Corneal densitometry in bilateral keratoconus patients with unilateral corneal Vogt’s striae: a contralateral eye study

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Abstract

Purpose To investigate corneal densitometry and correlations with corneal morphological parameters in patients with bilateral keratoconus (KC) with unilateral Vogt’s striae.

Methods This prospective contralateral study enrolled 112 patients (224 eyes) with evident KC characteristics (corneal topography with asymmetric bow-tie pattern, inferior steepening), and at least one KC sign (conical protrusion of the cornea at the apex, corneal stromal thinning, Fleischer ring, Vogt’s striae) on slit-lamp examination. Corneal densitometry and morphological parameters were measured using Pentacam HR.

Results The mean age was 23.93 ± 6.81 years. Fifty-two (23.22%), 111 (49.55%), and 61 (27.23%) eyes were in mild, moderate, and severe groups, respectively. Corneal densitometry values of the anterior 0–2 mm and 2–6 mm, intermediate 0–2 mm and 2–6 mm, posterior 2–6 mm, and total cornea 2–6 mm were significantly higher in eyes with Vogt’s striae (P < 0.05), whereas those of the anterior 6–10 mm, posterior 0–2 mm, and total cornea 6–10 mm were significantly lower in eyes with Vogt’s striae (P < 0.05). Anterior 0–2 mm and total cornea 2–6 mm corneal densitometry values were positively correlated with anterior K1 (A-K1), K2 (A-K2), Km (A-Km), Kmax (A-Kmax), anterior corneal elevation, and posterior corneal elevation (P < 0.05), and negatively correlated with central corneal thickness and thinnest corneal thickness in eyes with Vogt’s striae (P < 0.05). A-K2, A-Km, and A-Kmax were significantly correlated with the densitometry values of the anterior 0–2 mm and intermediate 0–2 mm in eyes without Vogt’s striae (P < 0.05).

Conclusion Vogt’s striae mainly occur on the anterior and intermediate layers during KC progression.

Keywords Keratoconus · Cornea · Corneal densitometry · Vogt’s striae · Contralateral eye study

Introduction

Keratoconus (KC) is a non-inflammatory and progressive corneal ectatic disorder characterized by central or paracentral thinning and steepening that produces a cone-shaped protrusion of the cornea.
that gradually impairs its optical features [1–3]. The incidence of KC ranges from 0.05 to 2.5% [4]. Slit-lamp biomicroscopy generally reveals stromal thinning, corneal scars, Fleischer’s ring, and Vogt’s striae in patients with progressive KC [5]. Vogt’s striae, one of the typical clinical signs of KC, are vertical lines parallel to the cone axis on the posterior stroma and Descemet’s membranes [6, 7]. Vogt’s striae can play an important role in the evaluation, classification, and monitoring of KC as they can reflect the severity of KC [8–13]. However, the cause of Vogt’s striae remains unclear. Mehmet et al. [14] evaluated alterations in the corneal keratocytes, endothelial cell densities, stromal nerve thickness, and sub-basal nerve density in KC patients using in vivo confocal microscopy (IVCM). The results demonstrated an association between the microstructural changes seen in KC and Vogt’s striae. To our knowledge, the correlation between corneal densitometry and the appearance of Vogt’s stria has not previously been studied.

Corneal densitometry, also known as corneal backscattering, is considered an indicator of corneal transparency [15]. Disarranged corneal histology, including changes in corneal lamellar array and spacing, haze clouding, inflammation, and scarring formation, may compromise corneal transparency [16–18]. Previous studies have demonstrated that the corneal densitometry values observed in KC are significantly different from those of a normal cornea [19, 20]. Anayol et al. [21] showed that patients with KC have significantly higher corneal densitometry values in the central cornea than healthy control subjects, and Lopes et al. [16] reported that the corneal densitometry level is higher in more advanced stages. Many previous articles have assessed corneal tomography, biomechanics, and endothelial cell distributions in KC eyes [22–24]; however, no study has assessed the corneal densitometry in patients with KC with unilateral corneal Vogt’s striae.

This study evaluated corneal densitometry at different positions using the Pentacam HR (Pentacam HR, Oculus, Inc., Wetzlar, Germany) to gain detailed insight into corneal densitometry and compare the corneal densitometric properties in patients with bilateral KC and unilateral corneal Vogt’s striae.

Methods

Participants

This prospective contralateral eye study was conducted at the Department of Refractive Surgery Center, Xi’an People’s Hospital (Xi’an Fourth Hospital) in Shaanxi Province (northwest China) between February 2018 and June 2020. The study enrolled 112 participants with bilateral KC and unilateral corneal Vogt’s striae.

