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Analysis of best corrected visual acuity following corneal refractive surgery comparing low and standard predicted postoperative keratometry

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ANALYSIS OF BEST CORRECTED VISUAL ACUITY FOLLOWING CORNEAL REFRACTIVE SURGERY COMPARING LOW AND STANDARD PREDICTED POSTOPERATIVE KERATOMETRY

by

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ABSTRACT

BACKGROUND: It is a commonly held view in the ophthalmologic community that eyes with sufficiently low calculated postoperative corneal keratometry, less than 35 diopters, should not undergo corrective refractive laser surgery (CRLS) due to the increased risk of best corrected visual acuity (BCVA) loss. Typical CRLS include Laser In-Situ Keratomileusis (LASIK), Photorefractive Keratectomy (PRK), and Laser-Assisted Sub-Epithelial Keratectomy (LASEK). Evidence for this claim in currently available literature is sparse and inconsistent.

PURPOSE: To further elucidate the relationship between calculated "flat" postoperative corneal keratometry and loss of BCVA. Additionally, to investigate the role of procedure type (LASIK, ASA, or LASEK) and degree of calculated postoperative corneal flatness on visual outcomes following CRLS.

METHODS: 222 eyes (111 candidates and 111 controls) were retrospectively analyzed and matched based on calculated postoperative keratometry compared to control subgroups with calculated postoperative keratometries ≥38 D and further stratified into subgroups 1b (K=38-38.99 D), 2b (K=39-39.99 D), 3b (K=40-40.9 9D), and 4b (K≥41 D). All of the

eyes had undergone LASIK, PRK, or LASEK between December 2008 and November 2016 at Boston Eye Group/Boston Laser in Brookline, MA.

RESULTS: Statistical analyses showed no significant differences between candidates and controls in preoperative BCVA (p=0.650) and postoperative BCVA (p=0.081). Subgroup matching showed no significant differences in the amount of tissue ablated in 1a & 1b (p=0.946), 2a & 2b (p=0.694), 3a & 3b (p=0.989), and 4a & 4b (p=0.986). There was also no significant change between preoperative and postoperative BCVA in subgroups 1a (p=0.367), 2a (p=0.297), 3a (p=0.576), 4a (p=0.669), 1b (p=0.458), 2b (p=0.227), 3b (p=0.071), or 4b (p=0.703). 3 of 111 (2.70%) candidate eyes and 1 (0.90%) control eye lost 1+ lines of BCVA following surgery. There was no statistical difference in 1+ lines of BCVA lost between these groups (p=0.313). Similarly, the type of CRLS undergone did not affect the rate of BCVA line loss (p=0.793).

CONCLUSION: Our evidence suggests that in a matched comparison of flat and normal mathematically predicted postoperative keratometries, there was no increase in BCVA lost due to flat keratometry.

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LIST OF ABBREVIATIONS

ASA	Advanced Surface Ablation
BCVA	Best Corrected Visual Acuity
CDVA	Corrected Distance Visual Acuity
CRLS	Corneal Refractive Laser Surgery
D	Diopter
GH	Games-Howell
LASEK	Laser Epithelial Keratomileusis
LASIK	Laser In-Situ Keratomileusis
LVC	Laser Vision Correction
PRK	Photorefractive Keratectomy
SE	Spherical Equivalence
VA	Visual Acuity

INTRODUCTION

In recent decades refractive surgery has become a safe, proven, and effective alternative to spectacles and contact lenses in the treatment of myopia, also known as "nearsightedness". [13] Myopia occurs when light entering the eye is bent too strongly and focuses at a point in front of the retina. The retina is a layer at the back of the eye which transmits the visual information it reads to the brain. As light converges before it reaches the retina, things near to a myope will be clear but things in the distance will be less so. Myopia is believed to be caused by a number of factors, ranging from genetics to axial length.[21]

Refractive Surgery

Refractive surgery is a group of procedures that correct for refractive error. Surgery typically involves the cornea, but may also involve the lens. The cornea lies at the front of the eye and is comprised of three main sections: the eyelid facing epithelium, the central stroma, and the inner endothelium. Each of these layers serves a distinct functional role. The regenerating epithelium protects the stroma from abrasion due to the eyelid and other environmental factors. The thick central stroma is comprised largely of connective tissue (keratocytes, nerves and dendritic cells), and largely defines the shape of the cornea as a whole. The endothelium is a single-layer membrane that separates the stroma from the anterior chamber of the eye and is not regenerative.[5] Refractive surgery allows for the corrections of myopia by changing the shape of the stroma, which in turn changes how light is refracted towards the retina.

There are 3 common refractive surgical procedures: LASIK (Laser In Situ Keratomileusis), LASEK (Laser Epithelial Keratomileusis), and PRK (Photorefractive Keratectomy). In an excimer laser-based refractive procedure an appropriate prescription is shaped from the patient's corneal stroma to compensate for their existing refractive error. In order to access the stromal layer, the epithelium is either lifted surgically (LASIK and LASEK) or removed chemically (PRK). Whether lifted or removed, the area of epithelium altered is typically a 4.5mm radius from the center of the cornea.[8] It is important not to remove a much wider radius than this, as it is possible to interfere with the stem cells that regrow the epithelium located at the corneal limbus. The corneal limbus is the intersection of the cornea and the sclera. A typical adult cornea has a diameter of about 11.7mm indicating that the limbus resides at a radius of about 5.85mm from the corneal center.[16]

