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Detection of postlaser vision correction ectasia with a new combined biomechanical index

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Purpose: To validate and evaluate the use of a new biomechanical index known as the Corvis biomechanical index–laser vision correction (CBI-LVC) as a method for separating stable post-LVC eyes from post-LVC eyes with ectasia.

Setting: 10 clinics from 9 countries.

Design: Retrospective, multicenter, clinical study.

Methods: The study was designed with 2 purposes: to develop the CBI-LVC, which combines dynamic corneal response (DCR) parameters provided by a high-speed dynamic Scheimpflug camera (CorVis ST; OCULUS Optikgeräte GmbH) and then to evaluate its ability to detect post-LVC ectasia. The CBI-LVC includes integrated inverse radius, applanation 1 (A1) velocity, A1 deflection amplitude, highest concavity and arclength, deformation amplitude ratio of 2 mm, and A1 arclength in millimeters. Logistic regression with Wald forward stepwise approach was used to identify the optimal combination of DCRs to create the CBI-LVC and then separate stable from LVC-induced ectasia. Eighty percentage of the database was used for training the software and 20% for validation.

Results: 736 eyes of 736 patients were included (685 stable LVC and 51 post-LVC ectasia). The receiver operating characteristic curve analysis showed an area under the curve of 0.991 when applying CBI-LVC in the validation dataset and 0.998 in the training dataset. A cutoff of 0.2 was able to separate stable LVC from ectasia with a sensitivity of 93.3% and a specificity of 97.8%.

Conclusions: The CBI-LVC was highly sensitive and specific in distinguishing stable from ectatic post-LVC eyes. Using CBI-LVC in routine practice, along with topography and tomography, can aid the early diagnosis of post-LVC ectasia and allow intervention prior to visually compromising progression.

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Laser vision correction (LVC) surgery with LASIK, photorefractive keratectomy (PRK), and Small-incision lenticule extraction (SMILE) are widely accepted procedures to correct refractive defects such as myopia, hyperopia, and astigmatism with an excellent safety profile.[1] A rare but feared complication of LVC (mostly LASIK but also reported after PRK and SMILE) is iatrogenic ectasia that deforms the cornea and causes significant visual loss.[2–4]

The incidence of ectasia after LASIK, which is the most commonly seen, is undetermined but has been

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reported to be between 0.04% and 0.2%.[5–7] The prevention/detection of this dramatic complication is a significant concern for refractive surgeons.[8] Early detection of post-LVC ectasia is critical, given the possibility to promptly treat these patients with crosslinking to stabilize the cornea.[9]

Much of the focus on postlaser vision correction ectasia has been on prevention with the identification of many intraoperative risk factors linked to an increase in the likelihood of post-LVC ectasia, including the following: increased flap thickness, using a microkeratome to create the flap, a high percentage tissue altered, and low residual stromal bed, although the sensitivity of the latter factor has been reported to be very low.[10–12] For this reason, many researchers have focused on preoperative characteristics that can increase post-LVC ectasia risk, particularly the need for more careful assessment of topography, tomography, and corneal epithelial maps.[13] The evaluation of corneal biomechanical properties is also increasingly used as a key part of the screening process to identify patients who have an increased susceptibility to develop iatrogenic ectasia after LVC.[14] Recent studies have also shown the importance of corneal biomechanics in the diagnosis of keratoconus, even in the early stages as for many it represents the primum movens in the development of the disease.[15–17]

These advancements in preoperative assessment have dramatically improved LVC safety record. However, indices such as the CBI and the TBI, which showed high sensitivity and specificity, were not created to detect when ectasia develops after refractive surgery.[15,16] The aim of this retrospective analysis study was to develop a new combined biomechanical index (CBI-LVC) based on the Dynamic Corneal Response parameters provided by the CorVis ST (OCULUS Optikgeräte GmbH) designed to separate stable corneas post-LVC from post-LVC ectasia.

MATERIALS AND METHODS

Population

Seven hundred thirty-six eyes of 736 patients were included in this retrospective multicenter study. The patients were included from 10 different clinics to include variability from different continents and to substantially increase the number of patients (particularly with post-LVC ectasia, which is a rare complication) and test the ability of the CBI-LVC in different ethnic groups. Each Institutional Review Board either ruled that approval was not required for this record review study (exempt category) or specifically approved the study. The research was conducted according to the tenets of the 1964 Declaration of Helsinki, revised in 2000. Subjects (or parents in case of pediatric subjects) provided written informed consent before using their data in the study. The participating centers were as follows: Humanitas Clinical Research Centre, Milan, Italy; ELZA Institute, Dietikon/Zurich, Switzerland; Center for Refractive Surgery Muenster, Muenster, Germany; Augenklinik am Neumarkt, Cologne, Germany; Eye Care, Miami, Florida; Department of Ophthalmology, the Federal University of the State of Rio de Janeiro (UNIRIO), Rio de Janeiro, Brazil; School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, China; Eyereum Eye Clinic, Seoul, Korea; Department of Ophthalmology, Osaka University Graduate School of Medicine, Osaka, Japan; Department of Cornea & Refractive Surgery, Medical Research Foundation, Chennai, India.

The enrolled patients were as follows: Group 1: post-LVC eyes that were stable for at least 24 months; Group 2: eyes with ectasia that developed after laser vision correction after at least 2 years postoperatively.

The planned ratio between cases (post-LVC ectasia) and controls (stable post-LVC) was determined to be at least 1:10, which was based on the published value of increasing the control-to-case ratio beyond 5 when P_0 (prevalence of ectasia, in this case) is expected to be less than about 0.15 (ectasia is 0.02%).[18] Stable post-LVC patients (PRK, LASIK, and SMILE were included) had no signs of progression/regression after LVC, with stable refraction and typical topography and tomography as confirmed by a masked examiner (R.V.). All patients in this group had a minimum of 2-year stable follow-up, which was defined as follows: No increase in posterior elevation of more than 10 mm in differential map; no increase in anterior curvature in sagittal map of more than 1.00 diopter (D) in differential map; no decrease in pachymetry of more than 20 μm in differential map; and no change in refraction of more than 1.00 D in spherical equivalent. Stability was also confirmed by one masked cornea expert (R.V., P.V., or R.A.) who evaluated postoperative maps.

Post-LVC ectasia was classified based on the evaluation of topography and tomography over time and a history of proven progression over a minimum of 3 months and worsening after refractive surgery. The definition was based on the occurrence of at least 2 of 4 of the following parameters based on published definitions of ectasia plus the confirmation of 2 corneal experts: Inferior topographic steepening of 5.00 D over time or more[5]; progressive focal steepening of more than 1.50 D in sagittal map[19]; decrease in uncorrected distance visual acuity of 2 or more lines on the Snellen chart[5]; and refractive change of 2.00 D or more of spherical equivalent.[20]

All cases in this group were confirmed by at least 2 experts, masked examiners (R.V., P.V., or R.A.). All patients had their examinations (including CorVis) before any treatment for ectasia was planned, such as corneal crosslinking (CXL). Similar to stable post-LVC cases, all patients with ectasia had their CorVis examinations after a minimum of 2 years post-LVC surgery. Exclusion criteria included any previous ocular surgery (including CXL) or disease and any concomitant or previous glaucoma or hypotonic therapies. All patients had a thorough ophthalmic examination, comprising the CorVis ST and Pentacam HR or Pentacam HR/AXL (OCULUS Optikgeräte GmbH) examinations.

CorVis ST Measurements

Only CorVis ST and Pentacam examinations with good quality scores that enabled calculation of all deformation and tomographic parameters were included in the analysis. All examinations with the CorVis ST were obtained by experienced technicians and captured by automatic release to ensure the absence of user dependency.

One eye per patient was randomly included in the analysis to exclude the bias of the relationship between bilateral eyes that could influence the result. Randomization was performed using the randomization module in the SPSS software package.

Dynamic Corneal Response Parameters

The CorVis ST elicits a set of Dynamic Corneal Response parameters (DCRs software, v. 6.08r22) based on the monitoring of the dynamic corneal response to air pressure. The DCRs that are currently part of the native software of the CorVis were previously described.[16,21,22] The logistic regression analysis (described further) selected the following DCRs: applanation 1 velocity (A1vel),

integrated inverse radius, applanation 1 deflection amplitude (A1Deflamplitude), highest concavity and applanation 1 arclength (HCArclength and A1Arclength, respectively), and deformation amplitude ratio (DAratio). All parameters used are described in Table 1.

Statistical Analysis

The statistical analysis was performed with SPSS Statistics for Windows software (v. 25.0, IBM Corp.). Receiver operating characteristic (ROC) curves were used to define the overall predictive accuracy of single DCRs and their combination, which is described as an area under the curve (AUC). The ROC curves were obtained by plotting sensitivity vs specificity and calculated for each value observed. An area of 100% implied that the test perfectly discriminates between groups.

As a first step, all 39 DCRs provided by the software (v. 6.08r22) of the CorVis ST were exported. Logistic regression with a forward stepwise approach was used to identify the optimal combination of parameters. Wald method was used to include parameters stepwise. (This method is based on a test for inclusion based on the significance of the score statistics and on a test for exclusion based on Wald statistics.) Of these 39 parameters, 6 DCRs were used for the creation the CBI-LVC. Eighty percentage of the database was randomly selected and used for training (database 1) and 20% for validation (database 2) to check for overfitting. Optimal cutoff points of the CBI-LVC were obtained from the ROC curves as those closest to the perfect classification point.

RESULTS

A total of 736 eyes of 736 patients were included. The mean age of the patients was 32.9 ± 12.3 years. It was 33.0 ± 12.1 years in the training dataset and 32.7 ± 12.6 years in the validation dataset. The mean Kmax and mean thinnest point were 54.20 ± 8.00 D and 435.7 ± 45.8 µm for ectasia patients post-LVC and 43.60 ± 1.70 D and 459.7 ± 44.9 µm for stable patients post-LVC, respectively. Table 2 tabulates the number of patients in each group, broken down by type of treatment: SMILE, LASIK, and PRK. There was no statistically significant difference ($P > .05$) regarding baseline characteristics between the training and validation datasets (age, sex, and ethnicity).

CBI-LVC

The stepwise logistic regression based on database 1 (training dataset) produced the following formula:

$$\text{CBI-LVC} = \text{EXP}\ (\text{Beta})/(1 + \text{EXP}(\text{Beta}))$$

where

$$\text{Beta} = \text{C1} * \text{integrated inverse radius} + \text{C2} * \text{A1vel} + \text{C3} * \text{A1Deflamplitude} + \text{C4} * \text{HCArclength} + \text{C5} * \text{DAratio 2 mm} + \text{C6} * \text{A1Arclength} + \text{C7}$$

and

$$\text{C1} = 5.2832,\ \text{C2} = -206.0078;\ \text{C3} = 390.0877,\ \text{C4} = -105.5705,\ \text{C5} = 1.8487,\ \text{C6} = 170.455,\ \text{and C7} = -79.899$$

Values of all constants used in the equation were highly significant ($P < .01$).

The ROC analysis of the training dataset (database 1) showed an AUC of 0.998 (Figure 1). The sensitivity and specificity were calculated on 2 different cutoff values: 0.2 and 0.5, which were chosen as best compromises between sensitivity and specificity. In database 1, a cutoff value of 0.5 provided a sensitivity of 91.7% and a specificity of 99.3%, whereas a cutoff of 0.2 showed a sensitivity of 100% and a specificity of 97.3%. The validation dataset (database 2) displayed an AUC of 0.991, and the cutoff value of 0.5 provided a sensitivity of 86.7% and a specificity of 98.5%, whereas a cutoff of 0.2 showed a sensitivity of 93.3% and a specificity of 97.8% (Figure 1).

DISCUSSION

The diagnosis of post-LVC ectasia (caused by LASIK, PRK, or SMILE) is a challenging task for refractive and cornea surgeons. Once ectasia is diagnosed, prompt crosslinking should be indicated to stop further progression.[8,9,23,24]

There are many indirect and direct ways to detect ectasia after refractive surgery, such as instability of refractive correction, subsequent regression, and progressive steepening and/or thinning.[19,25,26] Unfortunately, these well-established indicators are subjective, and they have the disadvantage of requiring proof of the deterioration of refraction and topography/tomography maps. In addition, the indicators that are used for preoperative screening are not helpful postrefractive surgery. Most of these indices are designed for the preoperative detection of KC and ectasia susceptibility

Table 1. Dynamic Corneal Response Parameters of CorVis ST Included for the Creation of the CVI-LVC.

Applanation velocity 1	Velocity of the cornea at the moment of first applanation (m/s).
Integrated inverse radius	This parameter is calculated based on the inverse concave radius curve. The inverse concave radius (1/R) is plotted over the duration of the air pulse, and the integrated sum (integrated inverse radius) is calculated between the first and second applanation events.
Applanation 1 deflection amplitude	Largest displacement of corneal apex in the anterior–posterior direction at the moment of first applanation.
Highest concavity arclength	Measurement (in mm) of the arclength at the moment of highest concavity
Applanation 1 arclength	Measurement (in mm) of the arclength at the moment of applanation 1
Deformation amplitude ratio	Describes the ratio between the deformation amplitude at the apex and the average deformation amplitude measured at 1 from the center

CBI-LVC = Corvis biomechanical index–laser vision correction

Table 2. Patients with Stable and Ectasia Post-LVC Previously Treated With LASIK, SMILE, or PRK.

No. of eyes	Post-LVC stable	Post-LVC ectasia
LASIK	145	50
SMILE	357	0
PRK	183	1
Total	685	51

LVC = laser vision correction; PRK = photorefractive keratectomy

(such as KISA score, BAD-D, CBI, and TBI) and, for this reason, are unable to distinguish between KC and post-refractive surgery, commonly appearing abnormal. In fact, corneas after LVC are thinner and flatter than normal and are classified as abnormal by these algorithms.

Because of this lack of an objective method for the detection of post-LVC ectasia, diagnosis is frequently made either when the disease is advanced or with the use of differential maps that show thinning, steepening, and increased elevation in a localized area. The drawback of this approach is that the patient must progress before being diagnosed and indicated for treatment with CXL.

As with keratoconus, in post-LVC ectasia, the changes in corneal biomechanics are believed to take place before any changes to refraction, topography, tomography, and epithelial maps are detectable. It is for these reasons that an assessment of corneal biomechanics may help in the early detection of this rare complication. Based on this, the aim of this multicenter study was to create and validate a biomechanical index with the goal of separating post-LVC ectasia from stable post-LVC with a large dataset.

The database included more than 700 subjects from 10 countries and 4 continents to consider possible variability in ethnic groups and to obtain a reasonable number of untreated post-LVC ectasia (because post-LVC ectasia is a relatively rare complication and patients are typically treated promptly with CXL, making these patients ineligible for inclusion). In addition, the size of the database allowed the validation of the indices and the exclusion of overfitting.

The main outcome of the study was the creation of the CBI-LVC, an index aimed to separate stable post-LVC patients from those with ectasia regardless of the type of LVC surgery performed. The study was a 2-stage process: first, the optimum combination of parameters for the CBI-LVC was defined. Second, its diagnostic capability was assessed.

The multivariate diagnostic model showed an AUC of more than 0.990 in both the validation and training datasets. We assessed 2 different cutoff points for the CBI-LVC: 0.2 and 0.5, which were chosen as best compromises between sensitivity and specificity. In the validation dataset, a cutoff of 0.5 provided a sensitivity of 86.7% and a specificity of 98.5%, whereas a cutoff of 0.2 showed a sensitivity of 93.3% and a specificity of 97.8%.

To the authors' knowledge, this is the first time that an index has achieved such a high level of sensitivity and specificity in separating stable post-LVC from post-LVC ectasia. Even if CBI-LVC sounds similar to the published CBI,[16] this newly created index is not an evolution of the CBI because it aims to diagnose a different disease (CBI-LVC ectasia after LVC and CBI keratoconus).

It is important to note that the CBI-LVC is purely a biomechanical index as it involves only biomechanical parameters and does not include shape or pachymetry indices (such as minimum pachymetry, ARTh, or simulated keratometry). This is a significant advantage as CBI-LVC would be less affected if the ectasia is developing in a thin or relatively thick cornea or if the cornea is steep or flat.

Currently, there are no validated indices to diagnose post-LVC ectasia in either subclinical or advanced stages. Randleman et al. suggested the diagnosis of ectasia as an inferior steepening of more than 5.00 D in postoperative topographic map, loss of 2 or more lines of visual acuity, and a change in manifest refraction of 2.00 D of either spherical or cylindrical power.[6] Another report by Twa et al. suggested 3 or 4 positive findings of 9 criteria, which included refractive, pachymetry, and topographic data that could be used to represent the clinical characteristics of post-LASIK.[27] Padmanabhan et al. also created a stratification model for the diagnosis of ectasia based on corrected distance visual acuity, refractive spherical equivalent, highest posterior elevation, spherical aberration, and anterior corneal surface asphericity.[19] These reports rely on relatively small databases with weak or no validation of the proposed diagnostic criteria.

As ectasia can develop up to 9 years postoperatively, this study did not prove the ability of the CBI-LVC to quantify corneal susceptibility to post-LVC ectasia or predict ectasia over the long-term.[28,29] Long-term studies are necessary to evaluate whether patients with high CBI-LVC but normal tomography will develop topographical and tomographical signs of ectasia.

The main strengths of this study are, first, the use of a validation dataset, which is of primary importance when assessing the accuracy of an index created with logistic regression to exclude overfitting. In addition, this study included a large number of patients, particularly with post-LVC ectasia (to the authors' knowledge, it is the largest number of included patients including biomechanical analysis). The main limitations of the study are the retrospective design and the lack of long-term follow-up after the

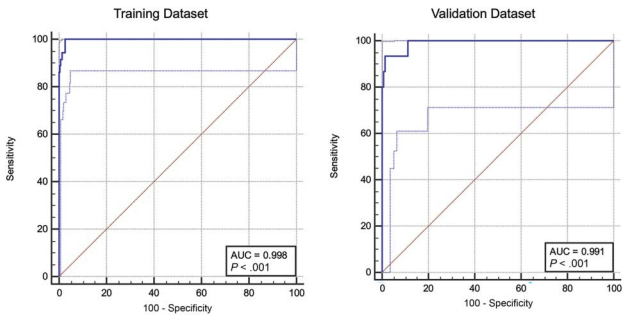

Figure 1. Showing the receiver operating characteristic (*solid line*) and 95% CI for receiver operating characteristic curve (*broken lines*) of the training dataset and validation datasets of the Corvis biomechanical index–laser vision correction applied to separate stable from ectasia postlaser vision correction.

refractive surgery in the stable group (minimum 2 years). With more years of follow-up and the presence of an early biomechanical assessment, it could be evaluated whether the CBI-LVC is able to predict ectasia even when the shape of the cornea is normal. In this study, only patients with clear ectasia were included. Currently, the CBI-LVC should not be seen as a tool to predict later development of post-LVC ectasia but rather as an index to diagnose it.

In conclusion, our study introduces the CBI-LVC for the diagnosis of post-Laser Vision Correction ectasia, which was shown to be highly sensitive and specific to separate stable from patients with post-LVC ectasia. The presence of a large external validation dataset confirmed the findings and recommended the use of CBI-LVC in everyday clinical practice, together with topography and tomography, to support the diagnosis of post-LVC ectasia.

WHAT WAS KNOWN

- Ectasia after laser vision correction (LVC) is a rare but severe disease that can cause significant visual loss.
- Standard ways to detect ectasia after refractive surgery are instability of refractive correction and subsequent regression, progressive steepening, and thinning.
- Similar to keratoconus, in post-LVC ectasia, the changes in corneal biomechanics are believed to appear earlier than refractive, topographic, tomographical, and epithelial maps changes are detectable.

WHAT THIS PAPER ADDS

- A new combined biomechanical index named Corvis biomechanical index–LVC is introduced for the diagnosis of post-LVC ectasia, which was shown to be highly sensitive and specific to separate patients with stable eyes from patients with post-LVC ectasia.