Among them, 25 (22.32%) patients used soft contact lenses and 16 (14.29%) used rigid gas permeable contact lenses (RGP). The participants were instructed to stop wearing soft contact lenses for 1 week and RGP for 3 weeks before the ophthalmic examination.

All participants underwent a comprehensive ophthalmic examination by the same ophthalmologist. The examination included patient history collection, slit-lamp biomicroscopy, and tests of uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), intraocular pressure (Topcon CT-80, Topcon Corporation, Tokyo, Japan), axial length (A-SCAN PLUS, Accutome, Inc., Florida, America), cycloplegic refraction, and funduscopy. Scheimpflug-based anterior segment tomography (Pentacam HR, Oculus, Inc.) was used to evaluate the corneal densitometry values and corneal topographic parameters, including the anterior flat keratometry value (A-K1) and anterior steep keratometry value (A-K2). In addition, the anterior mean keratometry value (A-Km), anterior maximum keratometry value (A-Kmax), central corneal thickness (CCT), thinnest corneal thickness (TCT), and conventional anterior corneal elevation (ACE) and posterior corneal elevation (PCE) of the cornea’s thinnest point were also evaluated.

The inclusion criteria included evolving KC, which was diagnosed based on the widely known criteria and the guidelines of the Collaborative Longitudinal Evaluation of Keratoconus Study [5]. The study participants were patients with evident KC characteristics (i.e., corneal topography with asymmetric bow-tie pattern with or without skewed axes, inferior steepening), and at least one KC sign (i.e., conical protrusion of the cornea at the apex, corneal stromal thinning, Fleischer ring, Vogt’s striae) on slit-lamp examination [25]. Among them, 112 patients with bilateral KC but unilateral corneal Vogt’s striae...
were enrolled. According to the staging scheme in the CLEK study [5], KC was divided into three groups based on the keratometry of the steepest corneal meridian: mild (<45.0 D), moderate (45.0–52.0 D), and severe (>52.0 D) [25].

The exclusion criteria included viral keratitis, corneal opacities, corneal scarring, ocular infection, history of corneal trauma, corneal refractive or intraocular surgery, and systemic diseases such as diabetes and connective tissue diseases.

The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board and Ethics Committee of the Xi’an People’s Hospital (Xi’an Fourth Hospital) (Ethical Approval Number: 20180157). Written informed consent was obtained from all participants.

Corneal densitometry

Corneal densitometry was performed using a rotating Scheimpflug imaging system (Pentacam HR; Oculus, Inc.). During the examination, the patient’s chin was placed on the chin rest and their forehead was placed against the forehead strap. The patient was asked to blink a few times and then open both eyes and stare at the fixation target. After attaining perfect alignment, the instrument automatically captured 25 Scheimpflug images by rotating 360° around the eye’s optical axis within 2 s. Three effective measurements (displaying the sign “OK”) were performed on each eye, and the average of the three values was used for the analyses. One experienced ophthalmologist obtained all measurements.

The corneal densitometry values were measured in grayscale units (GSUs) based on a minimum light scattering of 0 (maximum transparency) and a maximum light scattering of 100 (minimum transparency). The cornea in a 12-mm area was divided into four concentric radiation areas for local densitometry analysis, including the central area (diameter: 0–2 mm), an annulus with an inner diameter of 2 mm and an outer diameter of 6 mm (referred to as the 2–6 mm annulus), and a second annulus that was 6–10 mm in diameter (i.e., the 6–10 mm annulus). The outermost layer had a ring gap of 10–12 mm. The corneal densitometry measurements were performed at different corneal depths: the anterior cornea (the first 120 μm of the corneal thickness), the posterior cornea (the last 60 μm of the corneal thickness), and the intermediate layer.

Statistical analysis

The descriptive statistics were presented as means and standard deviations. SPSS version 26.0 (SPSS, Chicago, IL, USA) was implemented for all statistical analyses. The normal distribution of the parameters was assessed using the Kolmogorov–Smirnov test. Paired sample t tests and the Wilcoxon signed-rank test were performed to compare the parameters with a normal distribution and non-parametric parameters, respectively. Pearson’s correlation tests were performed to examine the correlations between the scale values fitting a normal distribution. Spearman correlation tests were implemented to determine the correlations between the data with a skewed distribution and ranked ordinal data. Two-sided P values of <0.05 were considered statistically significant.

Results

The study assessed 112 patients with bilateral KC and unilateral Vogt’s striae [65 men (58.04%) and 47 women (41.96%)]. Their mean age was 23.93 ± 6.81 years (range 15–38 years). Among the 224 eyes with KC, 52 (23.22%), 111 (49.55%), and 61 (27.23%) were in mild, moderate, and severe groups, respectively. In KC eyes with Vogt’s striae, nine (4.02%), 51 (22.76%), and 52 (23.21%) were in mild, moderate, and severe groups, respectively. Whereas in the KC eyes without Vogt’s striae, mild, moderate and severe KC were 43 (19.20%), 60 (26.79%), and nine (4.02%), respectively.