The most common refractive surgeries (LASIK, LASEK, and PRK) have near equivalent outcomes after stabilization,[3,8,22] and differ solely in how they remove the epithelium in order to access the stroma. Once the stroma is accessed, an excimer laser is used to alter its shape. The exact alteration is determined from the appropriate manifest refraction and the laser platform. In traditional refractive surgery the cornea is simply treated with the manifest refraction, centered on the pupil. Recent excimer laser platforms allow custom-wavefront and wavefront-guided surgery. Wavefront-based systems measure light as it travels through the eye in order to reduce aberrations caused by an individual's eye irregular shape. These systems give better visual acuity (VA) and outcomes when compared to traditional treatments.[12] In LASIK, the cornea is suctioned to give a flat surface, and then a "flap" of epithelium is cut from the cornea at a depth of 100-140μm.[9]

Since the corneal epithelium is typically about 50μm[5] this results in a flap that is both epithelium and stroma. The flap is cut with either a femtosecond laser or a microkeratome. The bladeless laser-based femtosecond technique has gained popularity in recent years, largely due to its safety and more consistent flap accuracy.[7,14] LASEK also creates a flap, but in a different manner than LASIK. In LASEK, the epithelium is loosened with a solution (such as 20% ethanol) and the epithelium is lifted as a hinged sheet. There is less postoperative pain when compared to PRK, but it takes a similar amount of time for vision to stabilize. In PRK there is no flap made. Instead the epithelium is chemically removed, usually with an alcohol or similar solvent. It can also be removed mechanically with a blade or rotating alger brush.[22] A metal trephine is pressed by the surgeon onto the cornea and the solvent is placed into the well for a short amount of time, generally less than one minute. Then it is washed away with copious amounts of saline and the newly pliable epithelium is removed with a small surgical sponge. This leaves a smooth surface ready for excimer laser treatment.[2]

"Flat" Corneal Keratometry

In the ophthalmology community it is a commonly-held belief that if excimer laser treatment of myopia reduces the curvature of the central cornea beyond a specific range, there may be a loss in achievable visual acuity.[23] This range has historically been defined as a postoperative keratometry value of <35 diopter (D).

Multiple investigations have examined the relationship between preoperative keratometry values and visual acuity following myopic laser vision correction. In 2001 Rao

et al.[15] studied preoperative keratometry from 103 myopic LASIK patients and compared it to their postoperative visual acuity. All patients were considered highly myopic, with manifest spherical equivalence (SE) ranging from -6.0 to -13.0 D. Regression analyses found that in eyes with similar preoperative manifest, eyes with "flatter" keratometry (<43.5 D) were more likely to contain residual prescription post-surgery compared to eyes with "steeper" keratometry (>44.5 D).

A series of 96 moderately myopic eyes, with SE from -2.00 to -5.99 D, were compared along similar lines in 2012. Christiansen et al.[3] found results contradictory to those found in high myopes. In their case flatter corneas (K<42 D) achieved better visual acuities than those with steeper corneas (K>46 D). A few explanations proposed include positive induced spherical aberrations, corneal asphericity, and tissue remodeling.

This issue has also been studied in hyperopic eyes. Cobo-Soriano et al.[4] studied 376 eyes with an average preoperative manifest SE of +4.04 D. They defined flat keratometry as <43 D and steep keratometry as greater or equal to that. They found that there was no dependence of postoperative results on preoperative keratometry. According to their results, they proposed that postoperative vision relied only the degree of hyperopia corrected and was independent of preoperative keratometry.

Although many studies[15,24] look at the overall change in keratometry and its effect on VA following refractive surgery, they do not explore if this change leaves the patients with flat keratometry postoperatively. As such, current literature fails to convincingly explore the relationship between predicted or measured flat postoperative keratometry and visual acuity. Varssano et al.[23] attempted to tackle this issue in 2013. An investigation into

PRK patients with postoperatively flat corneas (K<35 D) revealed no loss in corrected visual acuity (BCVA). However this study did not stratify the degree of corneal flatness and the amount of "flatness" affected BCVA. They also excluded patients undergoing LASIK or LASEK.

In 2015 Mostafa[11] looked at the degree of keratometric change following laser vision correction (LVC) and how it affected VA. Yet this investigation only included results from highly myopic patients, with manifest SE from -6 to -12 D. Another 2015 study[19] looked at postoperative keratometry, but only its relation to patient satisfaction and night-vision. Thus, the current body of literature would stand to benefit from further elucidation of the relationship between myopic corneal flattening following corrective refractive laser surgery (CRLS) and loss of BCVA.

OBJECTIVES

Our aim was to further investigate the relationship between degree of myopic corneal flattening following CRLS and loss of BCVA. Current belief is that patients at risk for significant postoperative corneal flattening should not undergo CRLS. To substantiate or refute this claim clinical data was retrospectively analyzed across eyes that had undergone LASIK, LASEK, or PRK.

We considered three main endpoints crucial to the elucidation of this topic. One, determine the existence of a relationship between predicted postoperative keratometry values of <38 D and loss of BCVA. Two, determine the existence of a relationship between VA outcomes and the degree of corneal flatness, as separated by keratometry subgroups: Subgroup 1a (K<35 D), Subgroup 2a (K=35-35.99 D), Subgroup 3a (K=36-36.99 D) and Subgroup 4a (K=37-37.99 D). Finally three, determine the existence of a relationship between CRLS type and postoperative BCVA loss.

METHODS

Study Design

A retrospective study was performed on eyes that had previously undergone refractive surgery Boston Eye Group/Boston Laser in Brookline, Massachusetts between December 2008 and November 2016. The refractive surgeries performed were LASIK or ASA (LASEK or PRK). Ablative excimer laser platforms used were the WaveLight EX500 Excimer Laser (Alcon Laboratories Inc., Fort Worth, TX) and the VISX STAR S4 IR Excimer Laser System (Abbott Medical Optics Inc., Santa Ana, CA). LASIK flaps were created with the IntraLase iFS60 Laser (Abbott Medical Optics Inc., Santa Ana, CA).

