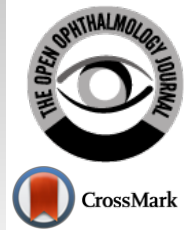




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RESEARCH ARTICLE

Corneal Indices Determined with Pentacam in Possible Candidates for Corneal Refractive Surgery

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Abstract:

Objective:

To describe the level of correlation of clinical refractive variables with corneal indices in Pentacam Scheimpflug tomography, demonstrate the usefulness of the study of corneal indices in the diagnosis of keratoconus (KC), and identify the corneal indexes with the greatest influence on the diagnosis of KC.

Methods:

A descriptive, retrospective, and cross-sectional study was conducted in 69 patients (138 eyes) with refractive disorders, possible candidates for corneal refractive surgery, at the Exilaser Ophthalmological Center, Cuenca, Ecuador, from March to August 2019. Corneal indices were studied using Pentacam. Statistical correlation methods, Levene's test, Fisher's exact test, Cramér's V coefficient, and multiple correspondence analyses were used.

Results:

The variables refractive cylinder and central keratometry had a direct correlation with the corneal indices ($p < 0.001$). An inverse correlation was obtained between central pachymetry and corneal indices ($p < 0.001$). A high level of dependence on central KC index (CKI) (Cramér $V = 0.785$) and KC index (KI) (Cramér $V = 0.775$) was obtained with the diagnosis of KC.

Conclusion:

Pentacam is a valuable tool in the analysis of corneal indices for the diagnosis of KC, given its high level of correlation with clinical refractive variables. The selection of candidates for refractive surgery, even when there is no diagnosis of KC, is strengthened with the analysis of the corneal indices. The indices with the most intense level of dependence with the diagnosis of KC are, in order, the following indices: CKI, KI, vertical asymmetry, minimum radius, and variation of the surface.

Keywords: Keratoconus, Indices, Pentacam, Keratometry, Cylinder, Pachymetry.

Article History

Received: April 4, 2020

Revised: May 26, 2020

Accepted: June 5, 2020

1. INTRODUCTION

Keratoconus (KC) is a corneal ectatic disorder that tends to be bilateral in most cases and is characterized by a progressive corneal thinning that results in corneal protrusion, irregular astigmatism, and visual impairment [1, 2]. Since the end of the last century, technological developments in this field have

enhanced the emergence of technologies that allow for an earlier and more effective KC diagnosis, thus decreasing long term complications associated with this disease.

Corneal topographic analysis has certainly been the most significant technological development. Corneal topography is a non-invasive imaging technique capable of representing the curvature, shape, and characteristics of a corneal surface effectively.

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Several commercial instruments that can be used to measure corneal thickness and curvatures are available, which vary according to the type of technology implemented. One of them is Pentacam, which is a system based on the Scheimpflug principle, with a great depth of focus that can be used to take pictures of a flat object that is not parallel to the image plane. It uses a rotating Scheimpflug camera and a monochromatic slit light source in combination with a static camera to obtain multiple images from specific angles through the optical axis [3].

Given the evident utility of corneal topographers, topographic indices have been developed, which are quantitative parameters that allow for the evaluation of the optical quality and corneal regularity in a more global way. Furthermore, they are algorithms that are included in most topographers, thus allowing for early diagnosis or an approach to the subclinical or clinical presence of corneal ectasia [4 - 6].

Corneal indices are numerical representations that simplify the interpretation of topographic results and the evolutionary study of corneal changes before and after surgery, thus acting as reference value controls [7 - 9]. They allow for a quantitative analysis of topographic information, and they are designed to simplify the distinction between normal corneas and pathological corneas even in subclinical states. They also include a combination of tomographic, topometric, and pachymetric parameters [6 - 9].

