Association Between the Percent Tissue Altered and Post–Laser In Situ Keratomileusis Ectasia in Eyes With Normal Preoperative Topography

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• PURPOSE: **To investigate the association of a novel metric, percent tissue altered, with the occurrence of ectasia after laser in situ keratomileusis (LASIK) in eyes with normal corneal topography and to compare this metric with other recognized risk factors.**

• DESIGN: **Retrospective case-control study.**

• METHODS: **The study included 30 eyes from 16 patients with bilateral normal preoperative Placido-based corneal topography that developed ectasia after LASIK (ectasia group) and 174 eyes from 88 consecutive patients with uncomplicated LASIK and at least 3 years of postoperative follow-up. The following metrics were evaluated: age, preoperative central corneal thickness, residual stromal bed, Ectasia Risk Score System scores, and percent tissue altered, derived from [PTA = (FT + AD)/CCT], where FT = flap thickness, AD = ablation depth, and CCT = preoperative central corneal thickness.**

• RESULTS: **In the ectasia group, percent tissue altered ≥40 was the most prevalent factor (97%), followed by age < 30 years (63%), residual stromal bed ≤300 μm (57%), and ectasia risk score ≥3 (43%) (*P* < .001 for all). Percent tissue altered ≥40 had the highest odds ratio (223), followed by residual stromal bed ≤300 μm (74) and ectasia risk score ≥4 (8). Stepwise logistic regression revealed percent tissue altered ≥40 as the single most significant independent variable (*P* < .0001).**

• CONCLUSIONS: **Percent tissue altered at the time of LASIK was significantly associated with the development of ectasia in eyes with normal preoperative topography and was a more robust indicator of risk than all other variables in this patient population. (Am J Ophthalmol 2014;158:87–95. © 2014 by Elsevier Inc. All rights reserved.)**

While most patients who have developed ectasia after laser in situ keratomileusis (LASIK) have, in retrospect, had identifiable risk factors, particularly irregular topographic patterns, that placed them at higher risk for this complication, ectasia cases in patients with normal preoperative topography still present a conundrum.[1–5] Postoperative corneal ectasia most likely represents a reduction in biomechanical integrity below the threshold required to maintain corneal shape and curvature. This could theoretically occur when a cornea already destined to manifest ectasia has surgery, when a preoperatively weak but clinically stable cornea has surgery, or when a relatively normal cornea is weakened below a safe threshold.

As corneal tensile strength is not uniform throughout the central corneal stroma, with a progressive weakening in the deeper 60%,[6–10] the relative extent of biomechanical alteration after refractive surgery, expressed as depth, definitely plays a role in postoperative weakening. Flap thickness factors directly into this alteration, as the anterior lamellar flap does not contribute significantly to postoperative corneal tensile strength.[11–13]

There is an integrated relationship between preoperative corneal thickness, ablation depth, and flap thickness in determining the relative amount of biomechanical change that has occurred after a LASIK procedure.[14,15] We have investigated a metric, the percent of anterior tissue depth altered, that describes this interaction[14] during excimer laser refractive surgery, which for LASIK can be described as:

$$PTA = (FT + AD)/CCT$$

where PTA = percent tissue altered, FT = flap thickness, AD = ablation depth, and CCT = preoperative central corneal thickness. This metric may more accurately represent the risk of ectasia than the individual components that comprise it.

The purpose of this study was to investigate the association of the percent tissue altered with the occurrence of ectasia after LASIK in eyes with normal preoperative Placido disk–based corneal topography and to compare this metric to other recognized risk factors.

Accepted for publication Apr 1, 2014.

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0002-9394/$36.00
http://dx.doi.org/10.1016/j.ajo.2014.04.002

METHODS

THIS RETROSPECTIVE COMPARATIVE CASE-CONTROL study included eyes that developed ectasia after LASIK for myopia and myopic astigmatism with bilateral normal preoperative Placido disk–based corneal topography identified in the authors' institutions (ectasia group), and a contemporaneous population composed of eyes with bilateral normal preoperative Placido disk–based corneal topography that underwent uncomplicated LASIK for myopia and myopic astigmatism at 1 author's institution (M.R.S.) without developing ectasia with at least 3 years of postoperative follow-up (control group). The study was approved by the Federal University of Rio de Janeiro Institutional Review Board (IRB) and the Emory University IRB before the study began and was conducted in adherence with the tenets of the Declaration of Helsinki.