In order to qualify as a "Candidate" in this study the patient must have had a calculated postoperative keratometry less than 38 D, based on their horizontal and vertical meridian keratometries. Similarly, qualifying for the "Control" group was based on a calculated postoperative keratometry being greater than or equal to 38 diopters. These two groups were then matched based on the amount of tissue ablated during their surgical procedure. Patients were excluded if they were hyperopic, had previously had an ocular surgery procedure to correct vision (including retinal procedures), were an ASA patient with less than three months of follow-up, or if their treatment was not wavefront-guided or optimized.

Postoperative Keratometry Calculation

The postoperative keratometry used to classify a patient into their Candidate or Control group and subgroup was based on the formulae proposed by Holladay et al.[6] and Varssano et al.[23] The preoperative spherical equivalent was achieved by multiplying the sum of the manifest preoperative sphere and half the manifest preoperative cylinder by 0.7. After refractive surgery it is expected to see a small amount of anterior corneal flattening, which is accounted for by taking 70% of the calculated spherical equivalence. This corrected spherical equivalence is then subtracted from the measured preoperative keratometry to give the approximate postoperative keratometry.

Data and Statistical Analysis

Prior to analysis or handling patient data was de-identified data and given an appropriate reference number. BCVA, as measured by the Snellen Visual Acuity Chart was converted to logMAR(BCVA) to allow for more detailed statistical analysis. Additionally, due to similarities in healing time, visual stability, and visual outcome, LASEK and PRK were combined into a single group called ASA (Advanced Surface Ablation), and considered as such for the purpose of statistical analyses.

Patients belonging to the Candidate (<38D) group were furthered sectioned into subgroups by their calculate postoperative keratometry: 1a (K<35D), 2a (K=35-35.99D), 3a (K=36-36.99D), 4a (K=37-37.99D). A similar type of stratification was applied to the Control (≥38) group, also giving four subgroups: 1b (K=38-38.99D), 2b (K=39-39.99D), 3b (K=40-40.99D), and 4b (K≥41D). Once subgroups were assigned Candidate and

Control, patients were matched with their appropriate counter subgroup (e.g. 1a & 1b). Matching was performed by pooling the subgroups to be matched, randomizing the data order, and selecting those with equal or near equal microns of tissue ablated.

Analyses were performed with IBM SPSS Statistics for Macintosh, Version 24. Graphs, figures, and charts were created in Microsoft Excel for Macintosh, Version 16.9. A number of analyses were performed including t-tests, Chi-Square tests, and ANOVAs. The appropriate test for each comparison was selected according to the variable types involved. For ANOVA post-hoc testing that involved samples of unequal size and variance, such as candidate or control subgroup comparisons, the Games-Howell (GH) test was used. This test was chosen due to its preference for more narrow confidence limits and higher statistical power than similar tests, such as Tamhane T2[20]. The null hypothesis of all analysis tests assumed equal means or equal qualitative distribution. A $p \leq 0.05$ (a probability less than 5%) was considered statistically significant and $p \leq 0.01$ (probability less than 1%) was considered very statistically significant, leading to a rejection of the null hypothesis and indicating that the data differed significantly.

RESULTS

A total of 111 eyes belonging to 92 patients were identified as candidates. A control population of 111 candidate eyes belonging to 89 individuals were selected by matching manifest refraction sphere and cylinder values with candidate patients.

Preoperative Data

Data collected from the overall candidate group showed a mean preoperative manifest sphere refraction of -5.3 D ± 1.76, mean manifest cylinder refraction of -1.07 D ± 0.87, mean spherical equivalence of -5.85 D ± 1.81, mean tissue ablated 81.52 μm ± 1.81 (Table 1), mean preoperative flat keratometry of 40.62 D ± 0.78, and mean steep keratometry of 41.80D ± 0.94 (Table 2). Data collected from the corresponding overall control group showed a mean preoperative manifest sphere refraction of -5.00 D ± 1.87, mean manifest cylinder refraction of -0.82 D ± 0.74, mean spherical equivalence of -5.41 D ± 1.84, mean flat keratometry of 44.22D ±0.99, and mean steep keratometry of 45.43 D ± 4.05.

A two-sample t-test assuming unequal variance was used to compare candidate and control mean preoperative manifest sphere refraction ($t(220) = -1.252$, $p=0.212$), mean preoperative manifest cylinder refraction ($t(220) = -2.418$, $\mathbf{p=0.016}$), mean preoperative spherical equivalence ($t(220) = -1.794$, $p=0.074$), and microns of tissue ablated ($t(220) = -0.052$, $p=0.958$). Although there was a significantly different preoperative manifest cylinder refraction between candidates and controls (Table 3), t-tests between paired

subgroups (e.g. 1a & 1b) with regards to cylindrical refraction did not indicate rejection of the null hypothesis (Table 4).

Table 3. Candidate and Control Comparison of Preoperative Manifest Sphere, Cylinder, Spherical Equivalence, and Amount of Tissue Ablated.

