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Corneal biomechanics: A diagnostic tool for differentiating high astigmatism and mild keratoconus

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Background: High astigmatism (HA) can be misinterpreted as keratoconus (KCN), is highly prone to developing KCN and is normally reconfirmed using corneal topography.

Aim: To determine the diagnostic value of corneal biomechanical parameters in distinguishing HA and normal eyes from mild KCN.

Setting: This is a comparative retrospective study.

Methods: This study assessed 55 eyes with mild KCN (stages I and II), 56 eyes with HA (> 2.0 DC) without KCN and 55 normal healthy eyes. Corneal biomechanical and tomography parameters were measured using the Corvis ST and Pentacam HR (Oculus Optikgeräte GmbH, Germany). Keratoconus was diagnosed through slit lamp examination and abnormal corneal tomography patterns. The Kruskal–Wallis test evaluated each parameter's distinguishing capability, and the receiver operating characteristic curve (ROC) analyzed the ability to differentiate high astigmatism and normal eyes from mild KCN.

Results: The Corvis biomechanical index (CBI) between HA and mild KCN reflected a lower area under the curve (AUC) of 0.859, with a sensitivity of 92.7% and specificity of 65.4%, than CBI between normal and mild KCN, with an AUC of 0.896. The AUC for the Belin / Ambrósio enhanced ectasia deviation index (BAD-D) was 0.993, while the tomographical and biomechanical index (TBI) achieved an AUC of 0.99.

Conclusion: Scheimpflug-derived biomechanical parameters effectively differentiated suspected HA and normal corneas from mild KCN corneas, indicating that corneal stiffness decreases at the early KCN stage.

Contribution: Oculus Corvis ST effectively screens for ectasia risk, enabling early detection of KCN in individuals with high astigmatism and asymmetric curvature.

Keywords: Corneal biomechanics; Oculus Corvis ST; Keratoconus; mild keratoconus; high astigmatism.

Introduction

Keratoconus (KCN) is a progressive, bilateral, but usually asymmetric, disorder, which results in the corneal stroma thinning and reshaping into a conical shape.[1,2] The precise aetiopathogenesis of KCN remains elusive, with potential contributions from genetic factors and, apparently more importantly, environmental influences such as eye rubbing and nocturnal ocular compression because of inappropriate sleeping positions.[2,3] While KCN was once considered a non-inflammatory disease, doubts have arisen as pro-inflammatory mediators have been detected in the tears and corneas of KC patients.[4] As the condition progresses, it leads to irregular astigmatism, impacting visual acuity. In the past 20 years, corneal crosslinking has emerged as one of the primary treatment options for stopping disease advancement, alongside glasses, hard contact lenses and keratoplasty procedures.[5,6,7] In advanced cases, as a consequence of breaks in the Bowman's layer or corneal hydrops, scarring may occur, in some cases even necessitating corneal transplantation.[8] While it was initially believed that Bowman's layer played a crucial role in corneal biomechanics, experimental findings have shown that the presence or absence of Bowman's layer not to result in a measurable difference in corneal stiffness.[9,10] This has been confirmed in the real world by millions of individuals who have undergone photorefractive keratectomy in the last three decades and still maintain a stable cornea despite the absence of Bowman's layer.[11] Thus, all this evidence demonstrates that the corneal stroma is primarily responsible for corneal strength, and therefore a breakdown of corneal stroma components may lead to tissue instability. In patients with KCN, the tear film contains proteolytic enzymes and inflammatory cytokines that may contribute to corneal thinning. These substances could disrupt the balance between synthesis and degradation of extracellular matrix and collagen fibrils, leading to a reduction in corneal thickness. These factors may potentially interfere with mechanical stability and cause viscosity imbalance of the cornea.[4,12]

Historically, diagnosing KCN involved observing scissor movement during retinoscopy and detecting irregular keratometry mires. Advanced stages of the condition were identified through subjective evaluation of clinical indicators.[1] Corneal tomography is currently used to detect early KCN. This method distinguishes standard patterns from ectatic pathological conditions by qualitatively and quantitatively measuring corneal morphology.[13] Astigmatism has also been analysed using Alpins method, measured by both refractive and corneal measurements using vector analysis has been recognised to discriminate between irregular and normal healthy astigmatism.[14,15,16] Vector parameters Ocular Residual Astigmatism (ORA) and Topographic Disparity (TD) are able to discriminate with good levels of precision between KCN and healthy corneas.[17,18]