Significant differences were observed in the refractive outcomes between KC eyes with and without Vogt’s striae (all P < 0.001). As shown in Table 1, KC eyes with Vogt’s striae had significantly higher absolute values for the sphere, cylinder, and spherical equivalents than the eyes without Vogt’s striae. UCVA and BCVA were significantly lower in KC eyes with Vogt’s striae than in those without Vogt’s striae (P < 0.001).

The main corneal morphological parameters are presented in Table 2. Significant differences were observed in the corneal morphological data A-K1, A-K2, A-Km A-Kmax, CCT, TCT, ACD, ACE, and
PCE) measured by the Pentacam HR between eyes with and without Vogt’s striae (all $P < 0.001$).

**Corneal densitometry**

As shown in Table 3, significant differences in the distribution of densitometry values were observed. Paired sample t tests and Wilcoxon signed-rank tests revealed that the corneal densitometry values of the anterior 0–2 mm and 2–6 mm, the intermediate 0–2 mm and 2–6 mm, the posterior 2–6 mm, and the total cornea 2–6 mm were significantly higher in eyes with Vogt’s striae than those in eyes without Vogt’s striae ($P < 0.05$). These values were significantly lower for the corneal densitometry values of the anterior 6–10 mm, the posterior 0–2 mm, and the total cornea 6–10 mm in eyes with Vogt’s striae ($P < 0.05$). No significant differences between the two groups were observed in other locations ($P > 0.05$).

**Corneal densitometry and morphological parameters**

The correlations between corneal densitometry and the morphological parameters in all KC eyes are shown in Table 4. The corneal densitometry values in the anterior (0–2 mm and 2–6 mm) and the total
cornea (0–2 mm and 2–6 mm) were positively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE, and PCE \( (P < 0.05) \) and negatively correlated with CCT \( (P < 0.05) \). However, the values were negatively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE, and PCE \( (P < 0.05) \) and positively correlated with CCT in the posterior 0–2 mm \( (P < 0.05) \).

In KC eyes with Vogt’s striae, the correlations between corneal densitometry and morphological parameters are shown in Table 5 and Fig. 1. The corneal densitometry values in the anterior 0–2 mm and the total cornea 2–6 mm were positively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE and PCE \( (P < 0.05) \) and negatively correlated with CCT and TCT \( (P < 0.05) \). The values in the posterior 0–2 mm were negatively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE and PCE \( (P < 0.05) \) and positively correlated with CCT \( (P < 0.05) \). The anterior 2–6 mm values were positively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE, and PCE \( (P < 0.05) \) and negatively correlated with TCT \( (P < 0.05) \).

As presented in Table 6, there was no correlation between A-K1 and the corneal densitometry values at any location in KC eyes without Vogt’s striae \( (P > 0.05) \). A-K2, A-Km, and A-Kmax were significantly correlated with the densitometry values of the anterior 0–2 mm and the intermediate 0–2 mm \( (P < 0.05) \), but not with the posterior 0–2 mm \( (P > 0.05) \). The corneal densitometry values in the intermediate 0–2 mm and 2–6 mm were negatively correlated with CCT and TCT \( (P < 0.05) \) and positively correlated with ACE and PCE in KC eyes without Vogt’s striae \( (P < 0.05) \).

Negative correlations were observed between ACD and the anterior 6–10 mm, the anterior-total, the intermediate 6–10 mm, the intermediate-total, the posterior 6–10 mm, the posterior-total, the total 6–10 mm, and total corneal densitometry values in all KC eyes \( (P < 0.05) \).

**Discussion**

Different manifestations of KC eyes’ clinical symptoms and signs occur at various periods [9, 26, 27]. Mild KC is usually difficult to detect with slit-lamp biomicroscopy. Fleischer’s ring and Vogt’s striae can be seen in the corneal inferior or center as the disease progresses. Vogt’s striae or stress lines are typical clinical signs of progressive KC [12]. We observed that the diopter, visual acuity, and corneal characteristics were significantly altered when Vogt’s striae appeared. However, the associations between the corneal morphological parameters, Vogt’s striae formation mechanisms, and where the striae first appeared remain ambiguous.