Subgroup Matching	Sphere	Cylinder	Spherical Equivalence	Tissue Ablated
Candidate & Control	p=0.212	***p*=0.016**	p=0.074	p=0.958

The same type of t-test was performed on each subgroup pair with regards to preoperative manifest sphere, cylinder, spherical equivalence, and tissue ablated. Between 1a & 1b, there were no significant differences between preoperative cylinder (t(26)=-1.368, p=.183) or tissue ablated (t(26)=0.069, p=0.946). However, there was a difference in preoperative manifest sphere (t(26)=0.403, ***p*=0.003**) and spherical equivalence (t(26)=-4.404, ***p*<0.001**). Between 2a & 2b, there were no differences in preoperative sphere (t(40)=-0.355, p=0.724), spherical equivalence (t(40)=-1.737, p=.090), or tissue ablated (t(40)=-0.396, p=0.694). There was a significant difference in preoperative cylinder (t(40)=-2.358, ***p*=.023**). When comparing 3a & 3b, there were no significant differences in preoperative sphere (t(58)=0.043, p=0.966), cylinder (t(58)=-1.626, p=0.109), spherical equivalence (t(58)=-0.233, p=0.817), and tissue ablated (t(58)=0.013, p=0.989). Similarly, comparisons of 4a & 4b along preoperative sphere (t(90)=-1.195, p=0.236), cylinder (t(90) = 0.041, p=0.968), spherical equivalence (t(90)=-1.221, p=0.226), and tissue ablated

(t(90)=0.018, p=0.986) did not reject the null hypothesis. The comparative p-values are summarized in Table 4.

Table 4. Candidate and Control Subgroup Comparison of Preoperative Manifest Sphere, Cylinder, Spherical Equivalence, and Amount of Tissue Ablated.

Subgroup Matching	Sphere	Cylinder	Spherical Equivalence	Tissue Ablated
1a & 1b	***p*=0.003**	p=0.183	***p*<0.001**	p=0.946
2a & 2b	p=0.724	***p*=0.023**	p=0.090	p=0.694
3a & 3b	p=0.966	p=0.109	p=0.817	p=0.989
4a & 4b	p=0.236	p=0.968	p=0.226	p=0.986

Preoperative BCVA in logMAR was also compared between candidate and control groups. The means, standard deviation, and range are given in Table 5. In a two-tailed t-test assuming unequal variance comparing the groups, there was no significant difference found (t(220)=-0.454, p=0.650).

Table 5. Candidate and Control Preoperative Visual Acuity in logMAR.

Group	Mean	Standard Deviation	Range
Candidate (N=111)	0.000757	0.0212431	0.2218
Control (N=111)	0.002142	0.0241392	0.2218
Total (N=222)	0.001450	0.0226964	0.2218

Preoperative BCVA was also quantified for each of the candidate and control subgroups (Table 6 and 7). In a one-way Anova comparison of candidate subgroups resulted in a significant difference between the groups ($F(3, 107)=3.001$, $\boldsymbol{p=0.034}$). When post-hoc testing was performed with the GH test, no significant differences resulted: 1a & 2a ($p=0.490$), 1a & 3a ($p=0.252$), 1a & 4a ($p=0.264$), 2a & 3a ($p=0.606$), 2a & 4a ($p=0.375$), and 3a & 4a ($p=1.000$). A similar comparison was performed with the control subgroups but maintained the null-hypothesis ($F(3, 107)=0.803$, $p=0.495$).

Table 6. Candidate and Control Stratified Subgroups and Preoperative BCVA.

Measure	Candidates				
	Subgroup 1a (K<35D) N=14	Subgroup 2a (K=35-35.99D) N=21	Subgroup 3a (K=36-36.99D) N=30	Subgroup 4a (K=37-37.99D) N=46	Total N=111
Mean BCVA [logMAR (BCVA)]	0.015271	0.002857	-0.002830	-0.002280	0.000757
Standard Deviation	0.0314254	0.0071714	0.0236058	0.0187147	0.0212431
Range [logMAR (BCVA)]	0.0969	0.0200	0.1449	0.1449	0.2218
Manifest Sphere (D)	-8.1250	-6.2381	-5.1167	-4.1467	-5.3063
Manifest Cylinder (D)	-1.3929	-1.8571	-0.7333	-0.8587	-1.0811
Spherical Equivalence (D)	-8.8236	-7.1688	-5.4853	-4.5789	-5.8492
Actual Ablation (μm)	107.21	98.33	79.40	67.41	81.52

Table 7. Candidate and Control Stratified Subgroups and Preoperative BCVA.

Measure	Control				
	Subgroup 1b (K=38-38.99D) N=14	Subgroup 2b (K=39-39.99D) N=21	Subgroup 3b (K=40-40.99D) N=30	Subgroup 4b (K≥41D) N=46	Total N=111
Mean BCVA [logMAR (BCVA)]	0.008350	0.004614	-0.002830	0.002367	0.002142
Standard Deviation	0.0260377	0.0171267	0.0236058	0.0266022	0.0241392
Range [logMAR (BCVA)]	0.0969	0.0769	0.1449	0.2218	0.2218
Manifest Sphere (D)	-6.9821	-6.0833	-5.1333	-3.8152	-5.0000
Manifest Cylinder (D)	-.9821	-1.0357	-.5250	-0.8641	-0.8198
Spherical Equivalence (D)	-7.4746	-6.6019	-5.3970	-4.2477	-5.4107
Actual Ablation (μm)	107.00	99.52	79.33	67.35	81.68

