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Predictors of Successful Outcome Following Intrastromal Corneal Ring Segments Implantation

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Abbreviations/Acronyms

ICRS: Intrastromal Corneal Ring Segments; **UCVA:** Uncorrected Visual Acuity; **CDVA:** Corrected Distance Visual Acuity; **LogMAR:** Logarithm of Minimum Angle of Resolution; **SE:** Spherical Equivalent; **IOP:** Intra-Ocular Pressure; **Km:** Mean keratometry; **CA:** Corneal Astigmatism; **WTR:** With-The-Rule; **ATR:** Against-The-Rule; **OBL:** Oblique; **SB:** Symmetric bow-tie; **AB:** Asymmetric bow-tie; **IS:** Inferior steepening; **SRAX:** Skewed radial axis; **Q:** Asphericity (Q-value); **CCT:** Central Corneal Thickness; **CTP:** Corneal Thinnest Point; **ORA**: Ocular Response Analyzer; **CH:** Corneal Hysteresis; **CRF:** Corneal Resistance Factor; **HOAs:** Higher-Orders Aberrations; **RMS** Root-Mean-Square; **SD:** Standard Deviation; **CI:** Confidence Interval.

ABSTRACT

Purpose: To assess the preoperative visual, refractive, corneal topo/tomographic, aberrometric and biomechanical parameters as predictive factors of a successful outcome 6 months following intrastromal corneal ring segments implantation.

Methods: 68 keratoconus eyes implanted with Keraring using femtosecond laser technology were assessed. The preoperative assessed parameters included uncorrected and corrected distance visual acuity (UDVA & CDVA), refraction, placido-based topography using TMS-4, Scheimplfug tomography using Pentacam HR, corneal biomechanical assessments using Ocular Response Analyzer (ORA) and the wavefront analysis using i-Trace aberrometer. Other variables were type of astigmatism based on orientation of the steep meridian, keratoconus staging based on the Amsler-Krumeich classification and the difference between the axes of refractive astigmatism, topographic astigmatism and comatic aberration based on a difference less or more than 30º. The success criterion was defined based on CDVA, a post-operative CDVA improvement at least two lines were considered as a success and otherwise were recognized as a failure following Keraring implantation.

Results: Only UDVA, coincidence of the most elevated points on the front and back corneal surfaces and the difference between UDVA and CDVA showed significant difference between the eyes with successful outcomes and those with unsuccessful results.($P<0.05$) Although corneal curvature and astigmatism were higher and corneal thickness was lower in the unsuccessful group, differences were not statistically significant.

Conclusion: It is expected that the greater difference between the preoperative uncorrected and corrected distance visual acuity (Δ UDVA-CDVA) and more coincidence of the most elevated points in the two corneal surfaces on the elevation maps increase the rate of successful outcome following the Keraring implantation.

Key Words: Keratoconus; Intrastromal corneal ring segments; Keraring; Corneal topography; Corneal biomechanics.

INTRODUCTION

Keratoconus is a non-inflammatory progressive ectatic disease leading to the corneal steepening, paracentral thinning, bulging and irregular astigmatism.[1] Although in the early stages of this disease, spectacle and contact lens usually provide an acceptable vision; however, when these two options fail to produce a satisfactory vision and patient does not tolerate contact lens, other therapeutic methods will be indicated.[2]

A minimally invasive additive surgical option to delay corneal transplants is implantation of intrastromal corneal ring segments (ICRS)[3-5] which also improve the patient's quality of life.[6] They produce gross corneal reshaping to more regularize corneal surface and improve visual acuity and contact lens tolerance,[7, 8] especially in the severe form of keratoconus compared to the milder form classified based on the preoperative distance corrected visual acuity.[9]

ICRS decrease the central corneal curvature,[10-13] this flattening effect and consequently reduction in myopic spherical equivalent are induced by the arc-shortening effect following the ring implantation in the mid-periphery of the cornea.[14-16] Other advantages of this technique are the preservation of corneal prolateness and its removability feature.[17] Furthermore, ICRS act as a second limbus and improve the structural integrity of the corneal tissue which provide some support for the eyes with keratoconus,[18] although no significant change in the corneal biomechanical parameters (corneal hysteresis and corneal resistance factor) obtained using the ocular response analyzer (ORA) was reported postoperatively.[19]

Examples of commercially available ICRS are Keraring (Mediphacos, Belo Horizonte, Brazil), Ferrara ring (Ferrara Ophthalmics, Brazil) and Intacs® (Addition Technologies, Des Plaines, IL, USA). Keraring is available in one or two segments with variable arc length from 90-210 degrees.[20]

In order to obtain the optimal clinical outcomes after the ICRS implantation, each manufacture provides a specific nomogram to help clinicians select the best ring characteristics according to clinical data. The available nomograms were mainly developed based on the distribution of ectatic corneal region, its symmetry status, and the spherical/cylindrical components of refractive error, while other factors such as preoperative visual acuity,[9] mean keratometry, corneal topographic pattern,[21] keratoconus grading,[15, 22, 23] aberrations,[10] coincidence between refractive, topographic and comatic axes,[24, 25] incision location,[24, 26] corneal biomechanical properties,[22, 27, 28] and internal astigmatism[15] may affect the surgical outcome.

It is necessary to consider that the purpose of ICRS implantation is to more regularize the cornea and to improve the patient visual quality, but it does not mean treating the disease or removing the need for spectacle. On the other hand, corneal response to ICRS in keratoconus is still highly unpredictable, as well as this method has a significant financial burden on the patient, so the patient selection is very important when suggesting this option.[27]

Therefore, this study was designed to assess the pre-operative visual, refractive, corneal topo/tomographic, aberrometric and biomechanical parameters as predictors of successful outcomes following the Kerаring implantation.