Corneal biomechanics is currently essential in monitoring KCN disease progression, which involves the *in vivo* measuring of cornea deformation when mechanical stress is applied.[13] The Corvis ST employs a single air puff to alter the shape of the cornea, while simultaneously capturing its response using a Scheimpflug camera. Additionally, this device measures various corneal parameters, including A½ length, A½ velocity, maximum concavity deformation amplitude, curvature radius, peak distance, thickness at the centre and pressure within the eye.[13,19,20] Corvis ST was recently introduced in clinics but has yet to be widely utilised. Moreover, few studies have tested the instrument's ability to distinguish between KCN and normal eyes.[21,22,23] The Corvis ST measurements of dynamic corneal response (DCR) parameters are highly replicable in healthy and KC eyes.[24,25] The Corvis biomechanical index (CBI) and tomographic and biomechanical index (TBI) also accurately differentiate healthy eyes from KCN eyes and subclinical ectasia.[26,27] Additional Corvis ST-derived metrics for distinguishing KCN eyes from normal ones include an evaluation of two rigidity parameters based on their deformation patterns. In theory, a cornea affected by KCN exhibits less stiffness compared to a healthy cornea.[28] Meanwhile, high astigmatism (HA) can be misinterpreted as KCN; thus, patients are often subjected to a corneal topography test for confirmation.

Individuals with HA are susceptible to developing KCN.[29,30] Among individuals with HA, 12.3% are identified as having KCN.[30] Twenty one out of 100 eyes with astigmatism of more than two diopters have KCN.[29] Patients with ≥ 2 D refractive astigmatism or 1 D to 2 D ATR (against the rule) should be further evaluated using corneal topography.[29] Increasingly, studies have demonstrated that corneal biomechanics possess high sensitivity in detecting early-stage KCN and forme fruste from normal eyes. Therefore, this study investigates the corneal biomechanics of individuals with HA and patients with mild KCN.

Methodology

Subject recruitment

This prospective cross-sectional, single-centre, observational study was conducted at the Department of Ophthalmology of an undisclosed hospital. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the undisclosed hospital. Informed consent was obtained from the participants before the study. Their data remained confidential and protected.

The participants were recruited between August 2021 and March 2023. The inclusion criteria for this study were healthy individuals aged between 13 years and 45 years. Those with severe astigmatism should have corneal astigmatism ≥ 2.0 D. Clinical examination and corneal tomography measured with the Oculus Pentacam were used to diagnose KCN. The three classes of topographic KCN classification (TKC) provided by the Pentacam HR, which follows the Amsler-Krumeich classification, were included in the early KCN group (TKC 1, TKC1–2 and TKC 2). TKC 1 was designated as KCN Stage I, whereas TKC 1–2 and TKC 2 were designated as KCN Stage II.[31,32] The exclusion criteria were individuals with a history of corneal or lenticular surgery, cataracts, corneal scarring, rigid contact lens usage, advanced KCN and concurrent ocular surface disorders.

A total of 166 eyes from 106 participants were selected and divided into three groups: early KCN (55 eyes, 41 participants), HA (56 eyes from 32 participants) and normal (55 eyes from 34 participants). The calculation of sample size for this research utilises the descriptive cross-sectional study formula (Equation 1):[33]

$$n = \frac{(Z1-\alpha/2)^2 (p)(q)}{(d)^2} \quad \text{[Eqn 1]}$$

n = Desired sample size
$Z\ 1-\alpha/2 = 1.96$
P = Expected prevalence based on previous research (1.66%)[34]
q = 1-p
d = Margin of error or precision
P = 0.0166 (keratoconus)
q = 0.9834
d = 0.05
n = 25.07 ~ 30 subjects for each group (20% drop out)

Each participant underwent the slit-lamp examination, Corvis ST and Pentacam HR, respectively. All measurements were performed by a trained optometrist, and only scans that the 'quality specification' (QS) function determined as 'OK' were included for analyses. In addition, healthy subjects and KCN patients were incentivised with a comprehensive ophthalmologic examination, which included slit lamp biomicroscopy of the anterior and fundus segments and a medical history review.