The following preoperative information was obtained for both ectasia and control cases: patient age; sex; preoperative central corneal thickness (CCT) based on ultrasound pachymetry; Placido disk–based color corneal topography; manifest refraction spherical equivalent (MRSE) in diopters (D); and best spectacle-corrected distance visual acuity (CDVA). Perioperative and postoperative information included date of surgery (year), LASIK flap thickness (measured), calculated central ablation depth, and calculated residual stromal bed thickness (CCT − measured flap thickness − calculated central ablation depth). LASIK flap measurements were taken intraoperatively with ultrasound pachymetry using the subtraction method or postoperatively with optical coherence tomography (OCT) or confocal microscopy. Specific cut-off values of recognized risk factors were identified for comparative purposes. These included individual metrics used in the Ectasia Risk Score System: patient age in years (<30), CCT (≤510 μm), residual stromal bed (≤300 μm), and preoperative myopia (≥8 D). We also calculated the original Ectasia Risk Score System[3] summed values for each group.

The percentage of anterior tissue depth altered during LASIK was obtained from the equation: Percent Tissue Altered = (Flap Thickness + Ablation Depth)/preoperative Central Corneal Thickness. Percent tissue altered was calculated for all eyes in the study and represents the percentage of anterior tissue that is modified during LASIK refractive surgery.

For this study, normal preoperative topography was defined as regular and symmetric patterns (including round, oval, or symmetric bowtie patterns) or mildly asymmetric (steepening ≤0.5 D and without a skewed radial axis) based on Placido disk analysis.[3] All patients included had bilateral normal Placido-based topographic patterns preoperatively.

Postoperative corneal ectasia was defined as progressive inferior steepening, increasing myopia, and astigmatism; loss of uncorrected visual acuity; and often loss of best-corrected acuity (CDVA).[2] All ectasia patients included in the analysis had uneventful surgery with initially good outcomes prior to developing the aforementioned findings.

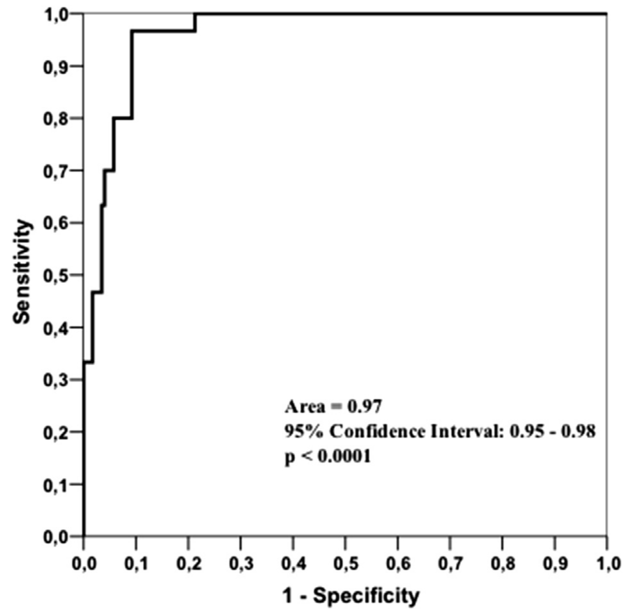

FIGURE 1. Receiver operating characteristic curve of the percent tissue altered for post–laser in situ keratomileusis (LASIK) ectasia risk analysis. A cut-off value of 40% provided the maximum combination of sensitivity (97%) and specificity (89%) to discriminate between post-LASIK ectasia cases and controls.

Inclusion criteria for both ectasia and control cases included having all relevant necessary preoperative and perioperative information for analysis. Eyes that developed ectasia with abnormal preoperative Placido disk–based color topography were excluded from this study. Topographically normal fellow eyes of eyes that had abnormal patterns were excluded. Patients with significant between-eye topographic asymmetry or family history of keratoconus were excluded.

