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Influence of the central corneal zone of patients on the measurement of keratometric parameters and the resultant KISA% index classification

Influencia de la zona central de la córnea sobre los parámetros queratométricos y el índice KISA%

A. F. Muñoz-Potosi[1*], L. G. Valdivieso-González[1], P. Rodríguez-Montero[2], A. Cruz-Félix[2], E. Tepichín-Rodríguez[2]

1. GICBA, Unidades Tecnológicas de Santander.

2. Instituto Nacional de Astrofísica Óptica y Electrónica.

(*) E-mail: amunozpotosi@gmail.com

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ABSTRACT:

Purpose: To analyze the influence of certain diameters of the corneal zone of a selected group of patients on the measured values of keratometric parameters and the resultant KISA% index classification.

Methods: One hundred and two eyes from fifty-one volunteers born in the central region of Mexico, between 25 and 40 years old, without previous diagnosis or treatment for keratoconus, were enrolled in this retrospective study. The same ophthalmologist evaluated all patients, and the same technician measured their keratometric parameters using the same topographer, an Orbscan II Topography System. The influence of the corneal zone on the resultant KISA% index was analyzed using the formalism of the Receiver Operating Characteristic (ROC) curves.

Results: As a consequence that the Area Under the ROC Curve (AUC) obtained with data for a 5.0 mm corneal zone diameter is larger than the AUC obtained for a 3.0 mm corneal zone, the ability to discern between normal and suspected eyes increased by 11%; between suspected eyes and those confirmed with keratoconus increased by 1.2%; and between normal eyes and those confirmed with keratoconus increased by 1.1%.

Conclusion: From the analysis of the resultant ROC curves and the AUC, we demonstrated that, for a 5.0 mm corneal zone, the KISA% index results in a more reliable diagnostic. The discrimination between normal and suspected eyes can be difficult under certain circumstances; however, we achieved a more accurate diagnostic for discriminating normal eyes from suspected eyes when a 5.0 mm corneal zone is used instead of a 3.0 mm corneal zone.

Key words: Keratoconus; ROC Curve; Diagnostic Techniques and Procedures; Corneal Topography.

RESUMEN:

Propósito: Analizar la influencia de diferentes diámetros de la zona corneal de un grupo seleccionado de pacientes, sobre los valores medidos de los parámetros queratométricos y la clasificación del índice KISA% resultante.

Métodos: En este estudio retrospectivo se incluyeron ciento dos ojos de cincuenta y un voluntarios nacidos en la región central de México, con edades entre 25 y 40 años, sin diagnóstico ni tratamiento previo para queratocono. El mismo oftalmólogo evaluó a todos los pacientes y el mismo técnico midió sus parámetros queratométricos utilizando un topógrafo corneal Orbscan II. La influencia de la zona corneal y el índice KISA% se analizaron utilizando el formalismo de las curvas características de receptor – operador (ROC).

Resultados: El área bajo la curva ROC (AUC) obtenida para una zona corneal de 5.0 mm es mayor que el AUC obtenida para una zona corneal de 3.0 mm, la capacidad de discernir entre ojos normales y sospechosos aumentó en un 11%; entre ojos sospechosos y confirmados con queratocono aumentó un 1.2%; y entre ojos normales y confirmados con queratocono aumentó un 1.1%.

Conclusión: A partir del análisis de las curvas ROC y el AUC, demostramos que, para una zona corneal de 5.0 mm, el índice KISA% es un diagnóstico más confiable. La discriminación entre ojos normales y sospechosos puede resultar difícil en determinadas circunstancias; sin embargo, logramos un diagnóstico más preciso para discriminar ojos normales de ojos sospechosos cuando se utiliza una zona corneal de 5.0 mm en lugar de una zona corneal de 3.0 mm.

Palabras clave: Queratocono, Curvas ROC, Técnicas de diagnóstico y procedimiento, Topografía corneal.

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1. Introduction

Keratoconus is a progressive disease and is the most common corneal ectasia with several genetic and etiologic factors involved. It produces changes in the shape of the cornea that affect the visual quality, increase the sensitivity to light, and create distortions in the image [1, 2]. In moderate or advanced stages, keratoconus is easily identified in clinical practice using standard procedures, such as slit-lamp, direct ophthalmoscopy, and retinoscopy examinations [1, 2]. However, early-stage keratoconus detection requires additional tests such as corneal topography, optical coherence tomography (OCT), corneal biomechanical, and aberrometry [3, 4]. Currently, many diagnostic tools exist for early-stage keratoconus detection [5-11].

Among the diagnostic tools for keratoconus detection, corneal topography devices are the most used because they provide a variety of corneal parameters and indices that offer an adequate diagnostic capacity [12, 13]. The most commonly used corneal topographers are based on Placido discs, which reconstruct the corneal shape using the reflection principle of concentric rings, and the Orbscan topographer, which uses an additional slit scanning system [14, 15].

Some authors have used information reported by the Orbscan for the early detection of keratoconus or its progress and have highlighted the importance of using the information given by the corneal topographic parameters calculated automatically by the Orbscan software [16-21]. These parameters are significantly higher when a suspected keratoconus eye is compared with a normal one [20, 22, 23]. Additionally, authors like Sonmez et al. [22] and Lim et al. [24] have carried out studies and they've acknowledged the importance of considering several corneal zone diameters, such as 3.0 mm and 5.0 mm, to compare the keratoconus group with the normal group and the keratoconus group with the keratoconus suspect group, respectively.

On the other hand, the Orbscan uses an algorithm to calculate the corneal irregularity indices in the 3.0 mm and 5.0 mm zones, which, according to Hassemi et al [25], can be crucial in screening patients. This is because the irregularity can be associated with loss of best-corrected vision, which was found to be strongly correlated with the maximum keratometry readings.

Following the above statement, no doubt analyzing the information provided by Orbscan for different corneal zones diameters can bring some advantages to the diagnosis of keratoconus. For this reason, it is convenient to choose a criterion that, using the information reported by commercial devices, allows quantifying and diagnosing keratoconus.

In this report, we consider the KISA% index, which was proposed by Rabinowitz and Rasheed in 1999[26]. The KISA% index has proved to be a reliable method to classify the degree of keratoconus with almost no overlapping between the classification groups [1]. The parameters used to calculate the KISA% index are measured at a specific corneal zone. However, to the best of our knowledge, analysis of the influence of the corneal zone and the measured parameters that lead to the calculated value of the KISA% index is almost absent.

Therefore, this report aims to analyze the influence of the corneal zone of a selected group of patients on the measurement values of keratometric parameters and the resultant KISA% index classification. This influence will be analyzed using the KISA% index's predictive ability. In particular, we will use the formalism of the ROC curves to analyze our results, as explained in the following sections.

2. Method

The quantitative indices of a selected group of patients were calculated from information reported by an Orbscan II Topography System, which provides the values of several topography parameters employed to calculate the KISA% index: the central corneal steeping (K), the degree of regular corneal astigmatism (AST), the difference between inferior and superior area (I–S), and the relative skewing of the steepest radial axes (SRAX).

The KISA% index is given by the equation: [26]

$$KISA\% = \frac{(K) \times (AST) \times (I - S) \times (SRAX) \times 100}{300}, \tag{1}$$

where the values of the parameters K, AST, I-S, which are given in diopters, and SRAX given in degrees, were directly obtained from the data displayed by the topography system employed (see Table 2). It is important to notice that, from the four parameters included in equation (1), the only parameter that is independent of the corneal zone is AST. For this reason, the KISA% index could vary depending on the selection of 3.0 mm or 5.0 mm corneal zone diameters.

This KISA% index, an effective and useful tool in our field, classifies the disease into four groups according to the numerical outcome from this criterion; eyes are classified as normal for KISA% values lower than 60%, suspect for values between 60% and 100%, early keratoconus for values over 100% and advanced keratoconus for values higher than 5000% [26-28].

Also, it is worth noting that, as mentioned by Rabinowitz, and due to the combination of the parameters, the KISA% may be greater than 100% and up to 10000% for advanced keratoconus [26]. However, additional criteria must be considered to evaluate equation (1); the precise description is beyond the scope of this work (see reference [26] for further details).

According to the above classification, we use the KISA% values to diagnose keratoconus in several corneal zone diameters. The influence of the corneal zone on the KISA% index was analyzed using the formalism of the ROC curves.

On the other hand, the ROC curve illustrates a trade-off between sensitivity and specificity for any diagnostic test that uses a continuous variable [29-34]. The sensitivity of a test for a given threshold is the ratio of the between the number of true positives (TP) to the sum of the true positives (TP) plus the number of false negatives (FN). It is a measure of the reliability of the test. The sensitivity of a test is defined as:

$$Sensitivity = \frac{TP}{TP + FN}, \quad (2)$$

for the same test, the specificity of the test, for the same given threshold, relates to the number of false positives (FP) and the number of true negatives (TN). It is the ratio of the number of true positives (TP). The specificity is defined as:

$$Specificity = 1 - \frac{FP}{FP + TN}. \quad (3)$$

Different values for sensitivity and specificity are calculated from a corresponding threshold. The threshold is a user-defined continuous variable, in this case, the KISA% index.

The ROC curve is obtained by plotting sensitivity versus (1–specificity). The details for the calculation of a ROC Curve are given in [29-32]. The AUC is commonly used for assessing the discrimination ability of prediction models [32]. The AUC value can be interpreted as the probability of correctly identifying the predicted risks in a specific population. It quantifies the separation between the distributions of diseased and non-diseased individuals. For instance, an AUC equal to the unity implies that the test perfectly differentiates between the different study groups, which means it can identify true positives and negatives. That is, it can improve the discernment between normal vs. suspected, suspected vs. keratoconus, and normal vs. keratoconus [35].

In this retrospective study, one hundred and two eyes from fifty-one volunteers whose relatives were diagnosed with keratoconus were enrolled. The subjects should not have had genetic diseases associated with keratoconus for inclusion in the study. Moreover, they should not have undergone photorefractive surgery or any other eye surgery that may have resulted in significant changes in corneal topography. Informed consent was obtained, and the subjects' age and gender were recorded. The same ophthalmologist evaluated all patients, and the same technician measured their keratometric parameters using the same topographer.

An Orbscan II Topography System was used to determine the patients' topographic parameters. This equipment can simultaneously analyze different corneal zones. In particular, the different parameters (K, I-S, AST, and SRAX) at 3.0 mm and 5.0 mm corneal zones were measured. Currently, there are devices, such as the Pentacam®, which can measure up to 7.0 mm of the corneal zone [36-38]; however, using Pentacam results to calculate or compare KISA% is beyond the scope of this paper.

3. Results

Of the 51 volunteers, 43% were female and 57% male; both eyes for each volunteer were diagnosed. All volunteers were born in the central region of Mexico, between 25 and 40 years old, with a mean age of 31.98±4.10 years. From the 102 eyes, the ophthalmologist's diagnosis was 51 eyes with confirmed keratoconus, 12 with suspected keratoconus, and 39 as normal eyes. The mean age was 33.20±3.99 years for the confirmed keratoconus group, 34.00±2.94 years for the suspected keratoconus group, and 30.22±3.83 years for the normal eyes group. (see Table 1). It is important to note that, 4 of our volunteers presented a different diagnosis in each eye. These patients are included in Table 1, as Double Diagnostic patients.

TABLE 1. Demographic characteristics of patients.

Characteristic	Norm.	Susp. KC	KC	Double diagnostic
No. of patients	18	4	25	4
Male gender	10 (55.5%)	2 (50%)	16 (64%)	1 (25%)
Age (yrs) mean ± SD	30.22 ± 3.83	34.00 ± 2.94	33.20 ± 3.99	30.25 ± 4.57
No. of eyes	39	12	51	N/A

KC, Keratoconus; Norm, normal eye; N/A, not applicable; SD, standard deviation; Susp. KC, suspected Keratoconus, yrs, years.

Table 2 shows typical parameters obtained for four volunteers with different diagnostics, using two corneal zones (3.0 mm and 5.0 mm), and the KISA% value determined by these parameters.

TABLE 2. Values reported by the Orbscan II for four different volunteers using two corneal zones.

Topographic indices	Case 1		Case 2		Case 3		Case 4	
	Corneal zone		Corneal zone		Corneal zone		Corneal zone	
	3.0 mm	5.0 mm	3.0 mm	5.0 mm	3.0 mm	5.0 mm	3.0 mm	5.0 mm
K value (D)	43.6	43.1	43.9	43.8	45.7	44.9	42.5	41.4
I-S value (D)	0.9	0.8	2.1	2.3	1.2	0.7	1.2	3.7
AST (D)	0.6	0.6	2.0	2.0	1.3	1.3	–0.3	–0.3
SRAX (deg)	88	94	89	95	96	174	87	89
KISA%	29.3	31.3	124.6	145.7	49.9	75.4	34.8	109.8

AST: degree of regular corneal astigmatism; D: diopters; deg: degree; I-S value: difference between inferior and superior area; KISA%: index criterion; K value: central corneal steeping; mm: millimeter; SRAX: relative skewing of the steepest radial axes.

In case 1, the eye remains classified as normal, independent of the corneal zone. Case 2 shows the parameters for an eye diagnosed with keratoconus obtained for 3.0 mm and 5.0 mm corneal zones. Similar to case 1, the diagnostic does not change. However, minor changes appear in the measured parameters that affect the KISA% value for eyes located in the boundary normal-suspect diagnostic. Case 3 shows an example where an eye, diagnosed as normal using a 3.0 mm corneal zone, changes to suspect when the parameters are measured using a 5.0 mm corneal zone. We also found that some eyes were diagnosed as normal when they were analyzed using a 3.0 mm corneal zone; however, when they were analyzed using a 5.0 mm corneal zone, they were diagnosed with keratoconus. Case 4 shows an example of this later situation.

As mentioned above, presenting our findings using the ROC curves is convenient. Figures 1 to 3 show the ROC curves for all 51 volunteers grouped according to the three intervals of KISA% index value calculated for 3.0 mm and 5.0 mm corneal zones and the diagnostic determined by an ophthalmologist expert in keratoconus. In these Figures, the solid line indicates that a 3.0 mm corneal zone was utilized, and the dashed line was obtained using a 5.0 mm corneal zone. The long and short dashed line at 45° is a reference one. ROC curves above this line mean that the test provides a good diagnostic prediction.

4. Discussion

It´s worth noting that clinically advanced keratoconus is relatively more straightforward to detect, as Rao et al [39] noted. Higher anterior and posterior corneal elevations reported by an Orbscan topographer have been consistently associated with patients diagnosed with confirmed keratoconus. The main problem is distinguishing suspected keratoconus eyes from normal ones, as Al-Timemy et al [40] mention. Consequently, there are many criteria and techniques to diagnose suspected keratoconus, Zéboulon et al [41] mentioned that corneal topography is the “gold standard” for diagnosing keratoconus.

Among several features, the Orbscan topographer calculates irregularity indices through keratometry values from the standard deviation of the axis-independent surface curvature and the mean astigmatism in 3.0 mm and 5.0 mm corneal zones [22, 25, 42, 43]. The irregularity indices evidence the optical surface irregularity [44]. Knowledge of these values can be beneficial in diagnosing corneal disease, especially ectatic conditions [42].

In addition, Sonmez et al [22] conclude that the mean values for different parameters from Orbscan data, such as the amount of astigmatism, central corneal power and irregularity indices at 3.0 mm and 5.0 mm were significantly higher in the keratoconus group compared with the normal group.

Moreover, to take advantage of all the information provided by Orbscan, Lim et al [24] have analyzed quantitative topographic parameters for the 3.0 mm and 5.0 mm irregularity to investigate the linear associations between the maximum keratometry and other corneal parameters obtained from Orbscan. They found that the means of the parameters are significantly higher in eyes in the keratoconus group than the keratoconus suspect; however, eyes in the keratoconus suspect group had higher 3.0 mm and 5.0 mm irregularity.

Hashemi et al [25] reported a strong correlation between these indices and the maximum keratometric readings. In contrast, Tummanapalli et al [45] highlighted that for a 5.0 mm corneal zone, the irregularity index of the posterior corneal surface exhibited high sensitivity and specificity in the early detection of subclinical keratoconus.

Sedghipour et al [1] research demonstrated that corneal topography is more effective for early diagnosis of keratoconus when compared to clinical examination. Corneal topography exhibited a sensitivity of 87% and a specificity of 92% for diagnosis. Nevertheless, the authors recommend that combining multiple topography indices can further enhance the accuracy in confirming the presence of keratoconus or suspected keratoconus.

Notably, studies on the influence of the corneal zone on the diagnosis of keratoconus are almost absent. In this study, we observed that the determination of the KISA% index, utilizing quantifiable topographic parameters obtained from an Orbscan device, exhibited variations when considering different corneal zones, specifically at 3.0 mm and 5.0 mm. The value of some parameters, such as keratometric astigmatism, simulated maximum and minimum K readings, and their corresponding meridian, do not depend on the corneal zone. In contrast, the value of parameters like mean power, the astigmatism power, and the steep and flat axes depend on the corneal zone. Aforementioned, the KISA% index value is determined by the product of indices that are dependent on the corneal zone (K, I-S, SRAX) and indices that are independent on the corneal zone (AST).

On the other hand, when the diagnostic accuracy of the KISA% index with that provided by a specialist was compared, we discovered that the ability to differentiate between diagnoses improved significantly, particularly for patients with normal eyes and those suspected of having keratoconus, when information from the 5.0 mm corneal zone was used.

As mentioned before, the larger the area under the ROC curve, the better the discernment of the employed test. Note that in Figures 1 to 3, the area under the dashed line is larger than that under the solid line. This difference means that, for measurements employing a 5.0 mm corneal zone, the KISA% index results in a better diagnosis. For the particular group of volunteers examined, the ability to distinguish between normal and suspected eyes increased by 11%; between suspected eyes and those confirmed with keratoconus increased by 1.2%; and between normal eyes and those confirmed with keratoconus, only by 1.1%.

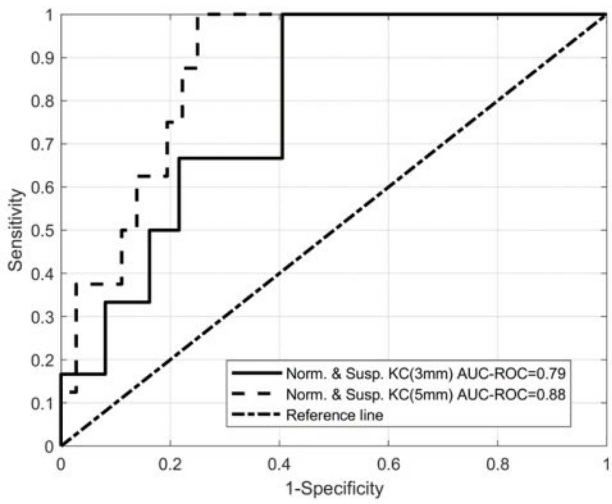

Fig.1. ROC curves for volunteers whose diagnostic is Normal eye (Norm.) and Suspected Keratoconus (Susp. KC); that is, for values of the KISA% index lower than 100%. AUC-ROC, area under the curve - receiver operating characteristic; Norm, normal eye; Susp. KC, suspected Keratoconus.