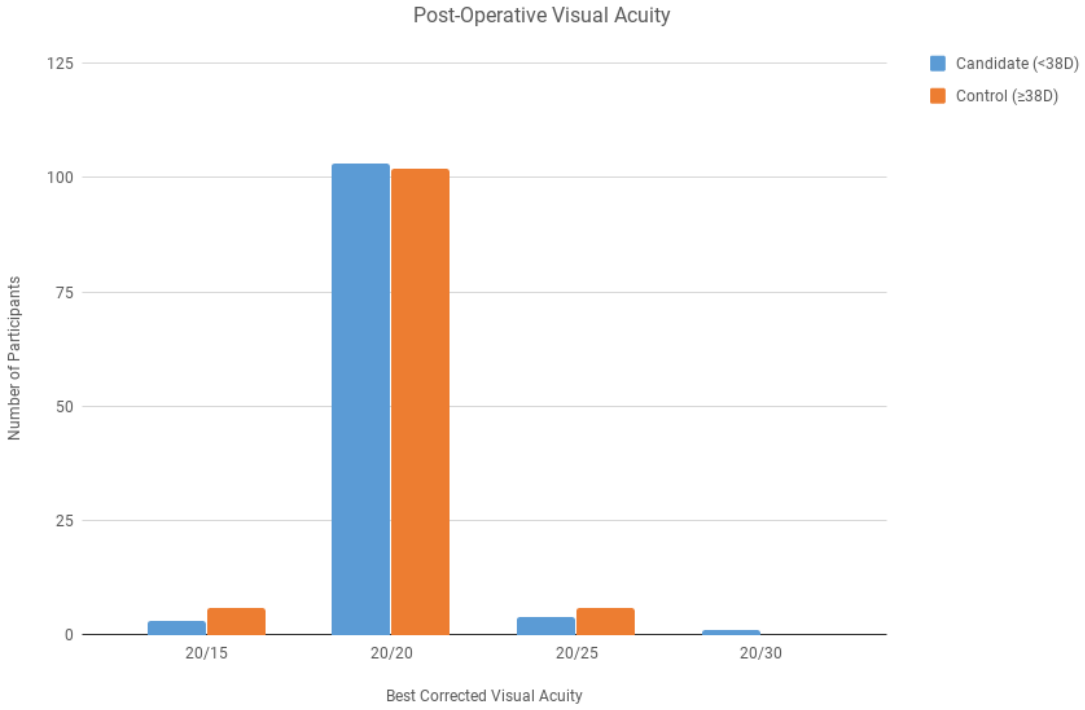
Postoperative Data

Data from the Candidate group showed a mean postoperative horizontal meridian keratometry of 36.53 D ± 1.15 and mean postoperative vertical meridian keratometry of 37.71 D ± 1.16. Data collected from the corresponding control group showed a mean postoperative flat keratometry of 40.44 D ±1.2, and mean postoperative steep keratometry of 41.7 D ± 4.17 (Table 8). Candidate vs. control postoperative BCVA data according to a Snellen measurement is presented visually in Figure 1.

Table 8. Candidate and Control Calculated Postoperative Horizontal Meridian ("Flat") and Vertical Meridian ("Steep") Keratometry.

Group	Measure	Calculated Postop Flat K (D)	Calculated Postop Steep K (D)
Candidate (N=111)	Mean	36.528437	37.712221
	Standard Deviation	1.1542562	1.1157949
	Range	4.7880	5.6750
Control (N=111)	Mean	40.435716	41.658144
	Standard Deviation	1.1970911	4.1744914
	Range	5.1520	44.5000
Total (N=222)	Mean	38.482077	39.685182
	Standard Deviation	2.2826276	3.6336809
	Range	10.0900	48.6625

Figure 1: Candidate vs. Control Postoperative Visual Acuity. Visual illustration of the postoperative BCVA of candidate patients with predicted postoperative keratometry values <38D vs. postoperative BCVA of control patients with predicted postoperative keratometry values ≥38D. X-axis represents visual acuity; Y-axis represents number of eyes.



Postoperative BCVA was compared between candidate and control groups with a two-tailed t-test assuming unequal variance. Relevant logMAR(BCVA) values can be found in Table 9. The null hypothesis was not rejected ($t(220)=1.754$, $p=0.081$). The corrected visual acuity was further analyzed along the candidate and control subgroups. A single factor ("one-way") ANOVA was conducted to compare the mean postoperative BCVA, in logMAR(BCVA), between the candidate subgroups 1a, 2a, 3a, and 4a (Table 10). The analysis of variance showed no significant difference between the subgroup means ($F(3, 107)=2.257$, $p=0.086$). Another one-way ANOVA was used to compare the control

subgroups 1b, 2b, 3b, and 4b (Table 11). There was a significant difference between these subgroup means (F(3, 107)=3.137, ***p*=0.028**). Upon GH post-hoc testing there was no significant difference found between any pairs: 1b & 2b (p=0.431), 1b & 3b (p=0.101), 1b & 4b (p=0.587), 2b & 3b (p=0.535), 2b & 4b (p=0.932), and 3b & 4b (p=0.238).

