mapping in refractive surgery evaluations. Am J Ophthalmol. 2022;240:125-34. doi: 10.1016/j.ajo.2022.02.021.
37. Loukovitis E, Sfakianakis K, Syrmakesi P, Tsotridou E, Orfanidou M, Bakaloudi DR, et al. Genetic aspects of keratoconus: a literature review exploring potential genetic contributions and possible genetic relationships with comorbidities. Ophthalmol Ther. 2018;7:263-92. doi: 10.1007/s40123-018-0144-8.

Corresponding Author/
Autor Correspondente:

Francisca Bragança
Largo Prof. Abel Salazar,
4099-001 Porto, Portugal
E-mail: franciscabraganca@hotmail.com

ORCID: 0000-0002-6702-6622