Statistical analyses were performed using JMP software (version 8.0; SAS Institute, Inc, Cary, North Carolina, USA). While percent tissue altered is a continuous variable, it was also evaluated as a discontinuous risk factor (cut-off) variable using 40 based on analysis of receiver operating characteristic (ROC) curve, which revealed a cut-off of 40.0 as the value with the maximized sum of sensitivity (97%) and specificity (89%), shown in Figure 1 and Table 1. Odds ratio values and the 95% confidence interval were calculated. The odds ratio represents the odds that an outcome will occur given a particular factor (risk factor, in case odds ratio >1, or protective factor, in case odds ratio <1), compared to the odds of the outcome occurring in the absence of that factor. Logistic stepwise regression was performed to investigate the significance as predictors of the event (ectasia). Normality of data was evaluated

TABLE 1. Receiver Operating Characteristic Table for Percent Tissue Altered Values Related to Post-LASIK Ectasia Risk for This Study Population

Cut-off Percent Tissue Altered Value (%)	Sensitivity (%)	Specificity (%)
48	27	100
47	33	100
46	33	98
45	53	97
44	63	96
43	77	94
42	87	91
41	90	91
40[a]	97	89
39	97	87
38	97	83
37	97	82
36	97	79
35	100	72
34	100	64

[a]The results of this table are derived from receiver operating characteristic (ROC) curve, and revealed a cut-off of 40% as the value with the maximized sum of sensitivity and specificity; PTA = Percent Tissue Altered (Flap Thickness + Ablation Depth)/Central Corneal Thickness.

with the Kolmogorov-Smirnov test. When parametric analysis was not possible the nonparametric Wilcoxon analysis was used to compare data between the 2 groups. The analysis of primary outcome measures was based on a non-normal distribution of the data. When parametric analysis was possible, the Student *t* test was used to compare the outcomes. Categorical variables were compared using either χ^2 or the Fisher test as appropriate. To correct for multiple comparisons performed in this study (Bonferroni method), only *P* values less than .007 were considered significant. Continuous data were expressed as mean values ± standard deviation and confidence interval. Categorical variables were expressed as frequency (n) and percent (%).

RESULTS

THE STUDY POPULATION INCLUDED 30 EYES FROM 16 patients in the ectasia group and 174 eyes from 87 consecutive patients in the control group. Ectasia cases had LASIK between 2002 and 2010; control cases had LASIK between 2008 and 2010, with a minimum of 3 years of uneventful follow-up. Table 2 shows the demographic data of eyes that developed ectasia with normal preoperative topography. In the ectasia group, 14 patients (28 eyes) developed ectasia bilaterally, while 2 (Cases 5 and 6) developed unilateral ectasia after bilateral LASIK. The fellow eyes of Cases 5 and 6 that did not develop ectasia presented percent tissue altered values of 38 and 37, respectively.

• **PATIENT VARIABLES: COMPARISON OF MEANS:** Percent tissue altered was significantly higher in patients with ectasia and normal topography compared to controls (Figure 2). Table 3 shows the comparison of a variety of preoperative variables between ectasia and control groups. Each variable was significantly different between populations. Analyzing the ectasia group, the mean measured flap thickness values (149.5 ± 23.2) were not statistically significant different than predicted flap thickness values (141.0 ± 17.8, *P* = .099).

• **PREVALENCE OF RISK FACTORS:** In the ectasia group (30 eyes), percent tissue altered ≥40 was the most prevalent evaluated variable (29 eyes, 97%), followed by age <30 (19 eyes, 63%), residual stromal bed ≤300 (17 eyes, 57%), and Ectasia Risk Score System ≥3 (13 eyes, 43%). Figure 3 highlights the prevalence of each of the risk variables considered as probable risk factors in the ectasia group. Table 4 shows the comparison of prevalence of each potential risk factor between the ectasia group and the control group. When comparing the prevalence of risk factors between ectasia and control groups, percent tissue altered ≥40, age <30, residual stromal bed ≤300, and Ectasia Risk Score System values ≥3 and Ectasia Risk Score System values ≥4 prevalence were significantly different. Prevalence of CCT ≤510 and MRSE ≥8 D were not significantly different between the groups.

• **ODDS RATIOS:** As seen in Table 3, percent tissue altered presented the highest odds ratio (including confidence interval), followed by residual stromal bed ≤300 μm, Ectasia Risk Score System ≥4, age <30, Ectasia Risk Score System ≥3, MRSE ≥8 D, and CCT ≤510 μm. However, CCT and MRSE included 1 in the confidence interval. For risk factors, residual stromal bed ≤260 μm and CCT ≤480 μm odds ratio could not be calculated because no patients of the control group presented the risk factor.