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**Table 3** Contralateral comparison of mean corneal densitometry values was measured by the Pentacam HR between KC eyes with Vogt’s striae and those without Vogt’s striae

| Location      | With Vogt’s striae | Without Vogt’s striae | t/S-value | \( P \) value |
|---------------|--------------------|-----------------------|-----------|--------------|
| Anterior 0–2  | 22.76 ± 3.01       | 21.97 ± 3.14          | 1301.0b   | <0.001*      |
| Anterior 2–6  | 21.65 ± 19.05      | 19.34 ± 2.56          | 1354.5b   | <0.001*      |
| Anterior 6–10 | 18.09 ± 3.64       | 18.87 ± 3.99          | −1428.5b  | <0.001*      |
| Anterior-total| 21.67 ± 3.04       | 22.03 ± 3.33          | −551.5b   | 0.070        |
| Intermediate 0–2| 15.50 ± 1.44      | 15.19 ± 1.59          | 4.007a    | 0.001*       |
| Intermediate 2–6| 13.39 ± 1.12      | 13.28 ± 1.20          | 732.0b    | 0.009*       |
| Intermediate 6–10| 12.98 ± 2.13      | 13.05 ± 2.10          | −435.0b   | 0.129        |
| Intermediate-total| 14.79 ± 1.63      | 14.89 ± 1.73          | −0.806a   | 0.422        |
| Posterior 0–2 | 10.46 ± 1.76       | 11.17 ± 1.38          | −1501.5b  | <0.001*      |
| Posterior 2–6 | 11.08 ± 0.95       | 10.72 ± 1.04          | 5.068a    | <0.001*      |
| Posterior 6–10| 11.11 ± 1.53       | 11.20 ± 1.41          | −483.5b   | 0.107        |
| Posterior-total| 11.77 ± 1.18       | 11.83 ± 1.14          | −0.643a   | 0.522        |
| Total 0–2     | 16.24 ± 1.42       | 16.11 ± 1.54          | 1.287a    | 0.201        |
| Total 2–6     | 14.78 ± 1.23       | 14.45 ± 1.29          | 4.914a    | <0.001*      |
| Total 6–10    | 14.06 ± 2.28       | 14.38 ± 2.36          | −1115.5b  | <0.001*      |
| Total         | 16.08 ± 1.62       | 16.25 ± 1.77          | −1.498a   | 0.137        |
Table 4  Correlation between the corneal densitometry values and morphological parameters measured by the Pentacam HR in all KC eyes