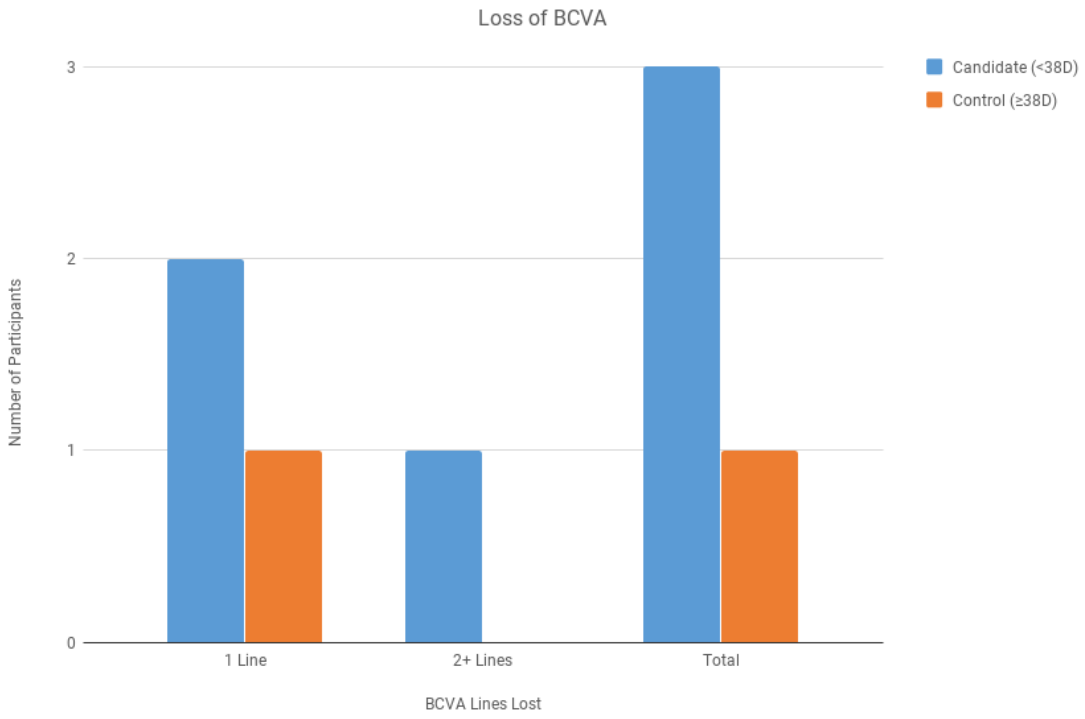
Table 9. Candidate and Control Postoperative Visual Acuity in logMAR.

Group	Mean	Standard Deviation	Range
Candidate (N=111)	0.004766	0.0319170	0.3010
Control (N=111)	-0.002871	0.0329542	0.2418
Total (N=222)	0.000947	0.0325918	0.3010

Loss of BCVA

Of the overall candidate patient group a total of 3 out of 111 eyes (2.70%) lost BCVA, with 2 eyes losing 1 line of BCVA and 1 eye losing 2+ lines of BCVA. Considering the control group, 1 out of 111 eyes (0.90%) lost 1 line of BCVA (Figure 2).

Figure 2: Candidate vs. Control vs. Total Loss of BCVA. Left: Candidate (2 eyes or 1.8% of candidate eyes losing BCVA) and Control (1 eye or 0.90% of control eyes losing BCVA) Loss of 1 Line BCVA. Middle: Candidate (1 eye or 0.90% of candidate eyes losing BCVA) and Control (0 eyes or 0.00% of control eyes losing BCVA) Loss of 2+ Lines BCVA. Right: Candidate (3 eyes) and Control (1 eye) Loss of Total BCVA. X-axis represents loss of BCVA categories; Y-axis represents number of eyes.



A more detailed look at the loss of postoperative BCVA is presented in Tables 12 and 13. These tables contain the number of persons in each subgroup falling into each BCVA lost category, as well as the percentage of BCVA lost and maintained.

Table 12. Candidate Eyes That Lost BCVA by Subgroup and Relative Frequency of Total Subgroup Population. The number of eyes within each subgroup that lost either 1 line or 2+ lines of BCVA as a percentage of each subgroup population where n is the number of subjects.

Measure	Candidate Subgroups				
	Subgroup 1a (K<35D) N=14	Subgroup 2a (K=35-35.99D) N=21	Subgroup 3a (K=36-36.99D) N=30	Subgroup 4a (K=37-37.99D) N=46	Total N=111
Loss of 1 Line BCVA	1 (7.14%)	0 (0%)	0 (0%)	1 (2.17%)	2 (1.80%)
Loss of 2+ Lines BCVA	0 (0%)	1 (4.76%)	0 (0%)	0 (0%)	1 (0.90%)
Total Loss of BCVA	1 (7.14%)	1 (4.76%)	0 (0%)	1 (2.17%)	3 (2.70%)
BCVA Not Lost	13 (92.86%)	20 (95.24%)	30 (100%)	45 (97.83%)	108 (97.30%)

Table 13. Control Eyes That Lost BCVA by Subgroup and Relative Frequency of Total Subgroup Population. The number of eyes within each subgroup that lost either 1 line or 2+ lines of BCVA as a percentage of each subgroup population where n is the number of subjects.

Measure	Control Subgroups				
	Subgroup 1b (K=38-38.99D) N=14	Subgroup 2b (K=39-39.99D) N=21	Subgroup 3b (K=40-40.99D) N=30	Subgroup 4b (K≥41) N=46	Total N=111
Loss of 1 Line BCVA	1 (7.14%)	0 (0%)	0 (0%)	0 (0%)	1 (0.90%)
Loss of 2+ Lines BCVA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total Loss of BCVA	1 (7.14%)	0 (0%)	0 (0%)	0 (0%)	0 (0.90%)
BCVA Not Lost	13 (92.86%)	21 (100.00%)	30 (100.00%)	46 (100%)	110 (99.10%)

To determine if more eyes within the candidate group lost BCVA in comparison to the control group, a Chi-Square test (χ^2) was performed. The relationship between these groups was not significant (χ^2 (1, N=222)=1.018, p=0.313). Two more Chi-Square tests were conducted to discover if BCVA changed among the candidate subgroups or control subgroups. Neither the control subgroups (χ^2 (3, N=111)=2.270, p=0.290) nor the candidate subgroups (χ^2 (3, N=111)=6.992, p=0.072) significantly differed from the other subgroups in their grouping category.