• **LOGISTIC STEPWISE REGRESSION:** Between ectasia cases and controls, the prevalence of percent tissue altered ≥40, residual stromal bed ≤300 μm, age <30, Ectasia Risk Score System values ≥4, and Ectasia Risk Score System values ≥3 all were significantly different, whereas MRSE −8 D or more and CCT ≤510 μm were not. To evaluate these factors further, a stepwise logistic regression analysis was performed. Using this approach, percent tissue altered ≥40 first and then residual stromal bed ≤300 μm remained independent significant variables (*P* < .0001); however, the other factors investigated were not significant independent predictors of ectasia in these analyses.

DISCUSSION

THIS AGGREGATE ANALYSIS PROVIDES EVIDENCE THAT THE percent tissue altered after LASIK is a significant factor in

TABLE 2. Post-LASIK Ectasia Study Population Patient Demographics

Case	Age (y)	Sex	MRSE	Preoperative CCT (μm)	Flap Thickness (μm)	Flap Creation Method	Tissue Ablated (μm)	RSB (μm)	ERSS	PTA
1	27	F	−5.33	542	161	MK	80	300	1	45
2	27	F	−5.00	540	164	MK	75	301	1	44
3	32	F	−6.37	524	141	FS	95.5	288	1	45
4	32	F	−6.37	522	143	FS	95.5	287	1	45
5	23	M	−6.07	532	160	FS	91	281	3	47
6	39	M	−7.80	568	177	MK	117	274	2	52
7	34	M	−8.67	541	162	MK	130	249	4	54
8	34	M	−8.67	540	130	MK	130	280	2	48
9	50	F	−7.47	580	150	MK	112	318	0	45
10	50	F	−6.80	580	150	MK	102	328	0	43
11	28	F	−7.00	529	160	MK	105	264	3	50
12	28	F	−6.47	526	159	MK	97	270	3	49
13	27	M	−5.93	512	131	FS	89	292	2	43
14	27	M	−4.80	529	140	FS	72	317	1	40
15	26	M	−7.53	540	153	MK	113	274	3	49
16	26	M	−7.00	540	122	MK	105	313	1	42
17	29	F	−4.93	588	186	MK	74	328	1	44
18	29	F	−5.93	594	180	MK	89	325	1	45
19	27	M	−3.00	550	201	MK	45	304	1	45
20	27	M	−3.07	546	189	MK	46	311	1	43
21	26	M	−7.75	525	130	MK	84	311	1	41
22	26	M	−9.00	530	130	MK	105	295	4	44
23	30	M	−5.63	527	140	MK	80	307	1	42
24	30	M	−6.75	509	150	MK	94	265	3	48
25	21	F	−5.63	497	170	MK	88	239	9	52
26	21	F	−4.63	480	155	MK	71	254	7	47
27	21	M	−4.75	529	125	MK	101	303	3	43
28	21	M	−5.25	522	120	MK	65	337	3	35
29	30	M	−6.00	498	110	MK	98	290	4	42
30	30	M	−5.50	500	110	MK	91	299	4	40

CCT = central corneal thickness; ERSS = Ectasia Risk Score System; FS = femtosecond laser; MK = mechanical microkeratome; MRSE = manifest refraction spherical equivalent (presented in diopters); PTA = percent tissue altered; RSB = residual stromal bed.

the development of ectasia after LASIK in eyes with normal preoperative Placido disk–based topography. Compared to other variables, percent tissue altered had higher prevalence, higher odds ratio, and higher predictive capabilities for ectasia risk than moderate to high Ectasia Risk Score System values, as well as the individual factors from that system, including residual stromal bed, central corneal thickness, spherical equivalent refraction, ablation depth, and age. This is the first study specifically investigating the concept of percent tissue altered and its role in post-LASIK ectasia.