| Location       | A-K1 r    | A-K1 P    | A-K2 r    | A-K2 P    | A-Km r   | A-Km P    | A-Kmax r  | A-Kmax P  | CCT r    | CCT P    | TCT r    | TCT P    | ACD r    | ACD P    | ACE r    | ACE P    | PCE r    | PCE P    |
|----------------|-----------|-----------|-----------|-----------|----------|-----------|-----------|-----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Anterior 0–2   | 0.266     | 0.000*    | 0.331     | 0.000*    | 0.322    | 0.000*    | 0.296     | 0.000*    | −0.194   | 0.004*   | −0.162   | 0.017*   | −0.029   | 0.672    | 0.250    | 0.000*   | 0.331    | 0.000*   |
| Anterior 2–6   | 0.193     | 0.004*    | 0.262     | 0.000*    | 0.243    | 0.000*    | 0.261     | 0.000*    | −0.153   | 0.024*   | −0.128   | 0.061    | −0.010   | 0.881    | 0.197    | 0.004*   | 0.273    | 0.000*   |
| Anterior 6–10  | −0.109    | 0.111     | −0.090    | 0.188     | −0.097   | 0.156     | −0.121    | 0.077     | 0.057    | 0.402    | 0.061    | 0.377    | −0.364   | 0.000*   | −0.204   | 0.003*   | −0.116   | 0.090    |
| Anterior-total | −0.036    | 0.596     | −0.024    | 0.724     | −0.026   | 0.709     | −0.026    | 0.706     | 0.017    | 0.807    | 0.035    | 0.612    | −0.273   | 0.000*   | −0.092   | 0.177    | −0.015   | 0.825    |
| Intermediate 0–2 | 0.0206    | 0.002*    | 0.262     | 0.000*    | 0.252    | 0.000*    | 0.221     | 0.001*    | −0.283   | 0.000*   | −0.292   | 0.000*   | −0.040   | 0.555    | 0.213    | 0.002*   | 0.263    | 0.000*   |
| Intermediate 2–6 | 0.0077    | 0.258     | 0.130     | 0.056     | 0.109    | 0.109     | 0.117     | 0.087     | −0.183   | 0.007*   | −0.211   | 0.002*   | −0.044   | 0.519    | 0.121    | 0.076    | 0.162    | 0.017*   |
| Intermediate 6–10 | −0.015    | 0.830     | 0.005     | 0.942     | −0.005   | 0.940     | −0.054    | 0.432     | −0.050   | 0.463    | −0.072   | 0.294    | −0.365   | 0.000*   | −0.126   | 0.065    | −0.065   | 0.341    |
| Intermediate-total | 0.021    | 0.761     | 0.004     | 0.949     | 0.013    | 0.848     | −0.030    | 0.657     | −0.059   | 0.391    | −0.091   | 0.185    | −0.321   | 0.000*   | −0.104   | 0.126    | −0.006   | 0.332    |
| Posterior 0–2  | −0.306    | 0.000*    | −0.291    | 0.000*    | −0.309   | 0.000*    | −0.306    | 0.000*    | 0.184    | 0.007*   | 0.132    | 0.054    | −0.037   | 0.586    | −0.249   | 0.000*   | −0.237   | 0.000*   |
| Posterior 2–6  | 0.188     | 0.005*    | 0.263     | 0.000*    | 0.231    | 0.001*    | 0.280     | 0.000*    | −0.195   | 0.004*   | −0.209   | 0.002*   | 0.070    | 0.305    | 0.278    | 0.000*   | 0.302    | 0.000*   |
| Posterior 6–10 | −0.048    | 0.480     | −0.039    | 0.564     | −0.045   | 0.509     | −0.080    | 0.245     | −0.026   | 0.702    | −0.043   | 0.533    | −0.339   | 0.000*   | −0.14    | 0.032*   | −0.095   | 0.163    |
| Posterior-total | −0.030    | 0.666     | −0.041    | 0.552     | −0.037   | 0.589     | −0.046    | 0.499     | −0.026   | 0.706    | −0.055   | 0.424    | −0.270   | 0.000*   | −0.099   | 0.148    | −0.073   | 0.289    |
| Total 0–2     | 0.151     | 0.026*    | 0.208     | 0.002*    | 0.199    | 0.003*    | 0.170     | 0.012*    | −0.173   | 0.011*   | −0.174   | 0.011*   | −0.065   | 0.338    | 0.154    | 0.023*   | 0.230    | 0.001*   |
| Total 2–6     | 0.202     | 0.003*    | 0.283     | 0.000*    | 0.256    | 0.000*    | 0.287     | 0.000*    | −0.220   | 0.001*   | −0.218   | 0.001*   | −0.013   | 0.853    | 0.244    | 0.000*   | 0.319    | 0.000*   |
| Total 6–10    | −0.083    | 0.227     | −0.059    | 0.387     | −0.071   | 0.299     | −0.102    | 0.135     | 0.025    | 0.719    | 0.015    | 0.825    | −0.390   | 0.000*   | −0.190   | 0.005*   | −0.106   | 0.121    |
| Total         | −0.018    | 0.797     | −0.019    | 0.782     | −0.016   | 0.812     | −0.040    | 0.563     | −0.001   | 0.987    | −0.004   | 0.956    | −0.350   | 0.000*   | −0.126   | 0.065    | −0.047   | 0.489    |

Spearman correlation coefficient analysis. *P < 0.05 is statistically significant.

A-K1, anterior flat keratometry; A-K2, anterior steep keratometry; A-Km, anterior mean keratometry; A-Kmax, anterior maximum keratometry; CCT, central corneal thickness; TCT, thinnest corneal thickness; ACD, anterior chamber depth; ACE, anterior corneal elevation; PCE, posterior corneal elevation.
Table 5 Correlation between the corneal densitometry values and morphological parameters measured by the Pentacam HR in eyes with Vogt’s striae