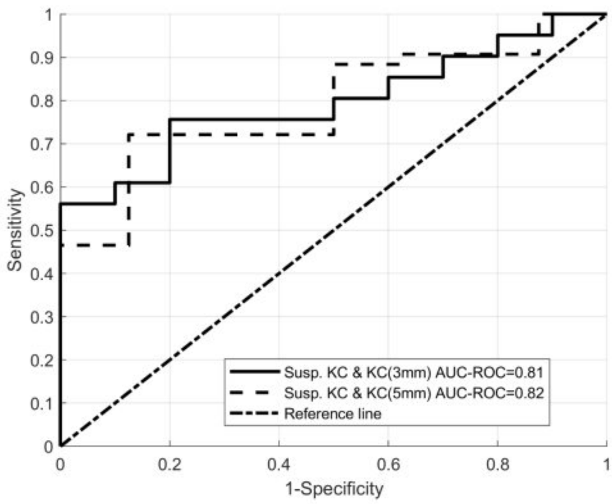

Fig.2. ROC curves for volunteers whose diagnostic is Suspected Keratoconus (Susp. KC) and Confirmed Keratoconus (KC). AUC-ROC, area under the curve - receiver operating characteristic; KC, Keratoconus; Susp. KC, suspected Keratoconus.

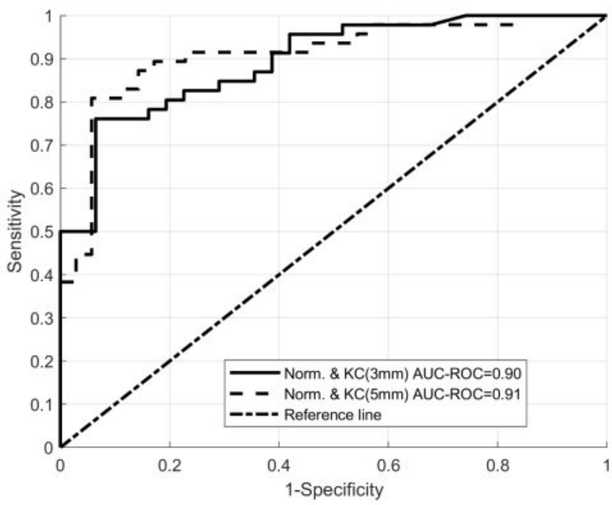

Fig.3. ROC curves for volunteers whose diagnostic is Normal eye (Norm.) and Confirmed Keratoconus (KC). AUC-ROC, area under the curve - receiver operating characteristic; Norm, normal eye; KC, Keratoconus.

Our results align with the literature since keratoconus is generally an asymmetric ectasia, and the quantification of the asymmetry can depend on the testing zone. Errors in this quantification can lead to different diagnostics or interpretations [46-49]. Although the increase in the power of discernment of the test can sometimes be slight, the effect can be significant on the patients' treatment.

5. Conclusions

We conducted an analysis to assess the impact of the corneal zone in a selected group of patients on keratometric parameters and the resulting KISA% index classification. We employed the ROC method to evaluate the predictive capability of these parameters. Our findings reveal that, in general, the area under the ROC curve obtained using data from a 5.0 mm corneal zone surpasses that obtained from a 3.0 mm corneal zone. This suggests that the KISA index yields a more reliable and accurate diagnosis when a 5.0 mm corneal zone is considered. Discriminating between normal and suspected eyes can be challenging in certain circumstances. However, we demonstrated that a more precise diagnosis is achievable for distinguishing normal eyes from suspected eyes when utilizing a 5.0 mm corneal zone as opposed to a 3.0 mm corneal zone.

Even though our proposal offers statistical justification for expanding the clinical examination's corneal zone from 3.0 mm to 5.0 mm, further research is needed, including a larger sample of patients and extending our proposal to encompass a broader corneal zone.

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