The main explanation for this finding most likely lies in the relative percentage contribution of the anterior stroma to the total corneal strength, which is modified after excimer laser refractive surgery, derived from the flap thickness creation and the ablation depth combined, since the flap itself provides no significant biomechanical contribution.[11–13] Since the cohesive tensile strength is not uniform throughout the central corneal stroma and the anterior 40% of the corneal stroma has significantly greater cohesive tensile strength,[6] removing this relevant part of the stroma may induce corneal weakening in increasing proportion as the threshold of 40% is reached and crossed. As compared to specific residual stromal bed or CCT values, percent tissue altered likely provides a more individualized measure of biomechanical alteration because it considers the relationship between thickness, tissue altered through ablation and flap creation, and ultimate residual stromal bed thickness.

This study demonstrated that percent tissue altered was much more sensitive than the absolute value of the residual stromal bed itself in predicting the risk of ectasia. This may partially explain why ectasia has occurred in corneas with normal thickness and normal expected residual stromal bed, even with normal topography before LASIK, if the combination of these factors resulted in a high percent tissue altered.

A recent study by Reinstein and associates[16] indirectly supports the role of percent tissue altered as the primary factor for predicting postoperative corneal biomechanical

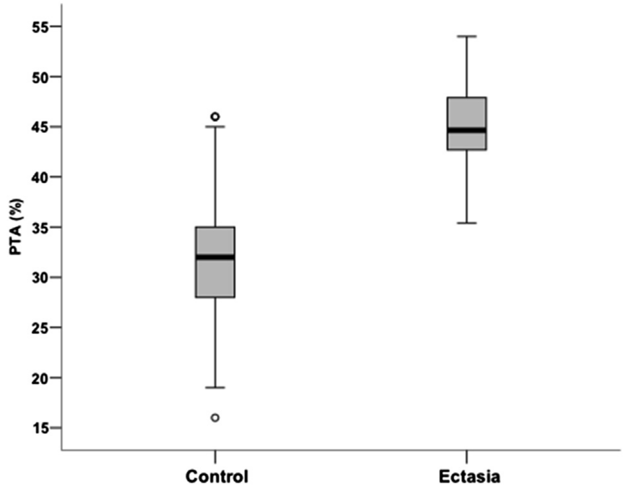

FIGURE 2. Box-plot graph of the percent tissue altered comparing the post–laser in situ keratomileusis (LASIK) ectasia group and controls. The bar inside each box represents the median and each box extends from the 25th percentile to the 75th percentile of the distribution in each group. The median of the percent tissue altered (PTA) values of the ectasia group is significantly higher than the control group ($P < .0001$) and the ectasia group has a tighter data spread than the control group.

properties after LASIK, photorefractive keratectomy, and small-incision lenticule extraction. In their mathematical model, the authors showed that the amount of anterior corneal tissue altered was more significant than residual stromal bed owing to the inherent differences in tissue strength. In their model they demonstrated that the thicker the cap for small-incision lenticule extraction (and therefore the deeper the lenticular tissue removal), and hence the lower the residual stromal bed thickness, the greater the residual tensile strength should be. This is, however, only a mathematical model at this time and requires direct testing to evaluate its accuracy.

The results of our study do corroborate residual stromal bed, central corneal thickness, and the amount of tissue ablated as independent risk factors for ectasia in varying degrees; however, rather than as an absolute value, they appear more important as part of the equation that ultimately generates the percentage of tissue depth altered after surgery. That is probably why absolute values and cut-off numbers for residual stromal bed have historically failed in determining the high-ectasia-risk patients. The results of our study also revealed that the measured central flap thickness was not thicker than estimated in most eyes developing ectasia after LASIK. This finding is agreement with the study published by Randleman and associates[17] that concludes that on average, the flap thickness is within what was predicted in eyes that developed ectasia.

The concept of the percent tissue altered may also be relevant in previous reports of both cases where ectasia developed despite paucity of risk factors and cases with uneventful outcomes despite having LASIK with some risk factor present. Table 5 lists recent case reports[5,18–21] of patients developing ectasia despite minimal risk factors. In each of these cases, percent tissue altered was significantly higher than 40. Analysis of older studies reporting ectasia in patients with normal topography[22,23] also corroborates the role of percent tissue altered on corneal ectasia after LASIK, with mean percent tissue altered values higher than 46%[22] and 48%.[23] However, these results should be viewed with greater caution owing to the inconsistencies in available data, especially in cases where both eyes were not available for analysis and when flap thickness was not available. In addition to these reports, Spadea and associates[24] investigated ectasia in a large series and, although the topographies are not available for review, when analyzing the eyes that were regarded by the authors as having normal preoperative topography the mean percent tissue altered value was 49.7%. Bühren and associates[25] investigated preoperative topographic characteristics of eyes that developed postoperative LASIK ectasia and present no classic patterns of subclinical keratoconus. Although the topographies are not strictly normal, the mean percent tissue altered value for the group was 46.6%.