METHODS

Pre-operative clinical findings 68 eyes of sixty eight keratoconic patients who were implanted with Keraring segments (Mediphacos, Belo Horiztone, Brazil) were included in this retrospective clinical study. Keratoconus was diagnosed based on corneal topo/tomography and slit-lamp observation and confirmed by an experienced corneal specialist (MRS).[29] All steps of this study followed the tenets of the Declaration of Helsinki.

Inclusion criteria were no history of corneal excimer laser refractive surgery, cross-linking; clear central cornea without any scar or other complications; no history of other eye diseases except keratoconus; contact lens intolerance; cornea thickness at least 450 and 350 micron at the insertion site and the thinnest point, respectively; no history of atopy, allergy, autoimmune disorders and herpetic disease.[13]

Preoperative assessments included determination of uncorrected and corrected distance visual acuity (UDVA& CDVA), refraction, placido-disk based topography with TMS-4 (Tomey Corp, Nagoya, Japan), and Scheimplfug tomography with Pentacam HR (Oculus; Wetzlar, Germany), corneal biomechanical assessments using the ocular response Analyzer (ORA, Reichert Ophthalmic Instruments, Buffalo, NY, USA); and wavefront analysis using i-

Trace aberrometer (Tracey Technologies, Houston, TX). It should be considered that the i-Trace aberrometer was previously shown to be valid for characterizing ocular aberrations in keratoconus.[30, 31] All measurements with the TMS-4, Pentacam, ORA and i-Trace were taken by the same experienced and qualified technician to avoid any bias.

Uncorrected and corrected distance visual acuity (UDVA & CDVA) was measured in decimal Snellen notation and converted to the logarithm of the minimum angle of resolution (LogMAR) for statistical analysis.

Recorded refractive error data included sphere, cylinder, axis and spherical equivalent (SE).

The corneal topography derived variables were corneal astigmatism (CA) and topography pattern based on the proposed patterns by Rabinowitz.[29]

Pentacam derived variables were mean keratometry in the central 3 mm of the front and back corneal surfaces; the magnitude and axis of front and back corneal astigmatisms (CA); maximum keratometry (K-Max); elevation pattern (skewed hourglass or sandy watch, isolated island, tongue-like extensions (including complete and incomplete positive bands) and irregular patterns); corneal asphericity expressed as the Q-value in the central 8-mm of the cornea in both surfaces; corneal thickness at the apex (CCT) and the corneal thinnest point (CTP) .

The obtained parameters from ORA were corneal hysteresis (CH) and corneal resistance factor (CRF).

The aberrometry data included the root-mean-square (RMS) of total higher-order aberration (HOAs) and the magnitude of preoperative coma and coma-like (3^{rd}, 5^{th} and 7^{th} orders) and trefoil (3^{rd}, 5^{th} and 7^{th} orders) calculated for simulated 6-mm pupil expressed in microns.

Refractive and corneal astigmatism were categorized based on the orientation of steep meridian into three groups, with-the-rule (WTR: 61 to 120 degrees), against-the-rule (ATR: 0 to 30 and 151 to 180 degrees) and oblique (OBL: 31 to 60 and 120 to 150 degrees) astigmatisms.[32]

Differences between each pair of the refractive astigmatism, topographic and comatic axes were determined and categorized into two groups, the group with a difference of <30º and the group with a difference of ≥30º.[25, 33]

Keratoconus staging according to the mean keratometry value was done based on the Amsler-Krumeich classification system into mild (up to 48D), moderate (≥48D to 52D), advanced (≥52D to 58D) and severe keratoconus (≥58D).[23]

The most elevated point was defined as the maximum positive values inside the cone area on the front and back elevation maps relative to the best fit sphere (BFS). Location of these points was obtained from the axes of the coordinates on their relevant maps. Coincidence was defined based on a difference of less than 1 mm in the position of the highest elevated points on both corneal surfaces; otherwise it was considered non coincidence.

The success criterion was defined based on CDVA comparison before and 6 months after the ring implantation. The implanted eyes were divided into two groups, the group with successful results and those with unsuccessful results 6 months following the surgery. A post-operative CDVA improvement a least two lines was considered as a success and otherwise was recognized as a failure.[34]

Implanted intrastromal corneal ring segments (ICRS)

Implanted ICRSs were Keraring (Mediphacos, Belo Horiztone, Brazil), they made of PMMA material (polymethylmethacrylate). There are two models of these segments (SI-5 and SI-6). The SI-5 was implanted in this study which is characterized by an optic zone 5 mm, isosceles triangular cross-section (base 600 µm and truncated apex 40 µm), thickness 150-350 µm by step range 50 µm, and arc lengths of 90, 120, 160, and 210 degrees.

Surgical Technique

Rings' selection and the surgical plan were based on the manufacture's proposed nomogram. Implanting one or two segments and symmetrical or asymmetrical segments were based on the distribution of the ectatic zone on the sagittal curvature map. Segment thickness was selected according to the ectatic area's distribution, spherical and cylindrical components of refractive errors. Incision location was chosen based on the corneal topographic steep meridian.[26] All Kerarings were implanted by the same surgeon (MRS).

Femtosecond laser was used to create the tunnel ring (Ziemer FEMTO LDV Z6) at a depth of approximately 80% of the corneal thickness at the implantation area (5 mm diameter around the pupil center). The inner and outer diameters of channels were set to 4.8 and 5.4 mm, respectively.