Ocular examinations

Corneal topography and biomechanics examination were performed on all subjects using the Pentacam HR and Corvis ST, respectively. Measurements of both eyes were conducted in a darkened room three times between 08:00 and 14:00. The Corvis ST allows dynamic and non-invasive corneal deformation imaging in response to a puff of air. An accurately controlled burst of air induces the cornea to deform and flatten, a process known as corneal applanation or the first applanation. The cornea continues to depress until it reaches its maximum concave state. Because of its viscoelastic properties, the cornea then rebounds from this concave position to a second point of applanation before ultimately returning to its original convex shape. The deformation is captured by a high-speed Scheimpflug camera, which displays the entire corneal cross-section in slow motion on a control panel. This camera is capable of recording at a rate of 4330 frames per second and spans a horizontal field of view measuring 8.5 mm.[35] In this study, the recording was performed within 30 ms, yielding 140 digital frames. The Corvis ST records standard tonometry and pachymetry data along with corneal movement throughout the deformation process. For inclusion in the study, all maps were required to have a 'OK' quality specification (QS) as determined by the machine. Corneal tomography measurements provided data on TKC and corneal astigmatism, including both power and axis information.

Statistical analysis

The empirical data were tabulated in Microsoft Excel 2016 (Microsoft Corp., Redmond, WA). Statistical analysis was performed using the Statistical Package for Social Sciences software version 27 (SPSS. IBM Corp., Armonk, New York, USA). The Kolmogorov-Smirnov test determined whether the quantitative data was normally distributed. Results demonstrating a normal distribution were expressed as mean ± standard deviation (s.d.), whereas the data not normally distributed were written as median (quartile range). The one-way analysis of variance (ANOVA) and Kruskal–Wallis test served to identify differences between the groups. Dunn's multiple comparison was the selected post hoc test used to compare two groups. A *P*-value of < 0.05 was deemed statistically significant. Sensitivity, specificity, cut-off points and area under the curve (AUC) were examined using logistic regression and receiver operating characteristic (ROC) curve analysis.

Ethical considerations

Ethical clearance to conduct this study was obtained from the National University of Malaysia (No. UKM PPI/111/8/JEP-2021-654).

Results

Study participants' characteristics

The participants were aged 26.47 ± 10.89 years on average and were primarily female (male: 48, female: 67) and Malay people (Malay people: 81, Chinese people: 8, Indian people: 13, other people: 3). The early KCN group comprised 20 male and 21 female participants with an average age of 29.31 ± 6.87 years. The HA group included 19 male and 13 female participants who were 20.16 ± 10.17 years old on average. Meanwhile, the normal group consisted of 12 males and 20 females with a mean age of 30.05 ± 12.13 years. The age distribution showed no statistically significant variation among the groups ($P = 0.078$).

Comparison of corneal topography and biomechanics between groups

The Corvis ST parameters abbreviations are detailed in Table 1. Table 2 presents the corneal astigmatism, mean keratometry (mean K), central corneal thickness (CCT) and the bio-mechanically corrected IOP (bIOPs) measured by the Corvis ST in different groups. The comparison of Corvis ST parameters among the three groups is shown in Table 3. Kruskal–Wallis analysis revealed that corneal biomechanical properties measured by Corvis ST differed significantly among the three groups ($P < 0.001$). Notable variances existed between mild KCN and normal groups for all parameters except for highest concavity peak distance (HCPD) ($P = 0.224$). Meanwhile, HA and mild KCN groups were significantly different for all parameters, excluding second applanation length (A2L) ($P = 0.078$) and highest concavity

TABLE 1: Corneal biomechanics parameters (Oculus Corvis ST).

Parameter	Details
A1L	First applanation length
A1V	Applanation-1 velocity
A2L	Second applanation length
A2V	Applanation-2 velocity
HCPD	Highest concavity peak distance
HCDA	Highest concavity deformation amplitude
HCR	Highest concavity radius
CCT	Central corneal thickness
bIOP	Bio-mechanically corrected intraocular pressure
ARTh	Ambrosio relational thickness horizontal
SPA1	Stiffness parameter at the first applanation
DA	Deformation amplitude ratio at 2 mm
IR	Integrated radius
CBI	Corvis biomechanical index
TBI	Tomographic and biomechanical Index
BAD	Belin / Ambrósio-enhanced ectasia deviation value

TABLE 2: Oculus Corvis ST Corneal biomechanics measurements for different groups.