As corneal refractive surgery evolves, professional expectations are higher and continuous improvements on presurgical evaluation and interpretation, as well as detection strategies and data analysis strategies in order to avoid the inappropriate inclusion or exclusion of candidates, are required. Early and accurate KC detection using indices has been widely discussed, and the sensitivities and specificities of several parameters have been compared. In addition, new algorithms and combined indices have been introduced for achieving earlier and more accurate KC detection [10 - 12].

The purpose of this study is to describe the level of correlation between clinical refractive variables and corneal indices, demonstrate the usefulness of studying corneal indices for KC diagnosis and identify the corneal indices that have the most influence on KC diagnosis.

2. MATERIALS AND METHODS

A descriptive, retrospective, and cross-sectional study was carried out on 69 patients (138 eyes) who had refractive disorders and were possible candidates for corneal refractive surgery at Centro Oftalmológico Exiláser, Cuenca, Ecuador, from March to August 2019.

2.1. Selection Criteria

Inclusion Criteria:

-Patients with refractive disorders (myopia, astigmatism, hyperopia) who requested refractive surgery

Exclusion Criteria:

-Patients who had undergone one or more prior corneal refractive surgeries

-Pregnant patients

-Patients who had undergone corneal transplant surgery

-Patients who had used contact lenses over the last 3 months

Subjective and objective ophthalmologic examinations as well as corneal topographies (Pentacam) were performed on all study patients. According to the clinical and topographic characteristics observed, patients were diagnosed with KC. For KC diagnosis, the presence of topographic/tomographic criteria of the disease determined with Pentacam (Belin-Ambrosio Enhanced Ectasia Display) was considered, as well as the presence of clinical alterations observed in the physical examination, such as irregularities in the corneal reflex, Munson's sign, and Rizzuti's sign, and the presence of Fleischer's ring and Vogt's striae. Not all diagnosed cases had clinical characteristics in slit lamp; however, the diagnosis was made by topography, visual acuity and refraction. All cases with KC were bilateral. As a result, the sample was divided into two groups:

N1 = 92: Patients with KC

N2 = 46: Patients without KC

2.2. Study Variables

Refractive cylinder: the refractive cylinder value expressed in the patient's subjective refraction (with a negative sign in the study), supported by autorefractometer and schiascopy, expressed in diopters.

Central pachymetry: measurement of the central corneal thickness expressed in micrometers. It is selected *via* Pentacam.

Central keratometry: the average of the corneal potency value observed in the 2, 3 and 4-mm diameter rings. It is expressed in diopters and selected *via* Pentacam.

Asphericity coefficient Q-value: it describes the changes in corneal curvature from the central to the peripheral areas. Value selected *via* Pentacam.

2.3. Corneal Indices

Surface Variation Index (SVI): shows the deviation of the individual corneal radius regarding the mean value. It can be normal (<37), abnormal (37-41), or pathological (≥41).

Vertical Asymmetry Index (VAI): shows the degree of symmetry between the corneal radius and the horizontal meridian. It can be normal (<0.28), abnormal (0.28-0.32), or pathological (≥0.32).

Keratoconus Index (KI): it is defined as the relationship between the mean values of the curvature radius in the upper and lower corneal segments. It can be normal (<1.07) or pathological (≥1.07).

Central Keratoconus Index (CKI): it is the relationship between the mean values of the curvature radius in a peripheral Placido ring divided by a central ring. It can be normal (<1.03) or pathological (≥1.03).

Index of Height Asymmetry (IHA): shows the degree of

symmetry between height data and the horizontal meridian. It can be normal (<19), abnormal (19–21), or pathological (≥21).

Index of Height Decentration (IHD): estimated using a Fourier analysis of height data and shows the degree of decentration in the vertical plane, which is calculated on a 3.0-mm radius ring. It can be normal (<0.014), abnormal (0.014–0.016), or pathological (≥0.016).

Minimum Radius (minR): shows the lowest curvature radius in all the analyzed area. It is high in KC. It can be normal (≤6.71) or pathological (>6.71).