Postoperative treatment was combination of Levofloxacin (Oftaquix, Santen Pharmaceutical, Japan) antibiotic eye drop 5mg/ml a, Fluorometholone 1% (Allergan Ltd, UK) corticosteroid eye drop administrated 4 times daily for 2 weeks and preservative-free artificial tear (Artelac Advanced, Bausch & Lomb, France) 8 times daily for 2 weeks and then 4 times daily for the next two weeks. In addition, a bandage contact lens (Biofinity, Cooper vision care, USA) made of a silicon hydrogel (Comflicon A) material approved for up to 6 nights/7 days of continuous wear with water content 48%, Dk = 128, base curve of 8.6 mm and overall diameter of 14 mm, was used for 2 weeks.

Statistical Analysis

Data were analyzed in SPSS.22 software using the independent-samples T test and its non-parametric equivalent (Mann-Whitney U test) for variables with no Gaussian distribution. The Bonferroni adjustment was applied to consider the potential bias associated to repeated testing significance. The Chi-square test was used for categorical variables. A p-value less than 0.05 was considered as significant in all tests.

RESULTS

Mean age was 30.03±7.96 (range: 21-60) years in keratoconus patients. 42 eyes were related to males. (68.1%)

Refractive errors and Visual acuity

The mean and standard deviation of refractive data (sphere, cylinder, axis and spherical equivalent, SE) and visual acuity before and 6 months after the Keraring implantation in all eyes and separately with attention to the final outcome are presented in Table 1.

Table 1:

Considering the preoperative variables presented in Table 1, only significant difference in UDVA was found between the two groups. ($P<0.05$) Specifically, there was a significant difference in comparison of different variables before and at 6 months after ring segment implantation in all cases as well as separately when the two groups were compared ($P<0.05$), except the cylinder axis in the group with successful results and UDVA, CDVA and cylinder axis in the group with unsuccessful results ($P>0.05$). The mean changes in sphere, refractive cylinder, SE, UDVA and CDVA in the group with successful results were 1.07 D, 3.70 D, 2.92 D, 0.57 LogMAR and 0.19 LogMAR, while these values in the other group were 0.95 D, 3.27 D, 2.58 D, 0.01 LogMAR and 0.00 LogMAR, respectively.

Corneal geometrical parameters using Pentacam

The mean and standard deviation of some preoperative indices obtained with the Pentacam system are shown in Table 2.

Table 2:

Although mean keratometry values and corneal astigmatism in both corneal surfaces and maximum keratometry value in the front surface were lower in the group with successful results but this differences were not significant statistically. Similarly the corneal thickness and corneal asphericity did not show significant difference between the two groups statistically. (P>0.05)

Standard corneal biomechanical parameters using ORA

The mean and standard deviations of corneal biomechanical parameters are displayed in Table 3.

Table 3:

In assessing the corneal biomechanical parameters using the ORA, the mean difference of CH and CRF in the studied groups were 0.02 and 0.16 mmHg, respectively with no significant difference between the two groups. (P>0.05)

Higher orders aberrations (HOAs) using iTrace

The mean and SD of total HOAs, coma and trefoil root mean square (RMS) were 1.70±1.10, 1.33±1.03, 0.64±0.47 µm in the group with successful results and 1.53±0.94, 1.07±0.80, 0.55±0.47 µm in the other groups, respectively, with no significant differences between the two groups using the Mann-Whitney U test. (P>0.05)

Frequency distribution of categorical variables

The distribution of various types of refractive and topographic (corneal) astigmatisms based on the orientation of steep meridian separately in the two groups is illustrated in Figure 1.

Figure 1:

ATR astigmatism was more frequent in the group with successful outcome while WTR and OBL astigmatisms were more prevalent in the other group. Types of topographic astigmatism in the successful group in a decreasing trend were OBL, ATR and WTR astigmatisms. In the unsuccessful group, WTR astigmatism was more prevalent type for both topographic and refractive astigmatisms. The Chi-square test did not show statistically significant differences in the distribution of different types of refractive (X^2= 4.392, df=2, P=0.080) and topographic (X^2= 4.705, df=2, P=0.095) astigmatisms between the two groups.

The frequency distribution of different elevation patterns on the front and back corneal surfaces and different corneal topography patterns separately in the two groups is shown in Figure 2.

Figure 2:

Tongue-like extensions were the most common pattern in the group with successful results and the irregular pattern was the most common pattern in the unsuccessful group in both corneal surfaces. There was not significant difference in the distribution of elevation patterns in the front (X^2= 1.397, df=2, P=0.497) and back (X^2= 2.927, df=2, P=0.231) corneal surfaces between the two groups. Among the observed patterns (SB, AB/IS, AB/SRAX, claw-like and junctional), the most common pattern in both groups was asymmetric bow-tie with skewed radial axis (AB/SRAX); however, there were not considerable differences in pattern distribution between the two groups. (X^2= 4.034, df=4, P=0.401)

The differences between refractive and topography axes and topography and coma axes were not statistically significant between the two groups. (P>0.05) As seen in Figure 3A, the refractive astigmatism axis and the axis of topographic astigmatism were considered almost consistent with less than 30 degrees of difference between them in

98% of the eyes with successful results; however, this factor did not show statistically significant difference between the two groups. (X^2=2.338, df=1, P=0.187) Difference between the topography and coma axes, and refractive astigmatism and coma axes were not significantly different between the two groups. (X^2=1.493, df=1, P=0.240) (Figure 3B)

Figure 3:

Evaluation of the coincidence of the most elevated point on the front and back corneal surfaces showed coincidence in 63.3% of eyes with successful results while no coincidence was evident in 68.4% of eyes with no successful outcomes. The Chi-square test showed a significant difference in the distribution of coincidence in the two groups. (X^2= 5.542, df=1, P=0.019)

Distribution of various stages of keratoconus separately in the two groups is illustrated in Figure 4.