Parameter	Mild keratoconus (*n* = 56)	High astigmatism (*n* = 55)	Normal (*n* = 55)	*P*
Gender (male/female)	20/21	19/13	12/20	0.078
Age (years)	29.31 ± 6.87	20.16 ± 10.17	30.15 ± 12.13	< 0.001
Corneal astigmatism (D)	2.77 ± 1.75	3.48 ± 1.01	1.08 ± 0.45	0.000
CCT (μm)	508.44 ± 48.52	561.29 ± 35.47	553.56 ± 35.19	< 0.001
bIOP (mmHg)	14.99 ± 2.15	16.66 ± 1.97	15.56 ± 1.98	< 0.001
Kmean (D)	46.67 ± 3.50	44.10 ± 1.58	43.41 ± 1.13	< 0.001

Notes: Data are presented as mean ± s.d. or median (IQR). The level of significance was set at $P < 0.05$.

CCT, central corneal thickness; bIOP, biomechanically corrected intraocular pressure; Kmean, mean keratometry; D, dioptre.

TABLE 3: Corvis ST eye assessments for different groups.

Parameter	Mild Keratoconus (n = 55)	High Astigmatism (n = 56)	Normal (n = 55)	P (KC, HA, NL)	P (KC vs NL)	P (HA vs NL)	P (KC vs HA)
CBI	0.70 ± 0.31	0.23 ± 0.26	0.18 ± 0.25	< 0.001	< 0.001	0.200	< 0.0010
TBI	0.98 ± 0.74	0.31 ± 0.27	0.26 ± 0.25	< 0.001	< 0.001	0.932	< 0.0010
BAD	5.88 ± 3.04	1.25 ± 0.75	1.08 ± 0.59	< 0.001	< 0.001	1.000	< 0.0010
SPA1	82.23 ± 16.42	108.10 ± 21.86	103.89 ± 20.24	< 0.001	< 0.001	0.785	< 0.0010
ARTh	376.94 ± 263.88	611.51 ± 279.22	675.70 ± 233.53	< 0.001	< 0.001	0.086	< 0.0010
DA	5.27 ± 0.90	4.66 ± 1.24	4.68 ± 0.43	< 0.001	< 0.001	0.038	< 0.0010
IR	10.67 ± 2.09	8.82 ± 1.27	8.58 ± 0.92	< 0.001	< 0.001	0.614	< 0.0010
A1L (mm)	1.97 ± 0.31	2.17 ± 0.34	2.08 ± 0.31	0.002	0.008	0.227	< 0.0010
A2L (mm)	1.49 ± 0.42	1.58 ± 0.46	1.73 ± 0.35	0.019	0.005	0.080	0.2977
A1V (m/s)	0.18 ± 0.22	0.16 ± 0.03	0.17 ± 0.03	< 0.001	0.001	0.080	< 0.0010
A2V (m/s)	-0.32 ± 0.07	-0.24 ± 0.13	-0.30 ± 0.05	< 0.001	0.002	0.116	< 0.0010
HCPD (mm)	5.12 ± 0.23	4.91 ± 0.31	5.08 ± 0.43	0.009	0.224	0.060	0.0020
HCR (mm)	5.91 ± 0.98	6.16 ± 1.01	6.80 ± 1.04	< 0.001	< 0.001	< 0.001	0.1340
HCDA (mm)	1.19 ± 0.11	1.07 ± 0.12	1.09 ± 0.13	< 0.001	< 0.001	0.559	< 0.0010

Notes: Data are presented as mean ± s.d. or median (IQR). The significant level was set at $P < 0.05$.