| Location         | A-K1       | A-K2       | A-Km       | A-Kmax     | CCT        | TCT        | ACD        | ACE        | PCE        |
|------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                  | r          | P          | r          | P          | r          | P          | r          | P          | r          |
| Anterior 0–2     | 0.275      | 0.004*     | 0.329      | 0.000*     | 0.325      | 0.001*     | 0.289      | 0.002*     | −0.279     | 0.003*     |
| Anterior 2–6     | 0.213      | 0.026*     | 0.301      | 0.001*     | 0.278      | 0.004*     | 0.311      | 0.001*     | −0.196     | 0.041*     |
| Anterior 6–10    | −0.103     | 0.286      | −0.018     | 0.846      | −0.057     | 0.558      | −0.018     | 0.846      | −0.023     | 0.808      |
| Anterior-total   | −0.048     | 0.620      | 0.030      | 0.754      | 0.003      | 0.974      | 0.046      | 0.630      | −0.043     | 0.652      |
| Intermediate 0–2 | 0.151      | 0.117      | 0.162      | 0.093      | 0.174      | 0.071      | 0.115      | 0.235      | −0.253     | 0.008*     |
| Intermediate 2–6 | 0.016      | 0.867      | 0.022      | 0.819      | 0.003      | 0.972      | 0.011      | 0.908      | −0.100     | 0.300      |
| Intermediate 6–10| −0.087     | 0.366      | −0.031     | 0.749      | −0.063     | 0.515      | −0.064     | 0.506      | −0.026     | 0.787      |
| Intermediate-total | −0.118   | 0.220      | −0.096     | 0.320      | −0.109     | 0.257      | −0.114     | 0.237      | −0.013     | 0.890      |
| Posterior 0–2    | −0.357     | 0.000*     | −0.357     | 0.000*     | −0.367     | 0.000*     | −0.344     | 0.000*     | 0.203      | 0.034*     |
| Posterior 2–6    | 0.131      | 0.175      | 0.179      | 0.062      | 0.165      | 0.087      | 0.252      | 0.008*     | −0.137     | 0.157      |
| Posterior 6–10   | −0.086     | 0.373      | −0.041     | 0.668      | −0.067     | 0.491      | −0.033     | 0.727      | −0.064     | 0.508      |
| Posterior-total  | −0.132     | 0.173      | −0.113     | 0.242      | −0.126     | 0.190      | −0.061     | 0.527      | −0.036     | 0.708      |
| Total 0–2        | 0.131      | 0.176      | 0.171      | 0.076      | 0.170      | 0.078      | 0.135      | 0.160      | −0.224     | 0.019*     |
| Total 2–6        | 0.199      | 0.038*     | 0.296      | 0.001*     | 0.264      | 0.005*     | 0.333      | 0.000*     | −0.236     | 0.013*     |
| Total 6–10       | −0.120     | 0.213      | −0.040     | 0.678      | −0.083     | 0.391      | −0.049     | 0.610      | −0.018     | 0.849      |
| Total            | −0.117     | 0.225      | −0.044     | 0.649      | −0.076     | 0.433      | −0.036     | 0.708      | −0.032     | 0.742      |

Spearman correlation coefficient analysis. *P < 0.05 is statistically significant.

A-K1, anterior flat keratometry; A-K2, anterior steep keratometry; A-Km, anterior mean keratometry; A-Kmax, anterior maximum keratometry; CCT, central corneal thickness; TCT, thinnest corneal thickness; ACD, anterior chamber depth; ACE, anterior corneal elevation; PCE, posterior corneal elevation
This study found that KC eyes with Vogt’s striae had significantly higher absolute values of the sphere, cylinder, and spherical equivalents than eyes without it. Furthermore, UCVA and BCVA were significantly lower in KC eyes with Vogt’s striae than those in eyes without it. This is consistent with the findings of previous research [28]. Sedaghat et al. [25] reported that the morphological parameters A-K1, A-K2, and A-Kmax measured by Pentacam HR were higher in KC eyes with Vogt’s striae than those in eyes without it. In the present study, additional morphological parameters were evaluated (i.e., CCT, TCT, ACD, ACE, and PCE), in addition to the standard parameters of A-K1, A-K2, A-Km, and A-Kmax. In addition to an increase in the anterior corneal curvature, the results indicated significant increases in ACE, PCE, and ACD and significant decreases in CCT and TCT in eyes with Vogt’s striae. Thus, we can conclude that the occurrence of Vogt’s striae positively correlates with KC’s severity. In the absence of corneal topography, KC severity can be assessed by observing the presence of Vogt’s striae under slit-lamp biomicroscopy during a clinical examination.

As demonstrated in a previous study, several factors (i.e., the size and arrangement of collagen fibrils) could influence corneal transparency and densitometry [29]. The disarrangement of the corneal collagen structure in KC patients [18] may lead to differences in corneal densitometry compared with that in healthy individuals [30, 31]. However, whether the presence of Vogt’s striae in KC causes changes in corneal densitometry and the sites that affect the changes in densitometry have not been reported.

In the current study, we found that corneal densitometry values of the anterior 0–2 mm and 2–6 mm and the intermediate 0–2 mm and 2–6 mm were significantly higher, and that of the posterior 0–2 mm was significantly lower in KC eyes with Vogt’s striae than in those without it. This is similar to the results observed by Shen et al. [32] in a study on corneal densitometry in KC. Alternations in corneal densitometry are related to the degree of changes in the structure of corneal collagen fiber [33]. Uçakhan et al. [34] and Ghosh et al. [35] reported that the presence of Vogt’s striae in the anterior stroma of KC eyes is usually present in moderate and severe KC. Erie et al. [36] and Hollingsworth et al. [6] reported a decrease in keratocyte density, with a 19% reduction in the anterior stroma and a 10% reduction in the posterior stroma. We hypothesize that KC eyes
Table 6  Correlation between the corneal densitometry values and morphological parameters measured by the Pentacam HR in eyes without Vogt’s striae