Figure 4:

Mild (44.9%) and moderate (57.9%) keratoconus eyes had the highest distribution in successful and unsuccessful groups, respectively. The graph shows that 85.7% and 94.7% of the eyes had a mean keratometry less than 52 D in successful and unsuccessful groups, respectively. The Chi-square test did not show significant differences in the distribution of different stages in the two groups. (X^2= 2.032, df=2, P=0.362)

The mean and standard deviations of difference between pre-operative UDVA and pre-operative CDVA, refractive and topographic axes, refractive and coma axes, topography and coma axes in the two groups are shown in Table 4.

Table 4:

With attention to Table 4, the only significant factor was the difference between UDVA and CDVA so that more difference was associated with better visual results post-operatively.

Mean and standard deviation ring characteristics including thickness, arc length and ring depth in the the eyes with and without successful surgical outcomes were 248.97±50.50 and 226.31±57.07 µm (P=0.140), 155.71±55.45 and 150.52±25.92 º (P=0.602), 400.36±30.92 and 393.68±23.14 µm (P=0.200), respectively. One segment ring was implanted in 45.6% and 13.2% of the eyes with and without successful outcomes, respectively; while double ring segments were used for 26.5% and 14.7% of the eyes with successful and unsuccessful results, respectively. There was significant difference in terms of ring segments distribution between the two groups using the Chi-square test. (X2= 1.428, df=1, P=0.232)

DISCUSSION

This study showed that among the pre-operative visual, refractive, corneal topographic, tomographic, aberrometric and biomechanical parameters, only UDVA, coincidence of the most elevated point on the front and back corneal surfaces and the difference between UDVA and CDVA (UDVA-CDVA) were significantly different between the groups with successful and unsuccessful results.

Alio et al. (2006) reported significant difference in the preoperative mean sphere and SE between a group with successful outcomes (≥3 lines improvement in CDVA) and a failure group (1 line loss in CDVA) following Intacs implantation.[27] However, these findings are in contrast with the present study, this difference may be attributed to the implanted ring's type (Keraring vs. Intacs) and different success criterion between these two studies. It should be considered that there is evidence of the significant changes in the corneal profile following Keraring and Intacs implantation, with more limited astigmatic correction and more induction of spherical aberration in the initial postoperative period with Intacs.[35]

Significant improvement in UDVA and CDVA were observed postoperatively in all eyes and separately in the group with successful results which is in the line of Alfonso et al.(2013) study.[33] Likewise, no significant improvement in the mean CDVA in the eyes with unsuccessful results contrasts with the results of Alio et al. (2006) study.[27] Difference in the used protocols as well as in the sample characteristics may account for this discrepancy.

The preoperative corneal geometrical parameters (curvature and thickness) were not significantly different between the two groups regarding the outcomes' success. Although the corneal curvature in both placido-based topography and Scheimpflug tomography in the front and back corneal surfaces were slightly flatter in the group with successful results, the current study was not able to confirm an association of significant higher mean keratometry with a failure of the results, as previously reported.[27] Outcomes analysis following Intacs implantation showed that the eyes with mean keratometry readings lower than 53 D had better postoperative results, so that more advanced keratoconus staging and higher induced myopic shift may be considered as the limiting factors of corneal reshaping by the ICRS.[27] Although the keratoconus stage was reported as a main predictor success following the ICRS implantation,[22] comparison of UDVA improvement between moderate and severe keratoconus showed greater increase in moderate keratoconus following Intacs implantation,[36] while the present study showed that the outcomes are independent of the keratoconus stage. This difference may be attributed to low sample size in previous study so that 7 eyes and 1 eye with mean KR ≥52 D were included in the groups with successful and unsuccessful results, respectively. However, this study did not find predictive values for the refractive error, keratometry readings, other corneal geometric properties and keratoconus staging to predict visual outcomes after the ring implantation based on the above mentioned preoperative factors.

Another new assessed parameter was the coincidence of most elevated point on the front and back corneal surface relative to the best fist sphere on the elevation maps. Interestingly, this parameter seems to have a predicting value since coincidence was seen in almost two-thirds of the eyes with successful results. The different position between the most elevated points on the corneal surfaces may be related to the degradation of the mechanical properties of the cornea. Possibly, structural weakening may result in loss of parallelism of both corneal surfaces and more difference in the most elevated points between the two surfaces. Indeed, it was demonstrated that the correlation between anterior and posterior corneal curvature becomes weaker as the stage of the disease is more advanced.[37] Likewise, Abu Ameerh et al. reported that the vertical apex location correlated well with the severity of the keratoconus while the horizontal location seemed to have no effect.[38]

More favorable results have been reported following ring implantation (Ferrara rings) in eyes with vertical orientation of the steep topographic meridian compared to the oblique meridians; in other words, better outcomes has been shown in eyes with vertical ring orientation.[26] These findings are not consistent with the current results, not showing the different types of topographic astigmatisms (and even refractive astigmatisms) based on the orientation of corneal steep meridian (WTR, ATR and OBL) superiority in the results.