KC, keratoconus; HA, high astigmatism; NL, normal; CBI, Corvis biomechanical index; TBI, tomographic and biomechanical Index; BAD-D, Belin / Ambrósio-enhanced ectasia deviation value; SPA1, stiffness parameter at the first applanation; ARTh, Ambrosio relational thickness horizontal; DA, deformation amplitude ratio at 2 mm; IR, integrated radius; A1L, first applanation length; A2L, second applanation length; A1V, applanation-1 velocity; A2V, applanation-2 velocity; HCPD, highest concavity peak distance; HCR, highest concavity radius; HCDA, highest concavity deformation amplitude.

radius (HCR) (P = 0.134). High astigmatism and normal groups statistically differed in deformation amplitude ratio at 2 mm (DA) and HCR ($P < 0.05$).

Diagnostic ability of Corvis St parameters between the groups

Comparison between early KCN and HA demonstrated significantly diagnostic accuracy for CBI (AUC = 0.859 [95% confidence interval {CI}: 0.785–0.933], sensitivity = 92.7%, specificity = 65.4%). Belin / Ambrósio enhanced ectasia deviation (BAD) index with (AUC = 0.991 [95% CI: 0.978–1.00], sensitivity = 100%, specificity = 80.4%), TBI (AUC = 0.993 [95% CI: 0.991–1.00], sensitivity = 100%, specificity = 88.5%) and stiffness parameter at the first applanation (SPA1) (AUC = 0.826 [95% CI: 0.745–0.890], sensitivity = 92.7%, specificity = 62.5%). Meanwhile, comparison between early KCN and normal groups recorded the best overall diagnostic accuracy in CBI (AUC = 0.896 [95% CI: 0.785–0.933], with sensitivity = 94.5%, specificity = 70.9%), BAD index (AUC = 0.991 [95% CI: 0.978–1.00], sensitivity = 100%, specificity = 85.5%), TBI (AUC = 0.974 [95% CI: 0.941–1.00], sensitivity = 100%, specificity = 89.1%), Ambrosio relational thickness horizontal, ARTh (AUC = 0.850 [95% CI: 0.779–0.920], sensitivity = 85.5%, specificity 69.1%) and integrated radius, IR (AUC = 0.850 [95% CI: 0.774–0.925], sensitivity = 85.5%, specificity = 69.1%) has been shown in Table 4. Overall, TBI and BAD index accurately distinguish mild KCN from HA and normal eyes.

Diagnostic ability of Corvis ST between the groups (controlled central corneal thickness, central corneal thickness)

Normal (n = 35), HA (n = 31) and KCN (n = 34) eyes whose mean CCT was not significantly different in the one-way ANOVA (P = 0.06) were used to form subgroups to control the CCT effects on Corvis ST parameters. The Bonferroni pairwise comparison reveals no significant difference in CCT between all subgroups: normal and HA (P = 0.656), normal and KCN (P = 0.07) and HA and KCN (P = 0.06). In addition, nine Corvis ST parameters with AUC > 0.7 in the previous analyses in the three subgroups were evaluated. Only TBI and BAD index exhibited high AUC, sensitivity and specificity to detect early KCN in normal and HA eyes when the CCT level is controlled. Comparison between HA and mild KCN yielded the following results: BAD index (AUC = 0.968 [95% CI: 0.921–1.00], sensitivity = 100% and specificity = 99.8%) and TBI (AUC = 0.983 [95% CI: 0.961–1.00], sensitivity = 97.4% and specificity = 99.9%). Meanwhile, the normal versus mild KCN results are presented as follows: BAD index (AUC = 0.975 [95% CI: 0.945–1.00], sensitivity = 97.1%, specificity = 88.9%) and TBI (AUC = 0.956 [95% CI: 0.901–1.00], sensitivity = 100%, specificity = 88.9%). The complete analysis is shown in Table 5.

Discussion

Identifying KCN at an early stage is critical to ensure timely intervention strategies. Nevertheless, there has been a significant therapeutic obstacle in accurately characterising the distinguishing features of early and marginal manifestations of this condition. Individuals with KCN and sub-clinical KCN exhibited a reduction in corneal biomechanical parameters compared to those with normal eyes.[21,36,37] Alterations in microscopic corneal structure may be observable at the initial stages of KCN, manifesting atypical mechanical stability before substantial corneal morphological abnormalities are detected.[38] Previous studies have provided evidence supporting the efficacy of corneal biomechanical testing in accurately distinguishing between moderate KCN and normal corneal conditions.[39,40,41] A cohort of mild KCN (Stages I and II) patients was chosen for this study to enhance the precision of Corvis ST in differentiating KCN from severe astigmatism.