In order to further investigate and understand the BCVA loss within each subgroup, preoperative and postoperative BCVAs were compared. For each subgroup, the

preoperative logMAR(BCVA) was compared with the postoperative logMAR(BCVA) via a one-way ANOVA for repeated measures. There was no significant change in any of the control (Table 14) or candidate (Table 15) subgroups.

Table 14. Candidate Subgroup Mean Preoperative and Postoperative BCVA Comparison.

Candidate Subgroup Pre- and Postoperative BCVA Comparison					
Subgroup	Subgroup 1a (K<35D) N=14	Subgroup 2a (K=35-35.99D) N=21	Subgroup 3a (K=36-36.99D) N=30	Subgroup 4a (K=37-37.99D) N=46	Total N=111
p-value	0.367	0.297	0.576	0.669	0.157

Table 15. Control Subgroup Mean Preoperative and Postoperative BCVA Comparison.

Candidate Subgroup Pre- and Postoperative BCVA Comparison					
Subgroup	Subgroup 1b (K=38-38.99D) N=14	Subgroup 2b (K=39-39.99D) N=21	Subgroup 3b (K=40-40.99D) N=30	Subgroup 4b (K≥41) N=46	Total N=111
p-value	0.458	0.227	0.071	0.703	0.100

Surgery Type

There were 111 candidate eyes. 104 (93.69%) underwent LASIK and 7 (6.31%) underwent ASA surgery. In comparison, of the 111 control eyes 83 (74.77%) underwent LASIK and 28 (25.23%) underwent ASA. A Chi-Square test for independence was performed to determine if one the groups (candidate or control) had a greater prevalence of ASA or LASIK in comparison to the along. This was found to be significant, with the

control group containing more ASA eyes (χ^2 (1, N=222)=14.958, ***p*<0.001**). Average follow-up time was 122 days for LASIK eyes and 229 days for ASA patients.

Overall, of both the candidate and control groups, 187 eyes underwent LASIK of which 3 eyes lost BCVA (1.60%). Similarly, 35 eyes underwent ASA and 1 eye lost BCVA (2.86%). To determine if these rates corresponded, a Chi-Square test was conducted to analyze whether a loss of BCVA was dependent on surgery type. The relationship between these groups was not significant, (χ^2 (1, N=222)=0.069, p=0.793). Additional Chi-Squares were performed on both the candidate and control subgroups. The candidate subgroups had no significant difference in the comparison of treatment type and loss of BCVA (χ^2 (1, N=111)=0.208, p=0.649). Similarly, the control subgroups also showed no differences along those criteria (χ^2 (1, N=111)=2.991, p=0.084).

Of the 3 candidate eyes that lost 1 or more lines of BCVA, all had undergone LASIK and had a mean follow-up time of 101 days. The 1 control eye that lost BCVA had been treated with ASA and had a mean follow-up period of 341. Also of note, is that none of the 4 eyes that lost BCVA had experienced intraoperative complications.

DISCUSSION

This investigation was undergone with the principle goal of discovering if patients with a flat calculated postoperative keratometry (<38 D) were at an increased risk of losing BCVA following CRLS. It also endeavored to determine if the degree of corneal flattening following surgery, as designated by calculated keratometry values (K<35 D, K=35-35.99 D, K=36-36.99 D, and K=37-37.99 D), was related to BCVA loss. Finally, we attempted to determine if type of refractive surgery had any role in postoperative VA, corneal flattening, or BCVA loss.

Candidate-Control Matching

When matching candidates and controls among their respective subgroups (e.g. 1a & 1b) we chose to focus on the amount of tissue actually ablated during surgery as opposed to matching based on preoperative manifest prescriptions. Multiple rationales led to this decision. Principally, we wanted to provide as accurate a match as possible when comparing postoperative keratometry. Those with flat K's tend to have higher myopic manifest SE than those with normal keratometry and we did not want this discrepancy to factor in to our comparisons. Furthermore it is extremely unlikely that the operating surgeon would chose to ablate more than 130μm of tissue, no matter the prescription or pupil size, due to the risk of corneal ectasia. For similar reasons it is extremely rare for a surgeon to perform refractive surgery on patients with keratoconus, a condition characterized by a unstable corneal structure. Corneal ectasia can result from too great an alteration of the cornea and can permanently impair vision. Vision is compromised when

the cornea's structure is comprised and as a result is too weak to properly refract light.[17,18] It follows that matching the amount of tissue removed between pairs should give a more robust pairing than manifest prescription.

There were significant differences found between candidate and control cylinder manifests (***p*=0.016**) and subgroup 2a & 2b cylinder (***p*=0.023**). There were also significant differences in subgroup 1a & 1b sphere (***p*=0.003**) and spherical equivalence (***p*<0.001**). As previously mentioned those with very large prescriptions were not fully treated if that would lead to an increase in risk of corneal ectasia. There were no statistically significant differences in the amount of tissue ablated between candidate and control or between candidate and control subgroups.

There was a significantly greater representation of those undergoing ASA as opposed to LASIK in the control group (***p*<0.001**). However, we do not feel this was a confounding factor or influenced results due to the lack of differences in postoperative visual outcome. Whether the patient had LASIK or ASA, there was no significant difference in either BCVA or BCVA loss. Therefore, we do not feel that these differences impacted our patient matching or results.

Overall Loss of BCVA

3 candidate eyes (2.70%) lost 1 or more lines of BCVA. There was only a single control eye (0.90%) that lost BCVA. Upon further analysis, there was no statistically significant difference (p=0.313) found between candidate (K<38 D) and control (K≥38 D) eyes. These results were similar to those by Varssano et al.[23], though they chose to use

different cutoff keratometry values to determine their candidate (K<35 D) and control (K≥35 D) groups.