Methods for Data Collection, Statistical Analysis, and Ethical Aspects

Data were obtained from the clinical records and Pentacam Scheimpflug tomography (Allegro Oculyzer II, WaveLight GmbH, Erlangen, Germany) results of each patient. Information was processed using SPSS 9.0 for Windows (SPSS, Inc.; Chicago, USA) package program. Pearson’s correlation coefficient was obtained between the variables of interest and each studied corneal index, and a correlation matrix was determined. The mean value of each corneal index was obtained for both study groups, and a comparison of these mean values was made for each index using a T-test for the comparison of two independent population means. After this, the variances observed in both groups were compared (Levene’s test) in order to determine their homoscedasticity and heteroscedasticity.

Subsequently, a categorical analysis of the different indicators was carried out. In order to do this, a category was assigned to each case (normal, suspicious, or pathological, according to the Pentacam values obtained for each index) and contingency tables were built for assessing the correlation between these categorical variables and KC. A multiple correspondence analysis of the categorical classification variables used for the different indicators was performed. For each case, a Fisher’s exact test was applied for determining whether it was dependent or independent; if it was dependent (which was the case for all the tests performed), the direction of such dependence was assessed by an analysis of the corrected standardized residuals. Cramér’s V coefficient was estimated to analyze the level of dependence.

3. RESULTS

As can be observed in Table 1, a direct statistically significant correlation was obtained between the refractive cylinder values and the corneal indices. That is to say that the higher a cylinder value is, the higher the corneal index is, this correlation being greater with the SVI.

As can be observed in Table 2, an inverse statistically significant correlation was obtained between the central pachymetry results and the corneal indices, this correlation being greater with the KI and the CKI. The lower a central pachymetry value is, the higher the KI and CKI values obtained.

Table 1. Correlation between refractive cylinder values and corneal indices.

Index	Pearson	p
SVI	0.680**	.000
VAI	0.481**	0.000
KI	0.456**	0.000
CKI	0.509**	0.000
IHA	0.425**	0.000
IHD	0.500**	0.000
minR	0.476**	0.000

** Correlation is significant at the 0.01 level (bilateral).

Abbreviations: SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

Table 2. Correlation between central pachymetry results and corneal indices.

Index	Pearson	P
SVI	-0.527**	0.000
VAI	-0.528**	0.000
KI	-0.645**	0.000
CKI	-0.758**	0.000
IHA	-0.359**	0.000
IHD	-0.578**	0.000
minR	-0.423**	0.000

** Correlation is significant at the 0.01 level (bilateral).

Abbreviations: SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

As can be observed in Table 3, a direct statistically significant correlation was obtained between the central keratometry value (central K) and the corneal indices, this correlation being greater with the KI and the CKI. The higher a central keratometry value is, the higher the KI and CKI values obtained.

Regarding the asphericity coefficient (Q-value), as shown in Table 4, the correlation coefficients obtained show a weak inverse relationship between the asphericity coefficient and the

corneal indices.

Table 5 shows the mean value for each corneal index in both study groups. When comparing these values, statistically significant differences were obtained between patients with KC and those without KC.

Table 6 shows the level of dependence of corneal indices with KC presence. Indices with the highest level of dependency are: CKI, KI, VAI, minR, and SVI.

Table 3. Correlation between central keratometry and corneal indices.

Index	Pearson	p
SVI	0.567**	0.000
VAI	0.481**	0.000
KI	0.668**	0.000
CKI	0.778**	0.000
IHA	0.286**	0.000
IHD	0.599**	0.000
minR	0.447**	0.000

** Correlation is significant at the 0.01 level (bilateral).

Abbreviations: SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

Table 4. Correlation between asphericity coefficient Q-values and corneal indices.

Index	Pearson	p
SVI	-0.356**	0.000
VAI	-0.169*	0.047
KI	-0.229**	0.007
CKI	-0.371**	0.000
IHA	-0.140	0.102
IHD	-0.218*	0.010
minR	-0.176	0.012

** Correlation is significant at the 0.01 level (bilateral).

* Correlation is significant at the 0.05 level (bilateral).

Abbreviations: SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

Table 5. Comparison between mean index values obtained for both groups.

-	Keratoconus	N	Mean	p
SVI	No	92	29.1522 ± 1.18821	<0.0001
	Yes	46	74.2959 ± 5.36396	
VAI	No	92	0.1635 ± .01327	<0.0001
	Yes	46	0.6511 ± .05918	
KI	No	92	1.0249 ± .00295	<0.0001
	Yes	46	1.1948 ± .02021	
CKI	No	92	1.0097 ± .00108	<0.0001
	Yes	46	1.0674 ± .00710	
minR	No	92	7.3890 ± .02948	<0.0001
	Yes	46	6.3359 ± .24087	
IHA	No	92	6.654 ± .7573	<0.0001
	Yes	46	25.763 ± 3.7786	

Abbreviations: SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

Table 6. Dependence level of corneal indices with KC diagnosis.

Indicator	Cramér's V
Q	0.409
SVI	0.682
VAI	0.755
KI	0.775
CKI	0.785
minR	0.754
IHA	0.556

Abbreviations: Q (corneal asphericity coefficient), SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

Table 7. Summary of the multiple correspondence analysis model.

Summary of the model				
Dimension	Cronbach's alpha	Variance explained		
		Total (Autovalues)	Inertia	% of variance
1	0.937	5.565	0.696	69.559
2	0.144	1.145	0.143	14.309
Total	-	6.709	0.839	-
Mean	0.802 ^a	3.355	0.419	41.934

^a. Average Cronbach's alpha is based on average autovalues.

Table 8. Multiple correspondence analysis model.

Discrimination measures			
-	Dimension		Mean
	1	2	
CKI1	0.757	0.005	0.381
Q1	0.314	0.039	0.177
SVI1	0.711	0.440	0.575
AVI1	0.815	0.118	0.467
KI1	0.782	0.000	0.391
CKI1	0.863	0.002	0.432
minR1	0.843	0.001	0.422
IHA1	0.480	0.539	0.509
Total active	5.565	1.145	3.355
% of variance	69.559	14.309	41.934

Abbreviations: Q (corneal asphericity coefficient), SVI (Surface variation index), VAI (Vertical asymmetry index), KI (Keratoconus index), CKI (Central keratoconus index), IHA (Index of height asymmetry), IHD (Index of height decentration), minR (Minimum radius).

A multiple correspondence analysis was performed on the categorical variables used to classify the different indicators. It can be observed that both dimensions together account for 83.9% of the total variability, Dimension 1 being the most significant as it accounts for 69.6% of the total variability (Tables 7 and 8).

Dimension 1 includes most of the evaluated indicators (KC, Q, SVI, VAI, KL, CKL, and minR); although IHA is significantly represented in Dimension 1, it is also significantly represented in Dimension 2, as can be observed in Table 7.

The presence of KC (yes) is highly correlated with the

pathological cases observed in the different indicators, with small distances between them, whereas the absence of KC (no) is highly correlated with the normal cases observed in the different indicators as well as in the suspicious indicators of SVI and, at a lower level (higher distance) with the altered cases of the same indicator. KC values (yes or no) should not be correlated with altered IHA values.

4. DISCUSSION

All the corneal indices studied showed a direct association with the refractive cylinder value. Patients with high cylinder values have a greater alteration of the corneal indices toward

figures that are considered pathological. The fact that a patient has a high cylinder value in his or her refraction formula is highly important in the examination for a possible ectasia; however, refractive cylinder results with more than 4 diopters may exist, with alterations in the corneal indices yielded by Pentacam, and without corneal ectasia. Therefore, it is important to consider the remaining clinical variables of each patient as well as the pachymetry results. One of the indices with the highest correlation with the refractive cylinder value was the SVI, which shows the deviation of the individual corneal radius regarding the mean value.

Regarding their association with pachymetry results, all the corneal indices increase up to figures that are considered to be pathological as the patient's central pachymetry value decreases. This correlation was greater with KI and CKI, which include the patient's pachymetry value in their analysis, thus turning into more comprehensive and specific indices for corneal ectasia diagnosis. Nevertheless, it is necessary to highlight that, although the remaining indices do not include corneal pachymetry results within their analysis, the changes observed toward pathological figures are particularly sensitive in patients with decreased pachymetry results.

Similar results were obtained with central keratometry, which directly correlated with several indices, particularly with KI and CKI, evidencing once more the influence of a high corneal curvature in the diagnosis of corneal ectasia. The lowest correlation was observed with the IHA.

Corneal asphericity coefficient Q-values did not show a correlation with the corneal index values obtained. The Q-value describes the changes in the corneal curvature from the central to the peripheral area.

The significant differences obtained between the mean index values estimated for both study groups suggest their usefulness in the diagnosis of corneal ectasia, which has been widely demonstrated in different studies [13 - 15]. However, further research into some elements that specify the variations observed in these values and their relationship with KC diagnosis is necessary. According to the results obtained, there are indices with a greater dependency level regarding KC diagnosis, such as CKI, KI, VAI, and SVI.

In this sense, we agree with prior researchers who showed CKI as a parameter for refractive detection which is highly capable of discriminating clinical KC from normal eyes [16 - 19]. Besides, research studying CKI increase and its relationship with early KC has been conducted. Bae reports an increase of CKI in the healthy eye of patients with unilateral KC; however, Huseynli reported that CKI is a poor parameter for preKC distinction [18, 20]. CKI is a valuable index capable of providing a quick reference in the identification of frank KC, and it is also highly useful to confirm clinical suspicions when used as a cross-reference parameter in relation to other indices.

According to the results obtained in this research, KI is one of the indices with the highest levels of dependence on KC, and it certainly represents an efficient diagnostic test used to discriminate between normal eyes and KC eyes. In this sense, we did not obtain results that were similar to the ones reported by Chan, who showed a KI diagnostic accuracy lower than other Pentacam indices obtained for KC diagnosis [16]. In contrast, the results obtained are consistent with those reported

by Orucoglu, who states that KI is an excellent indicator of KC diagnosis, with sensitivity and specificity levels higher than 90%, which are even higher than the ones obtained for CKI [21, 22]. Huseynli and Bae suggest that KI application should be limited to preKC patients [18, 20].

VAI is another parameter in which we obtained a high dependency level to the presence of corneal ectasia. Shetty obtained a high level of sensitivity in this index as a parameter for KC diagnosis [23]. Hashemi found that VAI was useful in preKC cases [17]. Arbelaez carried out a study with an index that was similar to the VAI, which showed a high predictive ability for preKC [24]. The importance of this index for diagnosing KC and determining the predictability of the disease is very clear; however, as it also happens with the previously analyzed indices, its full validity in preKC cases has not been shown.

SVI is also a highly sensitive parameter for KC diagnosis as it reflects the presence of irregular astigmatism. These results are consistent with those reported by different authors: a pathological SVI shows alterations of the corneal curvature [11, 17, 23]. Conversely, results that confirm its utility in preKC cases have also been obtained [22, 25]. An aspect that highlights the usefulness of this index demonstrated its importance in the postoperative follow-up of patients, as well as in KC progression in longitudinal analysis. In this sense, Kanellopoulos reports a high SVI sensitivity [26].

According to the results obtained, IHA, as opposed to the previously analyzed indices, did not have a high level of dependence on corneal ectasia. Different authors show a high sensitivity of IHA in KC detection and low sensitivity in preKC detection; for this reason, it is not very useful for the detection of the earliest corneal changes occurring toward ectasia [18, 20, 23].