This study demonstrated the efficacy of corneal biomechanical testing in accurately distinguishing between mild KCN and normal corneal characteristics. There were significant mean differences in several parameters measured by corneal

TABLE 4: Receiver operating characteristic (ROC) curve analysis of mild keratoconus, high astigmatism and normal eyes.

Parameters	Area under curve (AUC)	*P*	95% confidence interval (CI)	Cut-off	Sensitivity (%)	Specificity (%)
Mild keratoconus and high astigmatism						
CBI	0.859	< 0.001	0.800–0.931	0.220	92.7	65.4
TBI	0.993	< 0.001	0.991–1.000	0.615	100.0	88.5
BAD	0.991	< 0.001	0.984–1.000	1.745	100.0	80.4
ARTh	0.774	< 0.001	0.722–0.906	493.900	72.7	66.1
SPA1	0.826	< 0.001	0.745–0.890	102.200	92.7	62.5
DA	0.759	< 0.001	0.598–0.811	4.550	80.0	64.3
IR	0.844	< 0.001	0.767–0.919	9.350	72.7	62.5
AIL	0.688	0.018	0.522–0.731	1.570	73.0	64.0
A2L	0.664	0.003	0.563–0.764	1.580	56.4	51.8
A1V	0.723	0.050	0.630–0.744	0.165	80.0	58.9
A2V	0.702	0.050	0.602–0.796	-0.285	81.8	53.6
HCPD	0.665	0.050	0.564–0.762	5.025	72.7	51.8
HCR	0.580	0.050	0.444–0.661	6.185	58.2	51.8
HCDA	0.774	0.040	0.697–0.811	1.110	80.0	64.3
Mild keratoconus and normal						
CBI	0.896	< 0.001	0.785–0.933	0.180	94.5	70.9
TBI	0.974	< 0.001	0.941–1.000	0.630	100.0	89.1
BAD	0.991	< 0.001	0.978–1.000	1.735	100.0	85.5
ARTh	0.850	< 0.001	0.779–0.9200	554.850	85.5	69.1
SPA1	0.795	< 0.001	0.711–0.879	96.250	80.0	65.5
DA	0.729	< 0.001	0.631–0.827	4.750	69.1	63.6
IR	0.850	< 0.001	0.774–0.925	9.050	85.5	69.1
AIL	0.628	< 0.001	0.522–0.733	1.985	69.1	54.5
A2L	0.667	< 0.001	0.565–0.768	1.645	63.6	65.5
A1V	0.667	< 0.001	0.565–0.768	0.175	63.6	69.1
A2V	0.629	< 0.001	0.525–0.734	-0.295	76.4	54.4
HCPD	0.561	0266	0.453–0.670	5.070	58.2	52.7
HCR	0.814	< 0.001	0.733–0.897	6.485	80.0	70.9
HCDA	0.724	< 0.001	0.629–0.818	1.100	85.5	52.7

CBI, Corvis biomechanical index; TBI, tomographic and biomechanical index; BAD-D, Belin / Ambrósio-enhanced ectasia deviation value; SPA1, stiffness parameter at the first applanation; ARTh, Ambrosio relational thickness horizontal; DA, deformation amplitude ratio at 2 mm; IR, integrated radius; A1L, first applanation length; A2L, second applanation length; A1V, applanation-1 velocity; A2V, applanation-2 velocity; HCPD, highest concavity peak distance; HCR, highest concavity radius; HCDA, highest concavity deformation amplitude.

TABLE 5: Area under the curve (AUC) of corneal visualisation Scheimpflug technology (Corvis ST) parameters at 95% confidence interval (CI) and the best cut-offs for optimising sensitivity and specificity to separate normal and high astigmatism from keratoconic corneas in corneal thickness (CCT) controlled subgroups.