| Location  | A-K1 |          | A-K2 |          | A-Km |          | A-Kmax |          | CCT |          | TCT |          | ACD |          | ACE |          | PCE |          |
|-----------|------|----------|------|----------|------|----------|--------|----------|------|----------|-----|----------|-----|----------|-----|----------|-----|----------|
| r         | P    | r        | P    | r        | P    | r        | P      | r        | P    | r        | P   | r        | P   | r        | P   | r        |
| Anterior  |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| 0–2       | 0.100 | 0.302    | 0.257 | 0.007*   | 0.200 | 0.029*   | 0.241  | 0.011*   | 0.007 | 0.027*   | 0.075 | 0.054   | 0.101 | 0.016   | 0.302 | 0.029*   |
| 2–6       | 0.004 | 0.968    | 0.141 | 0.144    | 0.080 | 0.344    | 0.139  | 0.153    | 0.006 | 0.955    | 0.094 | 0.193   | 0.256 | 0.200   | 0.193 | 0.256   |
| 6–10      | 0.100 | 0.753    | 0.153 | 0.139    | 0.080 | 0.144    | 0.006 | 0.955    | 0.094 | 0.193    | 0.016 | 0.054   | 0.101 | 0.016   | 0.302 | 0.029*   |
| Anterior- |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| total     |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| Intermediate 0–2 | 0.185 | 0.054 | 0.265 | 0.005* | 0.252 | 0.006* | 0.264 | 0.005* | 0.271 | 0.004* | 0.285 | 0.002* | 0.265 | 0.005* | 0.322 | 0.000* |
| Intermediate 2–6 | 0.126 | 0.195 | 0.160 | 0.099 | 0.155 | 0.082 | 0.168 | 0.082 | 0.236 | 0.013* | 0.247 | 0.010* | 0.265 | 0.032* | 0.241 | 0.012* |
| Intermediate 6–10 | 0.097 | 0.318 | 0.054 | 0.578 | 0.079 | 0.445 | 0.038 | 0.694 | 0.093 | 0.339 | 0.094 | 0.338 | 0.326 | 0.000* | 0.100 | 0.922 |
| Intermediate-total | 0.180 | 0.063 | 0.068 | 0.486 | 0.119 | 0.163 | 0.002 | 0.984 | 0.109 | 0.262 | 0.122 | 0.210 | 0.303 | 0.000* | 0.010 | 0.922 |
| Posterior  |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| 0–2       | 0.041 | 0.673 | 0.086 | 0.374 | 0.065 | 0.647 | 0.122 | 0.208 | 0.003 | 0.974 | 0.026 | 0.792 | 0.050 | 0.470 | 0.035 | 0.716 |
| 2–6       | 0.072 | 0.460 | 0.137 | 0.156 | 0.108 | 0.203 | 0.144 | 0.135 | 0.078 | 0.421 | 0.066 | 0.496 | 0.085 | 0.207 | 0.214 | 0.026* |
| 6–10      | 0.073 | 0.455 | 0.012 | 0.898 | 0.036 | 0.674 | 0.086 | 0.379 | 0.053 | 0.583 | 0.041 | 0.676 | 0.301 | 0.000* | 0.010 | 0.936 |
| Posterior- |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| total     |      |          |      |          |      |          |        |          |      |          |      |          |      |          |      |          |
| Total 0–2 | 0.114 | 0.241 | 0.222 | 0.021* | 0.188 | 0.034* | 0.214 | 0.025* | 0.112 | 0.247 | 0.102 | 0.501 | 0.188 | 0.050 | 0.291 | 0.002* |
| Total 2–6 | 0.049 | 0.614 | 0.155 | 0.109 | 0.108 | 0.208 | 0.163 | 0.092 | 0.096 | 0.324 | 0.099 | 0.310 | 0.067 | 0.780 | 0.156 | 0.070 |
| Total 6–10 | 0.011 | 0.907 | 0.010 | 0.916 | 0.003 | 0.978 | 0.014 | 0.286 | 0.001 | 0.989 | 0.002 | 0.986 | 0.353 | 0.000* | 0.246 | 0.010* |
| Total     | 0.067 | 0.490 | 0.001 | 0.994 | 0.021 | 0.653 | 0.062 | 0.521 | 0.006 | 0.953 | 0.006 | 0.950 | 0.326 | 0.000* | 0.111 | 0.252 |

Spearman correlation coefficient analysis. *P < 0.05 is statistically significant

A-K1, anterior flat keratometry; A-K2, anterior steep keratometry; A-Km, anterior mean keratometry; A-Kmax, anterior maximum keratometry; CCT, central corneal thickness; TCT, thinnest corneal thickness; ACD, anterior chamber depth; ACE, anterior corneal elevation; PCE, posterior corneal elevation
with Vogt’s striae present with lesser epithelial cell density, lesser stromal keratocyte density in the anterior and intermediate stroma, greater stromal degeneration, and fewer intact corneal collagen fibrils. The abnormal separation of the collagen fibrils and wound healing reactions in stromal lamellae may lead to increased light scattering of the corneal tissue [37]. Hence, the corneal densitometry values of the anterior and intermediate corneal stroma are higher than those of the posterior stroma in KC eyes with Vogt’s striae (Fig. 2). Since the cone of KC is mainly located in the central area and under the temporal corneal area [38], corneal densitometry changes within the 0–6 mm area of the cornea are more evident.