In contrast, reports of successful LASIK in patients with thin corneas inversely support the role of percent tissue altered in ectasia risk. Table 6 lists recent studies[26–28] investigating safety of LASIK in thin corneas that have sufficient data published to calculate percent tissue altered; in each of these reports, even though the authors were not specifically using the percent tissue altered equation, the mean percent tissue altered value was significantly lower than 40 and therefore was most likely within the safety limits for LASIK even in thin corneas. With surface ablation the chances of having percent tissue altered greater than 40 are quite low, and studies have also shown that surface ablation is safe to treat either high corrections or thin corneas[26–30] (Table 6).

As evidenced by this study, the changes induced by the combination of the flap thickness and the ablation depth have a significant impact on corneal biomechanical properties.[14] Preoperative ectatic corneal disease, whether subtle or dramatic, clearly also has important biomechanical alterations that affect the suitability for LASIK. It seems logical that percent tissue altered will have different impact in screening eyes with more demonstrable topographic irregularities, since those corneas are by definition already showing evidence of abnormal weakening prior to any ablation, and that a biomechanical instability could occur in that group even when a lower threshold of percent tissue altered is surpassed or even without any surgery.

In this study, 19 of 174 control eyes (11%) also had percent tissue altered of 40 or higher. This finding highlights that some overlap between cases and controls in the primary variable evaluated may occur. It also demonstrates that, as a risk factor, the weakening predicted by a

TABLE 3. Comparison of Age and Corneal Thickness Alteration After LASIK Characteristics Between Post-LASIK Ectasia and Control Populations

Parameter	Post-LASIK Ectasia Cases[a] Mean Values ± SD (95% Confidence Interval)	Control Cases[b] Mean Values ± SD (95% Confidence Interval)	*P* Value (Wilcoxon Test)
Percent tissue altered (%)	45.1 ± 3.9 (43.6–46.6)	31.9 ± 5.8 (31.1–32.8)	<.0001[c]
Residual stromal bed (μm)	293.4 ± 24.8 (284.0–302.7)	378.4 ± 41.5 (372.2–384.6)	<.0001[c]
Flap thickness (μm)	149.9 ± 23.2 (141.3–158.6)	114.2 ± 15.6 (111.8–116.5)	<.0001[c]
Ablation depth (μm)	89.1 ± 21.6 (81.1–97.2)	63.6 ± 30.9 (58.9–68.2)	<.0001[c]
MRSE (diopters)	6.0 ± 1.6 (5.4–6.6)	4.2 ± 2.1 (3.9–4.5)	<.0001[c]
Central corneal thickness (μm)	534.6 ± 26.9 (524.6–544.7)	556.2 ± 31.3 (551.5–560.9)	.0005[c]
Age (y) (range)	29.3 ± 6.9 (26.7–31.9)	37.4 ± 10.0 (35.9–38.9)	<.0001[c]

MRSE = manifest refraction spherical equivalent.
[a]Ectasia cases: Eyes developing ectasia after laser in situ keratomileusis with normal preoperative topography.
[b]Control cases: Consecutive group of eyes that underwent uneventful laser in situ keratomileusis with at least 3 years follow-up.
[c]Statistically significant difference.