Corneal biomechanics is considered as an effective factor in the corneal response to ICRS so that the ring's effect will mostly depend on the corneal tissue biomechanical features. ICRS generates a peripheral force in the ectatic cornea leading to a central flattening, but the changes are related to corneal biomechanical behavior. Theoretically, ICRS should be having greater effect on the cornea with relatively lower elasticity modulus or softer corneas.[22, 27, 28] However, preoperative CH and CRF were not significantly different between the two groups. These findings may be attributed to the absence of severe keratoconus cases and very few cases with advanced disease, especially in unsuccessful groups, as well as, the limitation of ORA to characterize corneal biomechanical properties as it is still unknown the exact relationship between the obtained parameters using ORA and standard mechanical properties. [39] There were no significant relationship between success rate and coincidence of topographic astigmatism and comatic axes, refractive and topographic astigmatism axes, and refractive astigmatism and comatic axes in the present study.($P>0.05$) These findings are consistent with studies that reported considerable improvement in VA in the eyes (n=41) implanted with one Ferrara-type ICRS, regardless of the alignment of topographic and comatic axes.[25, 33]

Different incision locations, such as the topographic steep meridian, the positive cylinder axis, and even superior or temporal positions were reported in the literatures. Tu et al (2012) reported greater but non-significant reduction in refractive errors and keratometric astigmatism for incisions on the flat meridian compared to those performed on the steep meridian or oblique sites.[24] Although there is no general agreement on a particular reference site, in most studies, the steepest corneal meridian was used as an optimal location.[40] The location used in the current study was on the steepest topographic meridian.

Generally, the visual and ocular outcomes obtained following the ring implantation are not the result of a simple effect. They are the result of a multifactorial process which is mostly dependent on preoperative assessments and ring's characteristics, such as its thickness, insertion depth, diameter, arc length and etc. Another influential factor is the structure of the corneal stroma, with a loss of the common well-organized lamellar framework due to the degenerative process of keratoconus.[21] Therefore, more generalized assessments should be performed to better predict the final outcomes and the ring efficacy.

One limitation of this study was the low number of patients with advanced keratoconus in both groups. Although, the corneal deformation response measurement with the CorVis ST system from Oculus is another option which better examine the corneal dynamic behavior and supplies other aspects of biomechanical properties in addition to what the ORA system measured. [41] Possibly, the parameters obtained with the CorVis ST system may have better predictive value, but the clinical utility of this device in this field should be assessed in future researches.

In conclusion, this comprehensive analysis of pre-operative data showed that more difference between preoperative uncorrected and corrected distance visual acuity and more coincidence between the most elevated points in both corneal surfaces on the elevation maps are predictive factors for a successful outcome following Keraring implantation.

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Table 1: Mean and SD of refraction and visual acuity separately in the two groups created according to the achievement or not of a successful outcome. (n=68) (SD: Standard Deviation; CI: Confidence Interval; r: Correlation Coefficient; OP: Operation; SE: Spherical Equivalent; UDVA: Uncorrected Distance Visual Acuity; CDVA: Corrected Distance Visual Acuity; ^{Ŧ}: Independent samples T test or its non-parametric equivalent; $^{+}$: Wilcoxon signed ranks test; *: Non-parametric statistics)

Groups / Variables		**Successful Results (n=49) Mean±SD (95% CI)**	**No Successful Results (n=19) Mean±SD (95% CI)**	**Total (n=68) Mean±SD (95% CI)**	**P-value^{Ŧ}**
Sphere (D)	**Pre-Op**	-1.53±3.09 (-2.41, -0.64)	-1.97±2.23 (-3.04, -0.89)	-1.65±2.86 (-2.34, -0.96)	0.652*
	Post-Op	-0.44±2.41 (-1.13, 0.24)	-0.90±2.20 (-1.95, 0.16)	-0.57±2.35 (-1.13, 0.00)	0.702*
	P-value^{+}	0.001	0.006	0.000	
Cylinder (D)	**Pre-Op**	-5.79±2.51 (-6.51, -5.07)	-5.52±2.31 (-6.64, -4.41)	-5.72±2.44 (-6.31, -5.12)	0.676
	Post-Op	-2.07±2.03 (-2.66 -1.49)	-2.35±1.83 (-3.24, -1.47)	-2.15±1.97 (-2.63, -1.67)	0.967*
	P-value^{+}	0.000	0.000	0.000	
Axis (º)	**Pre-Op**	80.080±47.32 (67.20, 94.4039)	93.2568±63.94 (62.86, 124.51)	84.40±51.5652.31 (71.73, 97.06)	0.512*

	Post-Op	77.22±54.95 (61.43, 93.00)	87.68±57.78 (59.83, 115.53)	80.14±55.52 (66.70, 93.58)	0.460
	P-value+	0.802	0.658	0.599	
SE (D)	**Pre-Op**	-4.43±3.00 (-5.21, -3.52)	-4.73±2.54 (-5.79, -3.40)	-4.52±2.86 (-5.21, -3.82)	0.681
	Post-Op	-1.48±2.83 (-2.249, -0.66)	-2.07±2.2732 (-3.19, -0.945)	-1.64±2.70 (-2.30, -0.99)	0.448*
	P-value+	0.000	0.000	0.000	
UDVA (LogMAR)	**Pre-Op**	0.91±0.46 (0.77, 1.04)	0.58±0.27 (0.44, 0.71)	0.81±0.44 (0.71, 0.92)	0.005*
	Post-Op	0.34±0.26 (0.26, 0.42)	0.60±0.30 (0.46, 0.75)	0.41±0.29 (0.34, 0.49)	0.001*
	P-value+	0.000	0.305	0.000	
CDVA (LogMAR)	**Pre-Op**	0.36±0.24 (0.29, 0.423)	0.34±0.22 (0.24, 0.45)	0.35±0.23 (0.30, 0.41)	0.956*
	Post-Op	0.15±0.13 (0.12, 0.19)	0.35±0.30 (0.20, 0.49)	0.21±0.21 (0.16, 0.26)	0.011*
	P-value+	0.000	0.887	0.000	

Table 2: Mean and SD preoperative keratometry and Q-value in front and back corneal surfaces and corneal thickness using Pentacam. (n=68) (SD: Standard Deviation; CI: Confidence Interval; K: KeratometryCA: Corneal Astigmatism; Kmax: Maximum keratometry in front surface; Q: Asphericity (Q-value); CCT: Central Corneal Thickness; CTP: Corneal Thinnest Point; *: Non-parametric statistics)