Subgroup Loss of BCVA

No significant differences in BCVA loss were found between the candidate or control subgroups. This is supportive of statements by Varssano et al.[23] Their candidate group had no significant difference in BCVA loss compared to the control group. A study by Mostafa[11] stratified patients by degree of myopia (-6 to -7.9 D, -8 to -9.9 D, and -10 to -12 D) and measured their postoperative corrected distance visual acuity (CDVA) in eyes with postoperative keratometry 35 D. The study found that flat corneas and higher degrees of myopia led to worse CDVA outcomes postoperative. However, it is difficult to this study to the current investigation due to our lack of myopic stratification.

Multiple studies in the current literature have indicated that patients with a higher degree of myopia (especially -8 to -14 D) are at an increased risk of losing BCVA if they undergo CRLS, as summarized by a recent Cochrane review.[1] As mentioned previously, higher degrees of myopia require a larger percentage of corneal tissue to be laser altered and may greatly increase the risk of corneal ectasia.

Surgery Type

Our study had a larger percentage of candidate LASIK patients (93.69%) than controls (74.77%), which had a higher percentage of ASA patients (25.23%) than the candidate group (6.31%). This difference was significant (***p*<0.001**). However, there was no distinction made between the amount of BCVA lost and procedure type (p=0.793)

indicating that procedure type had no major role in determine BCVA outcome. This is further supported by a minimum required amount of follow-up time for LASIK and ASA patients, with ASA requiring longer to achieve BCVA stability. The average follow-up for LASIK eyes was 122 days and for ASA eyes was 229 days.

To our knowledge there is no other study in the current literature that considers the effect of procedure type (LASIK or ASA) on postoperative VA in flat corneas. Varssano et al.[23] investigated patients undergoing PRK and Mostafa[11] confined his research to LASIK patients.

Current Limitations and Future Studies

The most prominent limitation in this investigation is the use of mathematically predicted postoperative keratometry. Though this method is commonly used to help evaluate CRLS candidacy,[23] its validity as a predictive tool has not been exhaustively tested. Further large-scale studies comparing predicted and measure postoperative keratometry are warranted.

Our study is also hampered by a lack of measured postoperative keratometry. These values and their correlation to postoperative VA would further define our current findings and increase their validity. We recommend similar, large-scale, controlled studies to effectively evaluate this relationship.

Though we consider a fairly significant sample size (222 eyes), it is possible that sampling error may have skewed our results. Future investigations could possibly avoid

this by increasing sample size and/or including multiple surgery sites, potentially in significantly different geographic areas.

In conclusion, our evidence suggests there is no relationship between loss of BCVA and a postoperative corneal keratometry of less than 38 D.

APPENDIX

Table 1. Candidate and Control Preoperative Manifest Sphere, Cylinder, Spherical Equivalence, and Amount of Tissue Ablated.

Group	Measure	Sphere (D)	Cylinder (D)	Spherical Equivalence (D)	Tissue Ablated (μm)
Candidate (N=111)	Mean	-5.3063	-1.0811	-5.8492	81.52
	Standard Deviation	1.77280	.86875	1.80524	20.806
	Range	9.00	4.75	8.87	88
Control (N=111)	Mean	-5.0000	-.8198	-5.4107	81.68
	Standard Deviation	1.87204	.73560	1.83624	22.742
	Range	8.25	3.50	7.87	105
Total (N=222)	Mean	-5.1532	-.9505	-5.6300	81.60
	Standard Deviation	1.82543	.81371	1.82993	21.746
	Range	9.00	4.75	9.12	105

Table 2. Candidate and Control Preoperative Horizontal Meridian ("Flat") and Vertical Meridian ("Steep") Keratometry.

Group	Measure	Flat K (D)	Steep K (D)
Candidate (N=111)	Mean	40.62099	41.80468
	Standard Deviation	0.781309	0.940851
	Range	3.750	5.250
Control (N=111)	Mean	44.22243	45.44477
	Standard Deviation	0.992038	4.046393
	Range	5.000	44.000
Total (N=222)	Mean	42.42171	43.62473
	Standard Deviation	2.012697	3.452210
	Range	8.250	46.500

Table 10. Candidate Stratified Subgroups and Postoperative BCVA. Total number of persons in each stratified candidate group and associated postoperative BCVA.

Measure	Candidate: Postoperative BCVA				
	Subgroup 1a (K<35D) N=14	Subgroup 2a (K=35-35.99D) N=21	Subgroup 3a (K=36-36.99D) N=30	Subgroup 4a (K=37-37.99D) N=46	Total N=111
Mean BCVA [logMAR (BCVA)]	0.020764	0.012195	0.000503	-0.000715	0.005459
Standard Deviation	0.0382870	0.0383979	0.0221254	0.0307846	0.0326391
Range [logMAR (BCVA)]	0.0969	0.1761	0.1249	0.2418	0.3010

Table 11. Control Stratified Subgroups and Postoperative BCVA. Total number of persons in each stratified control group and associated postoperative BCVA.

Measure	Control Postoperative BCVA				
	Subgroup 1b (K=38-38.99D) N=14	Subgroup 2b (K=39-39.99D) N=21	Subgroup 3b (K=40-40.99D) N=30	Subgroup 4b (K≥41D) N=46	Total N=111
Mean BCVA [logMAR (BCVA)]	0.013843	-0.003090	-0.015987	0.000696	-0.002871
Standard Deviation	0.0360518	0.0240868	0.0436020	0.0241142	0.0329542
Range [logMAR (BCVA)]	0.1169	0.1249	0.1449	0.2218	0.2418

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