The results obtained for IHD were similar to those obtained for IHA. Bae states its usefulness in unilateral KC cases; besides, IHD has proven to be highly useful in preKC cases with high diagnostic accuracy [20]. However, Shetty states that this parameter lacks clinical accuracy in this sense [23]. Studies carried out in order to assess the usefulness of an index in preKC cases are always conditioned by selection bias in one way or another because the selection criteria for preKC cases as well as their definition may be controversial and may vary among several authors (subclinical, suspicious, and frustrated).

It is important to highlight that, regardless of the considerable usefulness of corneal indices in KC diagnosis, ophthalmologists should act based on the clinical criteria established for the disease, such as visual acuteness assessment, corneal aberration examination, family KC history, presence of an ocular allergy, and/or chronic eye-rubbing patients. They should not analyze corneal indices as isolated rigid variables as they are not capable of diagnosing corneal ectasia. The validity of the clinical method does not decrease with the analysis of these indices; on the contrary, it becomes stronger.

Ophthalmologists should not omit the area where their patients are examined; studies that identify regional differences in KC regarding its morphology and areas of higher prevalence are increasingly frequent [27 - 29]. This research was carried out in a city where a higher KC prevalence was reported in

comparison with the rest of the country; for this reason, if the examination takes place in areas with these characteristics, the index analysis should be deeper and be further selective when choosing candidates for corneal refractive procedures [30].

In contrast, the development of Pentacam as a diagnostic method has been optimized with new applications that go beyond the analysis of corneal indices. The Belin–Ambrosio analysis allows for a more comprehensive assessment of patients because of its multivariate potential, which has a greater contribution in patients with preKC as opposed to the study of corneal indices [31 - 34].

Current limitations of corneal indices include the fact that they have not been cross-validated for several reference surfaces. The Best-Fit Sphere (BFS) is the most common reference method; however, it may not be possible to apply it in patients with irregular astigmatism or severe astigmatism. For this reason, it is necessary to carry out index analysis with an improved BFS (better than the conventional BFS) and the best-fit toric ellipsoid (which is a better reference, used to identify cone height) [35, 36].

The study of corneal indices in specific populations with different age groups is another necessary aspect; most of the Pentacam normative database was obtained from refractive surgery candidates aged between 21 and 40 years old; moreover, for studying regional variabilities that may exist regarding emmetropic patients, patients with refractive defects and patients with corneal ectasia should be studied [18, 37 - 42]. It is also important to perform multicentric research on corneal indices of patients with preKC and to agree upon patient selection criteria. Another aspect to be considered is the determination of a corneal index capable of characterizing the predictability and the evolution of this disease.

CONCLUSION

Pentacam is a valuable tool in the analysis of corneal indices for KC diagnosis because of its high level of correlation with clinical refractive variables. The index values increase up to figures considered to be pathological in patients with high refractive cylinders, elevated keratometry results, and low pachymetry results.

The selection of candidates for refractive surgery, even when there is no KC diagnosis, is supported by the analysis of corneal indices because of the remarkable differences in the index values observed in patients without and with KC.

Indices with the highest dependency level toward KC diagnosis include, from the highest to the lowest level: CKI, KI, VAI, minR, and SVI.

The validity of the clinical methods does not decrease with the analysis of these indices.

LIST OF ABBREVIATIONS

Q	=	Corneal Asphericity Coefficient
SVI	=	Surface Variation Index.
VAI	=	Vertical Asymmetry Index.
KI	=	Keratoconus Index.
CKI	=	Central Keratoconus Index.

IHA	=	Index of Height Asymmetry.
IHD	=	Index of Height Decentration.
minR	=	Minimum radius.
N	=	Number.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Bioethics Committee of the Exilaser Ophthalmological Center, Cuenca, Ecuador (under approval number 9).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed written consent was obtained from all the patients when they were enrolled.

AVAILABILITY OF DATA AND MATERIALS

The databases of the current research are the property of the authors and are part of the statistical information of the Exilaser Ophthalmological Center, for which reason it is not possible to share it. Furthermore, these data will form part of future research by the institution.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

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