Groups / Variables	Successful Results (n=49) Mean±SD (95% CI)	No Successful Results (n=19) Mean±SD (95% CI)	Total (n=68) Mean±SD (95% CI)	P-value
Front Mean K (D)	47.90±3.32 (46.95, 48.86)	48.45±2.21 (47.38, 49.52)	48.05±3.04 (47.32, 48.79)	0.305*
Front CA (D)	4.86±2.71 (4.08, 5.64)	5.06±1.86 (4.17, 5.96)	4.92±2.49 (4.31, 5.52)	0.907*
Front CA Axis (º)	85.49±48.51 (71.56, 99.43)	76.60±59.51 (47.92, 105.28)	83.01±51.51 (70.54, 95.48)	0.432*
Front Q-value	-0.80±0.46 (-0.93, -0.66)	-0.89±0.51 (-1.14, -0.641)	-0.82±0.47 (-0.94, -0.71)	0.481
Front Kmax (D)	55.47±5.01 (54.03, 56.91)	56.42±4.25 (54.37, 58.47)	55.73±4.80 (54.57, 56.90)	0.435
Back Mean K (D)	-7.06±0.88 (-7.32, -6.81)	-7.17±0.52 (-7.43, -6.92)	-7.09±0.80 (-7.29, -6.90)	0.795*
Back CA (D)	0.70±0.98 (0.42, 0.99)	0.99±0.48 (0.75, 1.23)	0.78±0.88 (0.57, 1.00)	0.140*

Back CA Axis (º)	87.73±56.40 (71.53, 103.93)	74.30±68.09 (41.47, 107.12)	83.97±59.68 (69.53, 98.42)	0.274*
Back Q-value	-0.93±0.61 (-1.10, -0.75)	-1.04±0.64 (-1.35, -0.73)	-0.96±0.62 (-1.11, -0.81)	0.504
CCT (µm)	450.24±35.14 (440.15, 460.33)	437.15±31.03 (422.20, 452.11)	446.58±34.32 (438.27, 454.89)	0.142
CTP (µm)	446.46±36.11 (436.09, 456.84)	429.84±34.50 (413.20, 446.47)	441.82±36.20 (433.06, 450.58)	0.105*

Table 3: Mean and SD corneal hysteresis (CH) and corneal resistance factor (CRF). (n=68) (SD: Standard Deviation; CI: Confidence Interval; CH: Corneal Hysteresis; CRF: Corneal Resistance Factor; *: Non-parametric statistics)

Groups / Variables	Successful Results (n=49) Mean±SD (95% CI)	No Successful Results (n=19) Mean±SD (95% CI)	Total (n=68) Mean±SD (95% CI)	P-value
CH (mmHg)	8.31±1.18 (7.97, 8.65)	8.34±1.16 (7.77, 8.90)	8.32±1.17 (8.04, 8.60)	0.941
CRF (mmHg)	6.88±1.51 (6.44, 7.31)	7.04±1.59 (6.28, 7.81)	6.92±1.52 (6.55, 7.29)	0.699

Table 4: Mean and SD of difference between UDVA and CDVA, refractive and topographic axes, refractive and coma axes, topography and coma axes separately in the two groups (n=68)

Groups / Variables	Successful Results (n=49) Mean±SD (95%CI)	No Successful Results (n=19) Mean±SD (95%CI)	Total (n=68) Mean±SD (95%CI)	P-value
UDVA-CDVA	0.56±0.43 (0.44, 0.69)	0.21±0.21 (0.12, 0.31)	0.46±0.41 (0.36, 0.56)	0.002*
Refractive-Topography Axes	-2.65±16.61 (-7.42, 2.11)	10.73±64.17 (-20.19, 41.66)	1.08±36.61 (-7.77, 9.95)	0.859*
Refractive-Coma Axes	-22.20±58.61 (-40.94, -3.45)	-14.25±60.85 (-46.67, 18.17)	-19.93±58.81 (-35.68, -4.18)	0.659
Topography-Coma Axes	-21.20±58.44 (-39.89, -2.51)	-27.12±43.98 (-50.56, -3.68)	-22.89±54.38 (-37.45, -8.33)	0.412

FIGURE LEGENDS:

Figure 1: Distribution of different types of refractive (A) and topographic astigmatisms (B) with attention to the obtained results. (WTR: With-the-rule, ATR: Against-the-rule, OBL: Oblique)

Figure 2: Distribution of different elevation patterns on the front (A), back (B) corneal surfaces and different corneal topography patterns (C, SB: Symmetric bow-tie, AB: Asymmetric bow-tie, IS: Inferior steepening, SRAX: Skewed radial axis) separately in the two groups.

Figure 3: Frequency distribution of difference <30º or ≥30º between the refractive and topography axes (A), the topography axis with coma axis and refractive and coma axes (B) separately in groups with successful and unsuccessful results.

Figure 4: Frequency distribution of different keratoconus stages with attention to the obtained results.