As demonstrated in previous studies [24, 25, 28, 39], UCVA and BCVA were significantly lower in KC eyes with Vogt’s striae than that in eyes without it, and the corneal morphological parameters are clearly affected in those with Vogt’s striae. These results are consistent with our findings. Possible correlations between the corneal densitometry results and corneal morphological parameters in KC eyes with and without Vogt’s striae were evaluated. The corneal densitometry values in the anterior 0–2 mm and 2–6 mm and the total cornea (2–6 mm) were positively correlated with A-K1, A-K2, A-Km, A-Kmax, ACE, and PCE and negatively correlated with CCT and TCT in KC eyes with Vogt’s striae. The severity of KC is positively correlated with the anterior surface curvature and the elevation of anterior and posterior surfaces and is negatively correlated with corneal thickness [40]. Therefore, the corneal densitometry values within 0–6 mm of the anterior corneal layer can reflect KC severity. We speculate that the misalignment of the corneal collagen and the degeneration of fibronectin in the extracellular matrix occur in the anterior corneal stroma when Vogt’s striae appear in KC eyes.

Corneal densitometry values in the central area of the cornea can be used to evaluate the efficacy and impact of corneal collagen cross-linking surgery for KC [41].

In KC eyes without Vogt’s striae, we found that only A-K2, A-Km, and A-Kmax were correlated with the densitometry values of the anterior 0–2 mm and intermediate 0–2 mm. No correlation was observed between A-K1 and the corneal densitometry values at any location. Since the orientation of most stromal bands usually occurs in the steepest Sim K axis of the cornea [39], the corneal ultrastructure of the flat corneal axis is less altered in eyes with mild KC. We hypothesize that corneal densitometry in the central area may change in the early stages of KC. Therefore, corneal densitometry in the central region can be used as an auxiliary diagnostic indicator in the evaluation and diagnosis of early KC.

We could not determine the presence of a correlation between central corneal densitometry and ACD in KC eyes with and without Vogt’s striae. However, negative correlations were found between ACD and peripheral corneal densitometry in all patients. We postulate that those alternations in ACD may be associated with changes in corneal morphology, as described by other authors [3].

One limitation of our study is that the participants were not grouped by corneal curvature; this may have led to potential bias. However, the main objective of the current study was to investigate the changes in corneal densitometry in KC eyes with Vogt’s striae and to explore the regions with corneal collagen fiber alternations that occur with KC progression. Therefore, the curvature has little effect on our study. Another limitation of this study is that the examination of corneal densitometry in our study was not performed concurrently. Thus, we will control the inspection time more rigidly to reduce errors in future investigations.

![Fig. 2 Densitometry distribution from the anterior to the posterior layers over the annulus of 0–2 mm, 2–6 mm and 6–10 mm of a cornea in the KC eyes with Vogt’s striae](image)
Conclusions

This study demonstrated that the corneal densitometry values of the anterior and intermediate layers in the central corneal regions were higher in KC eyes with Vogt’s striae than in those without it. Furthermore, the densitometry of the anterior corneal stroma in the central region of the cornea was higher than that of the peripheral cornea in KC eyes with and without Vogt’s striae. Central corneal densitometry clearly correlates with A-K1, A-K2, A-Km, A-Kmax, CCT, TCT, ACD, ACE, and PCE in KC eyes with Vogt’s striae.

Based on the relationship between densitometry and KC severity [16], and the corneal densitometry values in different parts of KC with Vogt’s striae in the results, Vogt’s striae may occur mainly in the anterior and intermediate layers. In addition, the collagen fibers and structures in the central anterior cornea changed during KC progression. This result may explain how anterior corneal collagen cross-linking surgery can effectively prevent and control KC progression. It also indicates that more patients with KC with Vogt’s striae can be treated with deep anterior lamellar keratoplasty instead of penetrating keratoplasty.

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Availability of data and materials  The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest  The authors have no conflicts of interest to declare that are relevant to the content of this article.

Consent to participate  Written informed consent was obtained from at least one parent or legal guardian of each subject.

Ethical approval  This study protocol adhered to the tenets of the Declaration of Helsinki and received approval from the institutional review board and Ethics Committee of Xi’an People’s Hospital (Xi’an Fourth Hospital) (Ethical Approval Number: 20180157).

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