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A combination of topographic and pachymetric parameters in keratoconus diagnosis

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ABSTRACT

Purpose: To evaluate the utility of topographic and pachymetric parameters of *Scheimpflug* system in keratoconus diagnosis.
Methods: This study included 183 eyes of 183 patients with keratoconus (keratoconus group) and 131 eyes of 131 age and sex-matched healthy subjects (control group). Mean keratometry (*K*, front), topographic astigmatism, pupil-center pachymetry, apical pachymetry, thinnest pachymetry (*TP*), corneal volume and maximum *K* (*Kmax*) were obtained from the *Scheimpflug* imaging system. A receiver operating characteristic (ROC) analysis was performed and area under the curve (AUC) was calculated to determine the diagnostic ability of each parameter in eyes with ≤ stage 3, ≤ stage 2 and stage 1 keratoconus based on the Amsler–Krumeich grading system.
Results: The *Kmax* and *TP* showed the highest individual performance (with sensitivity–specificity of 92.9–92.4% and 89.6–93.3%, respectively) in diagnosis of keratoconus. The AUCs and sensitivity–specificity values for the *Kmax*/*TP* and $Kmax^2/TP$ were calculated to improve the diagnostic performance. As expected, sensitivity–specificity values significantly increased by using *Kmax*/*TP* (97.3–94.7% at the level ≥0.08) and $Kmax^2/TP$ (99.5–95.7% at the level ≥4.1) in discrimination of keratoconic eyes from normals. Moreover, $Kmax^2/TP$ had very high sensitivity (>99%) and specificity (>94%) in diagnosis of stage 1 and stage 2 keratoconus.
Conclusions: Although *Kmax* and *TP* appear to have high diagnostic ability in keratoconus, the use of either single parameter in isolation might be unsatisfactory in differential diagnosis. Therefore, the $Kmax^2/TP$ ratio has been introduced, which reflects major characteristics of keratoconus and might be used as an important criterion in keratoconus diagnosis.

1. Introduction

Keratoconus is a non-inflammatory corneal disease with progressive thinning and apical protrusion, which result in visual deterioration secondary to high myopia and irregular astigmatism [1]. The incidence of keratoconus in the general population is 1 per 2000 and no gender predominance was reported. The disease begins at puberty and shows progression until the third-fourth decade of life [1]. Clinical symptoms vary on the stage of the disease. A detailed patient history, refraction, keratometry and typical findings such as stromal thinning, iron deposits within the corneal epithelium (Fleischer's ring), vertical stress lines in the deep stroma (Vogt's striae), anterior stromal scars, Munson's sign, Rizzuti's phenomenon, scissoring reflex and oil droplet sign on retinoscopy sign on retinoscopy guide the clinician in diagnosis of moderate to advanced keratoconus [1–3]. However, in early cases and forme fruste (or subclinical) keratoconus, corrected distance visual acuity (CDVA) is generally 20/20 (Snellen equivalent) and typical signs are absent [1–3].

Corneal topography devices are widely used, and accepted as the reference method for keratoconus diagnosis [2,3]. A relatively new technology termed as *Scheimpflug* imaging, captures high-resolution slit images of the anterior segment structures from the anterior corneal surface to the posterior of the lens using a 360° rotating camera. The *Scheimpflug* system allows anterior chamber and lens assessment, pachymetric mapping of the entire cornea and corneal wavefront, as well as corneal topography [2,4]. Although topography devices provide valuable corneal data and typical patterns for keratoconus, it can be challenging to discriminate very early or subclinical keratoconus from normal. Thus,

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researchers have presented various indices and algorithms to assist clinicians for accurate diagnosis, such as central keratometry (*K*), topographic astigmatism, skewed steepest radial axis index (SRAX), the modified Rabinowitz–McDonnell indices (*K* and I–S values), the Maeda–Klyce (KCI% and keratoconus prediction index [KPI]) indices and the KISA% index [5–8].

In recent years, several topography based diagnostic algorithms have been developed to detect eyes with early keratoconus or forme fruste keratoconus, and the *Scheimpflug* technology has gained importance for the diagnosis, treatment planning and postoperative follow-up in the area of keratorefractive surgery [9–12].

In the current study, the performance of topographic and pachymetric parameters obtained from the *Scheimpflug* imaging system (Oculus Pentacam, Oculus Optikgerate GmbH, Wetzlar, Germany) in the diagnosis of keratoconus was measured. It was also shown that a combination of topographic and pachymetric data offers a highly sensitive and specific practical formula for distinguishing eyes with keratoconus from normal.

2. Materials and methods

2.1. Study group

This retrospective controlled study involved 183 eyes of 183 patients with a confirmed diagnosis of keratoconus (keratoconus group) and 131 eyes of 131 age and sex-matched healthy controls (control group). The study followed the tenets of the Declaration of Helsinki and local ethics committee approved the methodology.

All participants underwent a complete ophthalmological examination including CDVA measurement (Snellen charts), slit-lamp biomicroscopy, applanation tonometry, dilated retinoscopy and indirect fundus examination (with non-contact + 90 diopters [D] lens), and the *Scheimpflug* system anterior segment tomography (Oculus Pentacam, Oculus Optikgerate GmbH, Wetzlar, Germany).

2.2. Inclusion and exclusion criteria

Keratoconus diagnosis was confirmed using clinical and topographical findings as follows; biomicroscopic signs (corneal thinning, Fleischer's ring, Vogt's striae, Munson's sign, Rizzuti's phenomenon), retinoscopic evidences (oil droplet and scissoring reflex), typical topographical patterns previously described for keratoconus, inferior–superior value (I–S) on topographic map >1.5.

Control subjects (refractive surgery candidates) had normal biomicroscopic and topographical examination with a CDVA of 20/20 Snellen equivalent.

All patients and controls were aged between 18 and 40 years and had been asked not to wear their contact lenses for at least for one month prior to the examination day. In bilateral cases, one eye was selected randomly.

Subjects with history of any other corneal pathology, scarring or surgery, acute hydrops and dry eye were excluded from the study.

2.3. Corneal topography and pachymetry

The *Scheimpflug* ocular imaging system (Oculus Pentacam, Oculus Optikgerate GmbH, Wetzlar, Germany) was used for anterior segment tomography (corneal topography and pachymetry). This device captures up to 50 sectional images of anterior segment structures in about two seconds using a slit light source and a 360° rotating camera.

A single experienced technician performed the *Scheimpflug* imaging under scotopic conditions with undilated pupils (SV). Images were captured in automatic mode and a single test with a quality score (QS) over 95% was used for the statistical analysis.

Maps of sagittal curvature, corneal thickness, anterior and posterior elevation were acquired. The mean *K* (front), topographic astigmatism, pupil-center pachymetry, apical pachymetry, thinnest pachymetry (*TP*), corneal volume and maximum *K* (*Kmax*) values were recorded for each eye (Fig. 1).

In the keratoconus group, disease severity was graded according to the Amsler–Krumeich classification system as follows [13]:

Stage 1: Eccentric steepening; myopia, induced astigmatism, or both <5.00 D; mean central *K* <48 D.
Stage 2: Myopia, induced astigmatism, or both from 5.00 to 8.00 D; mean central *K* readings <53.00 D; absence of scarring; corneal thickness >400 μm.
Stage 3: Myopia, induced astigmatism, or both from 8.00 to 10.00 D; mean central *K* readings >53.00 D, absence of scarring; corneal thickness 300–400 μm.
Stage 4: Refraction not measurable; mean central *K* readings >55.00 D; central corneal scarring, corneal thickness < 200 μm.

Eyes with stage 4 keratoconus were not included into the study (because of the corneal scarring).

2.4. Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences software version 16.0 (SPSS Inc., Chicago, IL, USA) and MedCalc software version 12.6.1.0 (MedCalc Software bvba, Ostend, Belgium). The sample size in this study was tested using "*Power and Beta*" tool (under Procedures–Diagnostic tests–ROC curves) of the PASS software version 11.0.1 (NSCC, LLC, Utah, USA), and power of the present study was found to be 99% at 0.05 significance level (95% confidence interval). All variables were tested for normal distribution using the Kolmogorov–Smirnov method. Values were expressed as the mean ± standard deviation (SD). Categorical variables were analyzed using the Chi square test. The independent samples *t* test was used to determine difference between two groups in terms of quantitative variables. A receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) were assessed. The diagnostic power of the each *Scheimpflug* parameter was graded according to the AUC value as follows; excellent (0.90–1.00), good (0.80–0.89), fair (0.70–0.79), poor (0.60–0.69) and worthless (0.50–0.59). The ROC curve plots the true positives (sensitivity) against the false positives (100-specificity) for different threshold values [14]. Values on the ROC curve, which indicated best sensitivity–specificity pair, were accepted as the cut points [14]. At 95% confidence interval, a *P* value less than 0.05 was considered statistically significant.

3. Results

The study cohort comprised 183 eyes of 183 patients with a confirmed diagnosis of keratoconus (keratoconus group) and 131 eyes of 131 healthy subjects (control group). In the keratoconus group, 63 eyes (34.4%) had stage 1, 75 eyes (41%) had stage 2 and 45 eyes (24.6%) had stage 3 keratoconus based on the Amsler–Krumeich classification system [13]. Table 1 presents age, gender distribution and means for the *Scheimpflug* imaging system parameters (mean *K* [front], topographic astigmatism, pupil-center pachymetry, apical pachymetry, thinnest pachymetry, corneal volume and *Kmax*) in the keratoconus and control groups.

In the entire cohort, the ROC analyses and AUC values showed that *Kmax* and *TP* had the highest individual diagnostic ability