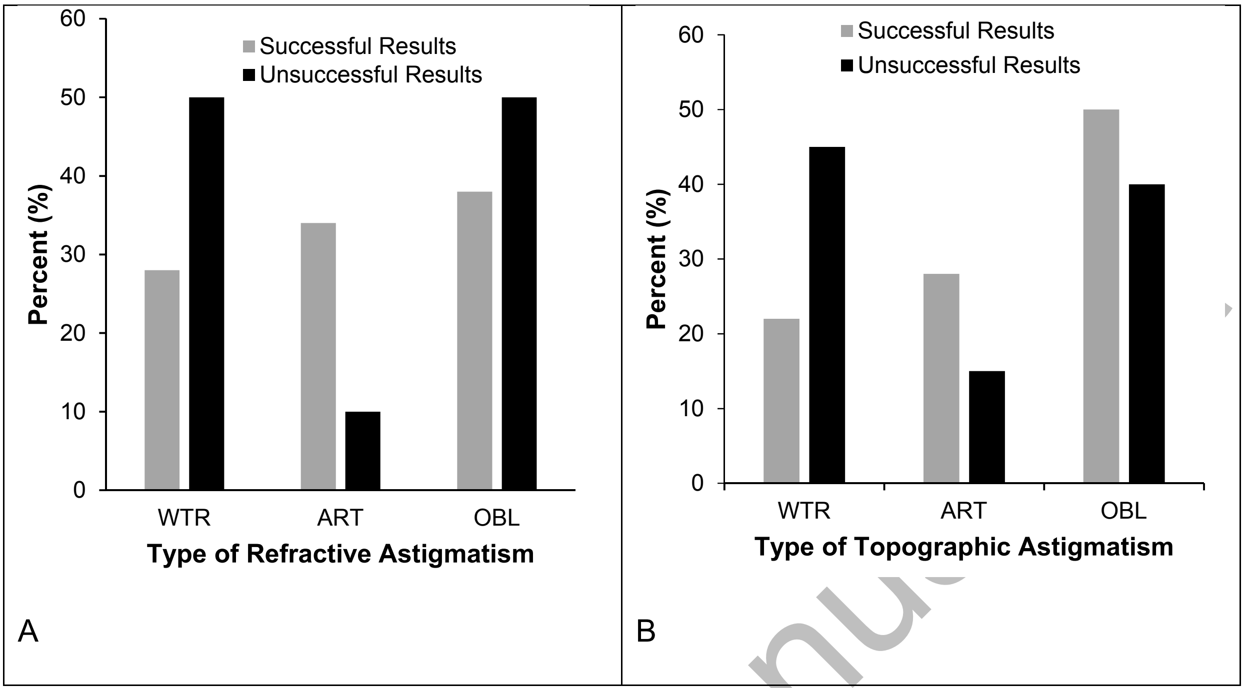

60
50
40
30
20
10
0
Percent (%)
Successful Results
Unsuccessful Results
WTR
ART
OBL
Type of Refractive Astigmatism
A
60
50
40
30
20
10
0
Percent (%)
Successful Results
Unsuccessful Results
WTR
ART
OBL
Type of Topographic Astigmatism
B