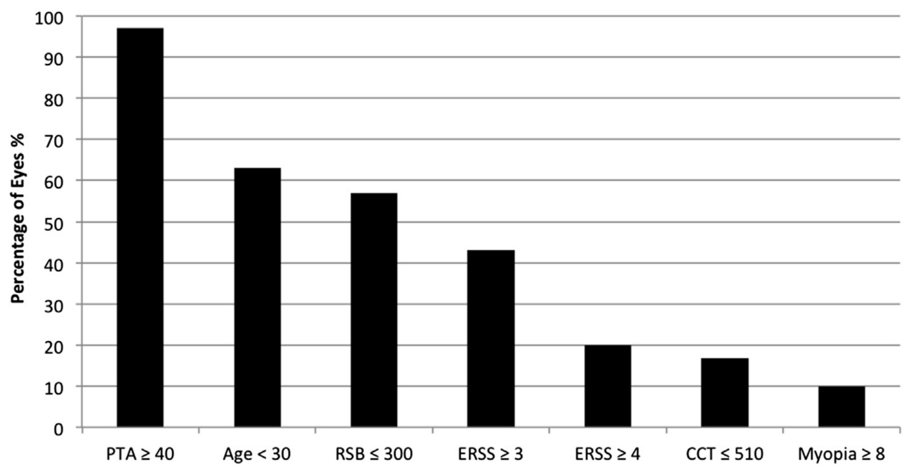

FIGURE 3. Relative prevalence of the individual variables investigated as possible ectasia risk factors in the post–laser in situ keratomileusis (LASIK) ectasia group. The percent tissue altered (PTA) ≥40 was by far the most prevalent risk factor (97%), followed by age < 30 years (63%), residual stromal bed (RSB) ≤300 μm (57%), Ectasia Risk Score System (ERSS) value ≥3 (43%), ERSS value ≥4 (20%), preoperative central corneal thickness (CCT) ≤510 μm (16%), and myopia ≥8 diopters (10%).

high percent tissue altered or any other factor does not mean ectasia will occur in all high-risk eyes; it merely means that these eyes carry increased risk for ectasia. Given the elective nature of LASIK, it seems logical that the balance of risk acceptance should be weighted toward minimizing risk, especially when other excellent procedures are available for refractive correction.[31]

Although it has been shown that most ectasia cases occur within the first 18 months after surgery,[3] the fact that it has not happened after 3 years (36 months) in our control group does not completely exclude the possibility of that event occurring in the future. Still, we considered it a reasonable follow-up time for the purposes of the study, given the difficulty in observing large numbers of successful LASIK cases over time owing to limited patient follow-up.

This study relied on Placido-based analysis for corneal evaluation. Other testing technologies are available and have been used for patient screening, including Scanning-slit,[32] Scheimpflug,[33] dual Scheimpflug,[34,35] and optical coherence tomography.[36] These technologies are widely available and used in many clinical practices, including our own. However, although each of these technologies has shown promise, none to date have proven to be more effective or reliable at detecting keratoconus suspect features than Placido imaging. In a recent study by Bae and associates,[37] the authors evaluated patients with what they termed unilateral keratoconus and compared these to a normal population. They found that anterior curvature metrics were the most robust discriminators between normal and suspect eyes and that most thickness, anterior, and posterior elevation metrics were unable to distinguish suspect eyes from normal, suggesting that anterior curvature changes may be the first detectable metric. We hope that future comparative analyses will provide a better

TABLE 4. Prevalence of Individual Proposed Ectasia Risk Factors in Post-LASIK Ectasia and Control Eyes

Risk Factor	Post-LASIK Ectasia Group	Control Group	*P* Value	Odds Ratio	Confidence Interval	Sensitivity	Specificity	Negative Predictive Value
PTA[a] ≥40%	97%	11%	<.0001[b]	223.3	(28.8–1729.7)	97%	89%	99.4%
RSB ≤300 μm	57%	2%	<.0001[b]	74.5	(19.3–287.7)	57%	98%	92.9%
CCT ≤510 μm	16%	6%	.065	2.9	(0.9–9.2)	16%	93%	86.7%
ERSS ≥4	20%	3%	.001[b]	8.4	(2.4–29.8)	20%	97%	87.5%
ERSS ≥3	43%	12%	.0002[b]	5.3	(2.2–12.3)	43%	87%	89.9%
MRSE ≥8 D	10%	7%	.547	1.5	(0.4–5.7)	10%	93%	85.7%
Age (y) <30	63%	24%	<.0001[b]	5.4	(2.4–12.3)	63%	75%	92.3%

CCT = central corneal thickness; D = diopters; ERSS = Ectasia Risk Score System; MRSE = manifest refractive spherical equivalent; PTA = percent tissue altered; RSB = residual stromal bed.

Ectasia group is composed of ectasia cases after laser in situ keratomileusis with normal preoperative topography and control group is composed of consecutive uneventful laser in situ keratomileusis eyes with at least 3 years follow-up.

[a]Percent Tissue Altered = (Flap Thickness + Ablation Depth)/preoperative Central Corneal Thickness.

[b]Difference statistically significant.

TABLE 5. Calculated Percent Tissue Altered Values From Published Studies of Post-LASIK Ectasia Cases With Normal Preoperative Topography

Study	Corneal Topography	Preoperative CCT (μm)	Flap Thickness (μm)	Tissue Ablated (μm)	RSB (μm)	ERSS	PTA[c] (%)
Klein et al[5,a]	Normal	556	140	119	297	1	46
Saad et al[18]	Normal	555	157	92	306	0	45
Saad et al[18]	Normal	575	149	116	310	0	46
Ambrósio et al[19,b]	Normal	532	160	97	275	2	48
Ambrósio et al[19,b]	Normal	528	165	81	282	2	46
Goncalves et al[20]	Normal	543	160	101	281	4	48
Goncalves et al[20]	Normal	564	160	104	301	3	47
Alió et al[21]	Normal	558	114	191	253	6	54
Alió et al[21]	Normal	560	114	193	253	7	55

CCT = central corneal thickness; ERSS = Ectasia Risk Score System; PTA = percent tissue altered; RSB = residual stromal bed.

[a]Case number 3 from Klein's study.

[b]The right eye never had surgery but would have been considered at high risk as well.

[c]Percent Tissue Altered = (Flap Thickness + Ablation Depth)/preoperative Central Corneal Thickness.

TABLE 6. Calculated Percent Tissue Altered Values From Published Studies Reporting Safety of LASIK or Surface Ablation in Thin Corneas

Study	Preoperative CCT (μm)	Tissue Altered (μm)	PTA
Djodeyre et al[26]	462	123	26
Kymionis et al [27]	485	140	29
Tomita et al[28]	487	166	34
Alió et al[29]	500	104	20
Djodeyre et al[26]	458	110	24
Kymionis et al[27]	482	114	23
de Benito-Llopis et al[30]	481	80	16

CCT = central corneal thickness; PTA = percent tissue altered.

understanding of the relative and combined utility of these devices in patient screening.

There are certain limitations to this study. Because this was a retrospective study, the data available were limited, which limited the number of cases that could be analyzed. Epithelial thickness measurements were not obtained to give a completely accurate analysis of stromal tissue altered. Epithelial thickness may play a small role in percent tissue altered measurements. Normal epithelial thickness does not vary significantly by overall corneal thickness, so the relative stroma altered in any percent tissue altered measurement will increase slightly (generally less than 1%) with increasing corneal thickness. Further, there are significant differences in epithelial thickness profiles between keratoconic and normal corneas[38–41] and there may be significant differences in epithelial thickness between normal corneas and keratoconus suspects, although this has yet to be substantiated. However, since this study population investigated only preoperatively normal corneas, and the variation of epithelium thickness in normal individuals is minimal, we believe the epithelium layer would not have a significant influence in this analysis. Additional tomographic information was not available and was therefore not analyzed. This was not the purpose of this study; however, future work with a data set containing data to determine percent tissue altered in addition to other proposed screening metrics would further elucidate the importance of percent tissue altered in screening. The relationship between percent tissue altered and other screening metrics, including patient age and topographic patterns, remains to be determined and will be the focus of future work.

In conclusion, the results of our study provide scientific evidence of the association of percent tissue altered with post-LASIK ectasia in eyes with normal corneal topography, and therefore this measure should be taken into account as a screening parameter for refractive surgery candidates.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported. Supported in part by an unrestricted Emory University Department of Ophthalmology departmental grant from Research to Prevent Blindness, Inc, New York, New York, USA (grant number P30 EYO6360). Contributions of authors: design and conduct of the study (M.R.S., J.B.R.); collection (M.R.S., B.F.G., G.R.M., M.L.R.M., J.B.R.), management (M.R.S., D.S., J.B.R.), analysis (M.R.S., S.E.W., J.B.R.), and interpretation of the data (M.R.S., J.B.R.); and preparation (M.R.S., D.S., B.F.G., M.L.R.M., S.E.W., J.B.R.), review (M.R.S., S.E.W., J.B.R.), or approval of the manuscript (M.R.S., S.E.W., J.B.R.).

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Biosketch

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