REFERENCES

1. Kim TI, Alio Del Barrio JL, Wilkins M, Cochener B, Ang M. Refractive surgery. Lancet 2019;393:2085–2098
2. Rao SN, Epstein RJ. Early onset ectasia following laser in situ keratomileusus: case report and literature review. J Refract Surg 2002;18:177–184
3. Giri P, Azar DT. Risk profiles of ectasia after keratorefractive surgery. Curr Opin Ophthalmol 2017;28:337–342
4. Rabinowitz YS. Ectasia after laser in situ keratomileusis. Curr Opin Ophthalmol 2006;17:421–426
5. Randleman JB. Post-laser in-situ keratomileusis ectasia: current understanding and future directions. Curr Opin Ophthalmol 2006;17:406–412
6. Randleman JB, Russell B, Ward MA, Thompson KP, Stulting RD. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology 2003;110:267–275
7. Rad AS, Jabbarvand M, Saifi N. Progressive keratectasia after laser in situ keratomileusis. J Refract Surg 2004;20:S718–S722
8. Ambrosio R Jr. Post-LASIK ectasia: twenty years of a conundrum. Semin Ophthalmol 2019;34:66–68
9. Wan Q, Wang D, Ye H, Tang J, Han Y. A review and meta-analysis of corneal cross-linking for post-laser vision correction ectasia. J Curr Ophthalmol 2017;29:145–153
10. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. Ophthalmology 2008;115:37–50
11. Ambrosio R Jr, Dawson DG, Belin MW. Association between the percent tissue altered and post-laser in situ keratomileusis ectasia in eyes with normal preoperative topography. Am J Ophthalmol 2014;158:1358–1359
12. Santhiago MR, Smadja D, Gomes BF, Mello GR, Monteiro ML, Wilson SE, Randleman JB. 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 e81
13. Santhiago MR, Giacomin NT, Smadja D, Bechara SJ. Ectasia risk factors in refractive surgery. Clin Ophthalmol 2016;10:713–720
14. Koh S, Ambrosio R Jr, Inoue R, Maeda N, Miki A, Nishida K. Detection of subclinical corneal ectasia using corneal tomographic and biomechanical assessments in a Japanese population. J Refract Surg 2019;35:383–390
15. Ambrosio R Jr, Lopes BT, Faria-Correia F, Salomao MQ, Buhren J, Roberts CJ, Elsheikh A, Vinciguerra R, Vinciguerra P. Integration of Scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg 2017;33:434–443
16. Vinciguerra R, Elsheikh A, Roberts CJ, Ambrósio JR, Sung Yong Kang D, Lopes B, Morenghi E, Azzolini C, Vinciguerra P. Detection of keratoconus with a new Corvis ST biomechanical index. J Refract Surg 2016;32:803–810
17. Vinciguerra R, Ambrosio R Jr, Roberts CJ, Azzolini C, Vinciguerra P. Biomechanical characterization of subclinical keratoconus without topographic or tomographic abnormalities. J Refract Surg 2017;33:399–407
18. Hennessy S, Bilker WB, Berlin JA, Strom BL. Factors influencing the optimal control-to-case ratio in matched case-control studies. Am J Epidemiol 1999;149:195–197
19. Padmanabhan P, Rachapalle Reddi S, Sivakumar PD. Topographic, tomographic, and aberrometric characteristics of post-LASIK ectasia. Optom Vis Sci 2016;93:1364–1370
20. Zhang M, Zhang F, Li Y, Song Y, Wang Z. Early diagnosis of keratoconus in Chinese myopic eyes by combining Corvis ST with Pentacam. Curr Eye Res 2019;45:118–123
21. Vinciguerra R, Elsheikh A, Roberts CJ, Ambrosio R Jr, Kang DS, Lopes BT, Morenghi E, Azzolini C, Vinciguerra P. Influence of pachymetry and intraocular pressure on dynamic corneal response parameters in healthy patients. J Refract Surg 2016;32:550–561
22. Roberts CJ, Mahmoud AM, Bons JP, Hossain A, Elsheikh A, Vinciguerra R, Vinciguerra P, Ambrosio R Jr. Introduction of two novel Stiffness parameters and interpretation of air puff-induced biomechanical deformation parameters with a dynamic Scheimpflug analyzer. J Refract Surg 2017;33:266–273
23. Randleman JB, Stulting RD. Ectasia after photorefractive keratectomy. Ophthalmology 2007;114:396; author reply 396-397
24. Moshirfar M, Albarracin JC, Desautels JD, Birdsong OC, Linn SH, Hoopes PCSr. Ectasia following small-incision lenticule extraction (SMILE): a review of the literature. Clin Ophthalmol 2017;11:1683–1688
25. Kanellopoulos AJ, Asimellis G. Refractive and keratometric stability in high myopic LASIK with high-frequency femtosecond and excimer lasers. J Refract Surg 2013;29:832–837
26. Yan MK, Chang JS, Chan TC. Refractive regression after laser in situ keratomileusis. Clin Exp Ophthalmol 2018;46:934–944
27. Twa MD, Nichols JJ, Joslin CE, Kollbaum PS, Edrington TB, Bullimore MA, Mitchell GL, Cruickshanks KJ, Schanzlin DJ. Characteristics of corneal ectasia after LASIK for myopia. Cornea 2004;23:447–457
28. Bohac M, Koncarevic M, Pasalic A, Biscevic A, Merlak M, Gabric N, Patel S. Incidence and clinical characteristics of post LASIK ectasia: a review of over 30,000 LASIK cases. Semin Ophthalmol 2018;33:869–877
29. Hafezi F, Koller T, Derhartunian V, Seiler T. Pregnancy may trigger late onset of keratectasia after LASIK. J Refract Surg 2012;28:242–243

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