Figure 1

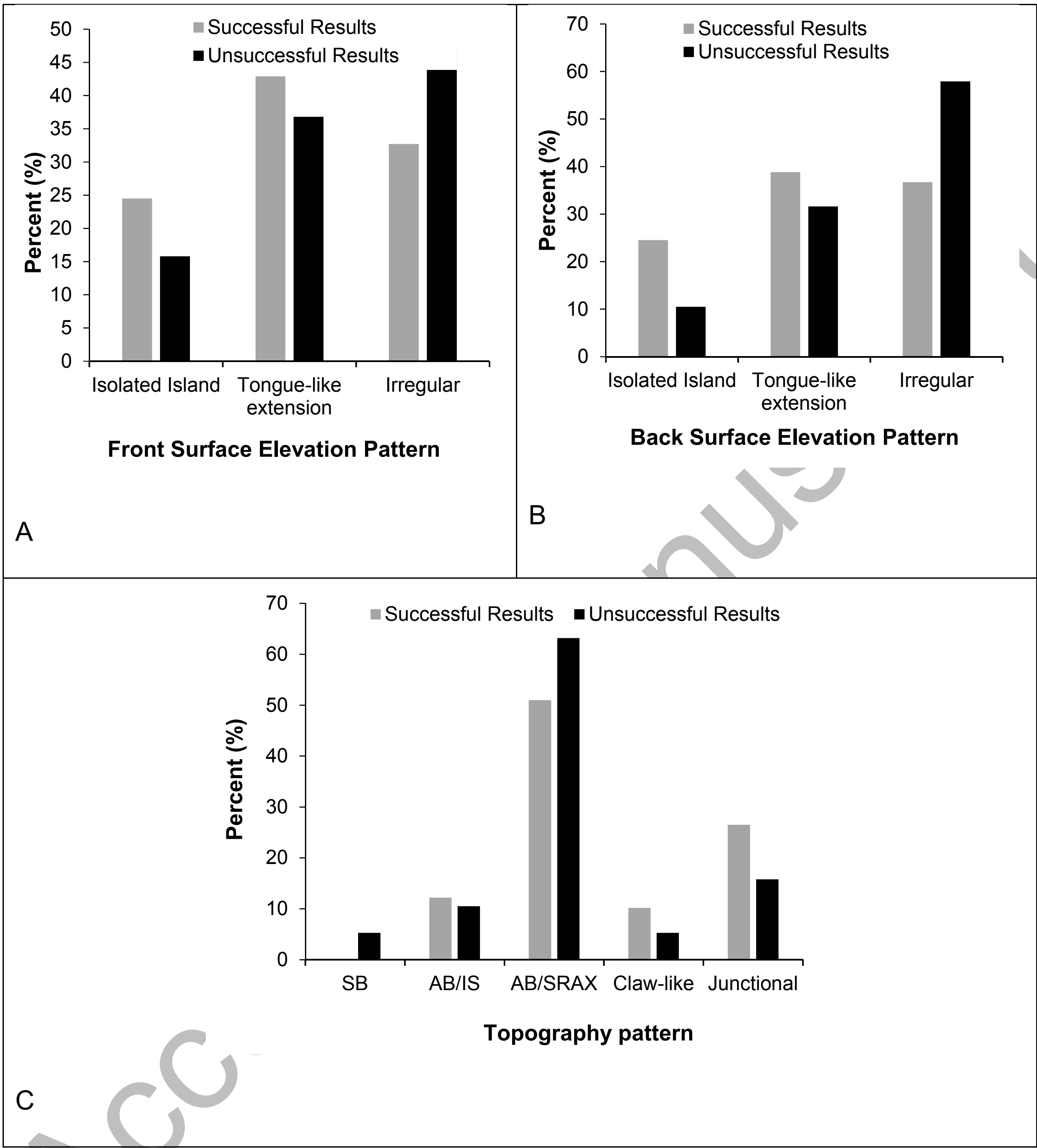
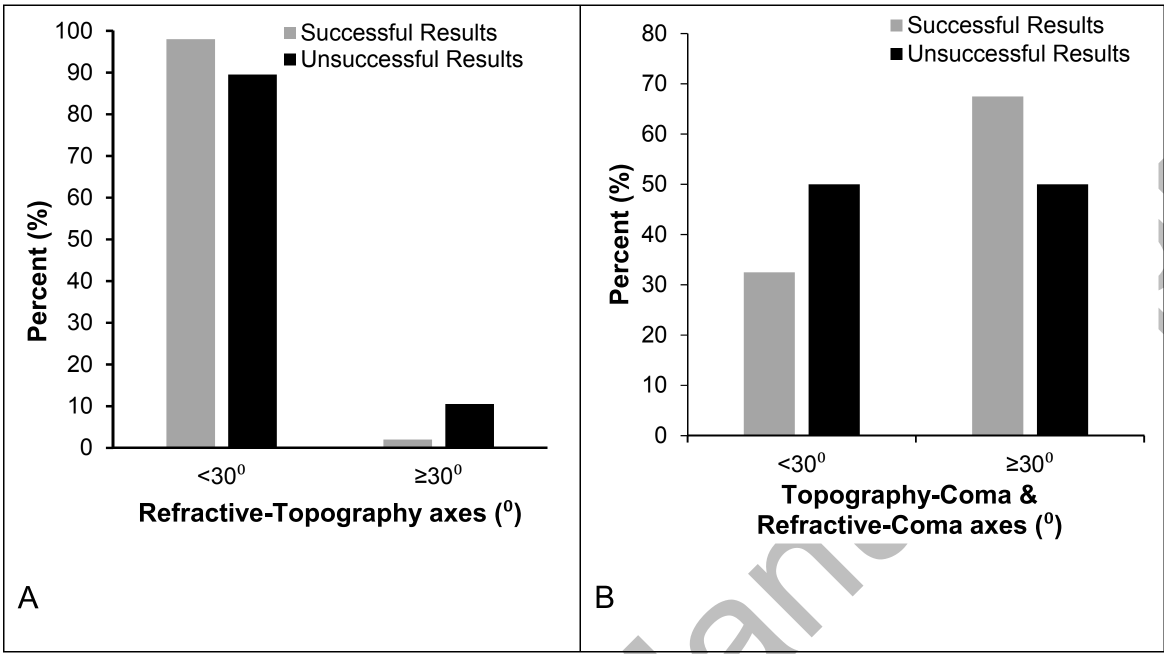

Successful Results
Unsuccessful Results
Percent (%)
Isolated Island
Tongue-like extension
Irregular
Front Surface Elevation Pattern
A
Successful Results
Unsuccessful Results
Percent (%)
Isolated Island
Tongue-like extension
Irregular
Back Surface Elevation Pattern
B
Successful Results
Unsuccessful Results
Percent (%)
SB
AB/IS
AB/SRAX
Claw-like
Junctional
Topography pattern
C

Figure 2:



Successful Results
Unsuccessful Results
Percent (%)
100
90
80
70
60
50
40
30
20
10
0
<30⁰
≥30⁰
Refractive-Topography axes (⁰)
A
Successful Results
Unsuccessful Results
Percent (%)
80
70
60
50
40
30
20
10
0
<30⁰
≥30⁰
Topography-Coma &
Refractive-Coma axes (⁰)
B

Figure 3:

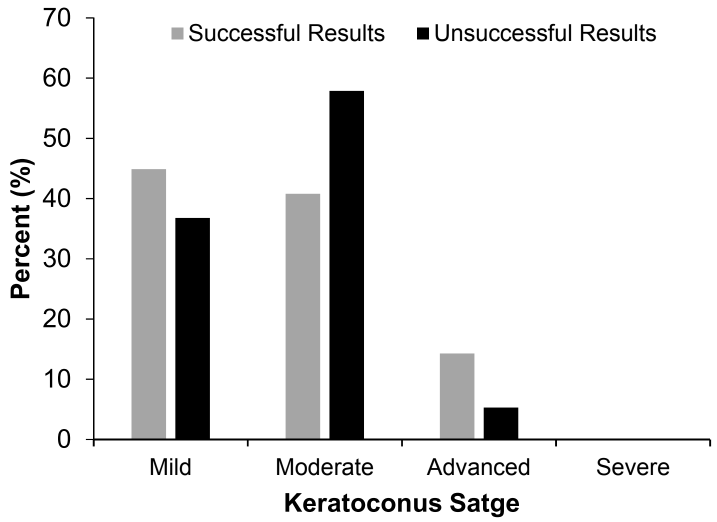

Successful Results
Unsuccessful Results
Percent (%)
70
60
50
40
30
20
10
0
Mild
Moderate
Advanced
Severe
Keratoconus Satge

Figure 4: