Contact Lens and Anterior Eye xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Contact Lens and Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Evaluation of the diagnostic ability of vector parameters characterizing the corneal astigmatism and regularity in clinical and subclinical keratoconus

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ARTICLE INFO

Article history:
Received 25 August 2016
Received in revised form 12 November 2016
Accepted 28 November 2016

Keywords:
Keratoconus
Subclinical keratoconus
Ocular residual astigmatism
Topography disparity
Corneal astigmatism

ABSTRACT

Purpose: To evaluate the diagnostic ability of the vector parameters ocular residual astigmatism (ORA), topography disparity (TD) and topographic astigmatism CorT (anterior and total) for the detection of clinical and subclinical keratoconus, and to develop a detection model based on them.
Methods: This study comprised a total of 61 keratoconus eyes (KC group), 19 eyes with subclinical keratoconus (SKC group) and 100 healthy eyes (control group). In all cases, a complete eye exam was performed including an analysis of the corneal structure with the Sirius system (Costruzione Strumenti Oftalmici, CSO). Likewise, the iASSORT software (ASSORT Pty) was used to calculate in all cases the vector parameters ORA, TD and CorT.
Results: Significant differences among groups were found in ORA, TD and CorT (anterior and total) ($p < 0.001$). The diagnostic ability of ORA (cutoff 1.255 D, sensitivity/specificity 82%/92%) and TD (cutoff 1.035 D, sensitivity/specificity 78.5%/86%) for the detection of keratoconus was good, whereas anterior and total CorT showed a poorer diagnostic ability. ORA (cutoff 0.925 D, sensitivity/specificity 63.2%/77%) and TD (cutoff 0.710 D, sensitivity/specificity 74%/68%) showed an acceptable diagnostic ability for the detection of subclinical keratoconus, but anterior and total CorT did not. A detection model for subclinical keratoconus was obtained by logistic regression analysis involving TD, anterior corneal spherical aberration and posterior high order aberrations.
Conclusions: The vector parameters ORA and TD are useful for the diagnosis of clinical and subclinical keratoconus. In this last condition, the combination of TD with corneal aberrometric data provides a consistent detection model.

1. Introduction

Keratoconus characterization and diagnosis can be currently performed with accuracy by means of a variety of techniques and technologies. Slit lamp examination allows the detection of biomicroscopic signs, such as stromal thinning, conical protrusion, Fleischer ring and Vogt striae [1]. With the help of current topography systems, the conical protrusion and infero-superior asymmetry associated to keratoconus can be easily detected with high levels of accuracy [2–4]. However, the detection of subclinical keratoconus, which could be considered a very early stage of keratoconus, is significantly more complex, as it is characterized by a normal-appearing cornea on slit lamp biomicroscopy, the crucial factor being the comprehensive analysis of corneal topography [4,5]. In addition, there are other complementary techniques or descriptors that facilitate the detection of subclinical keratoconus, such as corneal aberrations, pachymetry, asphericity, or the analysis of corneal biomechanical properties [3,6–10].

Vector analysis may be another tool that could be useful for the detection of keratoconus [11]. The ocular residual astigmatism (ORA) is defined as the vector difference between the corneal astigmatism and refractive astigmatism calculated from the corneal plane [12]. It is the result of the combination of astigmatism of the lens, the posterior surface of the cornea and the contribution of visual perception analysis [12]. The topography disparity (TD) is another vector parameter that characterizes the regularity of the cornea and it is calculated as

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http://dx.doi.org/10.1016/j.clae.2016.11.008
1367-0484/

the vectorial difference between the regular astigmatism of the superior and inferior hemidivisions of the cornea [12]. In a previous preliminary study, the magnitude of these vector parameters has been found to be significantly higher in keratoconus and even in subclinical keratoconus [11]. Another recently defined vector parameter is the topographic astigmatism CorT that characterizes the corneal astigmatism considering an analysis of astigmatism meridians, expanding the region of cornea examined, increasing the accuracy in the estimation of corneal astigmatism compared to simulated keratometry, and providing greater consistency when corneal astigmatism is measured in irregular corneas [13]. The aim of the current study was to evaluate the distribution of ORA, TD and CorT parameters in healthy eyes and in eyes with clinical and subclinical keratoconus, to determine the diagnostic ability of these parameters to detect these conditions, and to define, if possible, a predictive model of detection of subclinical keratoconus considering this vector parameters as well as other clinical variables.

2. Material and methods

2.1. Clinical study

This retrospective comparative study was comprised by 61 keratoconic eyes of 38 patients, 19 eyes with subclinical keratoconus of 16 patients, and a control group with 100 eyes from 100 patients (only one eye was randomly selected in each patient to avoid the interference in the analysis of the correlation that often exists between the two eyes of the same person). This study was conducted at the Department of Ophthalmology (OFTALMAR) of the Vithas Medimar International Hospital (Alicante, Spain). Patients from the control group were selected randomly retrospectively from those attending to the anterior segment consultation of our hospital using a random number sequence. The inclusion criteria for each group were the following:

- Control group: healthy eyes that did not meet the exclusion criteria.
- Keratoconus group: keratoconus diagnosed according to the standard criteria, which is the presence of an asymmetric bowtie pattern in corneal topography and at least on keratoconus sign on slit-lamp examination, such as stromal thining, conical protusion on the cornea at the apex, Fleischer ring, Vogt striae or anterior stromal scar [1,3].
- Subclinical keratoconus group: any eye with corneal topography showing an abnormal localized steepening or an asymmetric bow tie pattern combined with a normal-appearing cornea at slit-lamp biomicroscopy and at least one of the following signs: steep keratometric curvature greater than 47 D, oblique cylinder greater than 1.5 D, central corneal thickness less than 500 μm or clinical keratoconus in the follow eye [5,7,10].

As monocular keratoconus is rare and even though keratoconus tends to be an asymmetric condition, the fellow eye generally exhibits clinical signs at a later time [1]. In our sample, the monocular keratoconus cases included had subclinical keratoconus in the fellow eye or they had keratoconus with a previous surgical treatment, such as intracorneal ring segment implantation or corneal collagen crosslinking. For this reason, only the data from one eye was included in the keratoconus group in such cases.

Exclusion criteria in all groups were previous ocular surgery and any other active ocular disease. This study was approved by the hospital ethics committee and was then performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2.2. Examination protocol

All patients underwent a complete eye examination including the following tests: anamnesis, measurement of uncorrected (UDVA) and corrected distance visual acuity (CDVA), manifest refraction, slit-lamp biomicroscopy, and corneal and anterior segment analysis by the Sirius system (Costruzione Strumenti Oftalmici, Italy) which combines a rotating Scheimpflug camera with a Placido disk to provide more accurate analysis of the geometry of the cornea. Specifically, the following parameters were evaluated and recorded with this topography system: anterior (Ka) and posterior average keratometry (Kp), anterior (ACA) and posterior corneal astigmatism (PCA), minimum corneal thickness (MCT), anterior (Qa) and posterior corneal asphericity (Qp), corneal volume (CV), anterior chamber depth (ACD), anterior corneal (HOAa) and posterior corneal high order aberration root mean square (HOAp), anterior (SAa) and posterior spherical aberration Zernike term (SAp), and anterior (COMAa) and posterior coma root mean square (COMAp). Besides all these tests, ORA, TD and CorT were calculated using the iASSORT software (ASSORT Pty. Ltd., Chhentenham, Australia) which uses the Sirius system data as well as combines topographic and refractive data for a complete vector astigmatic analysis [13]. The CorT parameter was calculated for the anterior surface and also for the whole cornea considering the contribution of both corneal surfaces, using the methodology described by Alpins et al. [13].

2.3. Statistical analysis

SPSS statistics software package version 15.0 (IBM, Armonk, EEUU) was used for the statistical analysis. Normality of all data was checked by means of the Kolmogorov-Smirnov test. Comparison between groups was performed using the one-way analysis of variance (ANOVA) if variables were normally distributed or using the Kruskal-Wallis test if one or more variables were not normally distributed. The post-hoc comparative analysis for the ANOVA was performed with the Bonferroni test when the variances were homogeneous and the T2 Tamhane test when the variances were not homogeneous, while the Mann-Whitney tests with the Bonferroni's adjustment was used for the post-hoc analysis of the Kruskal-Wallis test. Differences were considered to be statistically significant when the associated p-value was <0.05.

The diagnostic ability of ORA, TD and CorT parameters to detect keratoconus and subclinical keratoconus was determined using the receiver operating characteristic (ROC) curve analysis. ROC curves show the relationship between sensitivity (pathological cases that are correctly detected) and 1-specificity (non-pathological cases that have a negative test result). Furthermore, this analysis provides the area under the curve and its corresponding statistical significance that allows the clinician to determine the diagnostic accuracy of any clinical parameter evaluated. Likewise, an optimal cutoff is defined, which corresponds to the point of the curve which has high sensitivity while maintaining a high specificity (compromise between sensitivity and specificity).

Finally, a stepwise backward logistic regression was performed to define the key parameters involved in the detection of subclinical keratoconus. Hosmer-Lemeshow adjustment was used to assess the overall goodness of fit of the model, and R^2 Cox and Snell and R^2 Nagelkerke were used to study the variance rate explained by the variables of the model. The specific relationship between the parameters of the final model was evaluated with the model coefficients (B) and the odds ratios that represent the value of increased likelihood that a category of the dependent variable is

Please cite this article in press as: A. Martínez-Abad, et al., Evaluation of the diagnostic ability of vector parameters characterizing the corneal astigmatism and regularity in clinical and subclinical keratoconus, Contact Lens & Anterior Eye (2016), http://dx.doi.org/10.1016/j.clae.2016.11.008