Parameters	Area under curve (AUC)	*P*	95 % confidence interval (CI)	Cut-off (≥)	Sensitivity (%)	Specificity (%)
Mild keratoconus and high astigmatism						
CBI	0.759	0.049	0.633–0.871	0.220	84.2	61.7
TBI	0.983	< 0.001	0.961–1.000	0.595	97.4	99.9
BAD	0.968	0.001	0.921–1.000	1.745	100.0	99.8
ARTh	0.643	0.050	0.520–0.790	507.250	63.2	63.0
SPA1	0.745	0.001	0.616–0.865	100.500	84.2	63.0
DA	0.647	0.040	0.513–0.790	4.450	81.6	51.9
IR	0.667	0.020	0.591–0.842	9.150	71.1	51.9
HCR	0.540	0.581	0.388–0.663	5.880	71.1	44.4
HCDA	0.736	0.001	0.651–0.896	1.105	73.7	63.0
Mild Keratoconus and Normal						
CBI	0.786	< 0.001	0.677–0.896	0.220	85.3	66.7
TBI	0.956	< 0.001	0.901–1.000	0.615	100.0	88.9
BAD	0.975	< 0.001	0.945–1.000	1.960	97.1	88.9
ARTh	0.742	0.001	0.627–0.857	557.400	73.5	66.9
SPA1	0.708	0.003	0.585–0.830	95.500	70.6	66.9
DA	0.562	0.072	0.420–0.704	5.050	47.1	72.2
IR	0.809	< 0.001	0.708–0.910	8.950	82.4	61.1
HCR	0.741	0.001	0.624–0.857	6.550	76.5	63.9
HCDA	0.648	0.030	0.519–0.778	1.105	79.4	50.0

CBI, Corvis biomechanical index; TBI, tomographic and biomechanical Index; BAD-D, Belin / Ambrósio-enhanced ectasia deviation value; SPA1, stiffness parameter at the first applanation; ARTh, Ambrosio relational thickness horizontal; DA, deformation amplitude ratio at 2 mm; IR, integrated radius; HCR, highest concavity radius; HCDA, highest concavity deformation amplitude.

Scheimpflug tomography among the three study groups. The KCN eyes demonstrated poor biomechanics and diminished strength. The ROC curve analysis compared mild KCN with HA and produced significant findings. As indicated by elevated AUC values, CBI, TBI and BAD exhibited a notable capacity for discrimination. Meanwhile, SPA1, ARTh, DA and IR demonstrated favourable AUC values, which indicate a modest ability to distinguish between the two conditions.

An earlier report coined CBI as a comprehensive metric incorporating several corneal deformation attributes. When employing a threshold value of 0.5, CBI exhibited a specificity of 100% and a sensitivity of 94.1% in distinguishing between KCN and healthy eyes.[19] In addition, in a case series of 12 patients, one eye exhibited normal tomographic and topographic results, while the other eye showed abnormalities. Nevertheless, the CBI was found to be abnormal in both eyes of all patients.[42] These findings corroborate our research, demonstrating that CBI exhibits a strong predictive capacity to distinguish early-stage KCN from normal cases. Furthermore, multiple research studies have supported our observation that TBI demonstrates high sensitivity in identifying ectasia, especially in the detection of early-stage KCN.[43] For detecting KCN, the TBI combines corneal tomography data from the Pentacam system with biomechanical information gathered by the Corvis ST device.[43] At a cut-off value of 0.76, TBI recorded 100% sensitivity and specificity in diagnosing clinical ectasia.[44] Another study compared corneal tomography, Pentacam HR and Corvis ST and discovered that TBI (threshold = 0.63) had the highest diagnostic accuracy in identifying mild ectasia eyes.[40]

This investigation revealed a significant difference in CCT between the normal and KCN groups ($P < 0.001$). This disparity in CCT may introduce a potential bias when comparing corneal biomechanical parameters, as discussed in previous studies.[45,46] In a separate investigation, Corvis ST was used to measure the central concave curvature at the point of maximum concavity and CCT, which were elevated among individuals with subclinical KCN.[47] This study mitigated the influence of CCT on Corvis ST parameters by dividing the participants into three distinct subgroups based on their level of astigmatism: HA, normal and KCN. The CCT measurements of these subgroups were not significantly different from one another ($P = 0.06$). The assessment of the differentiating value of nine parameters, which had demonstrated superior distinguishing ability in prior analyses (AUC > 0.7), was conducted in the three novel subgroups. TBI and BAD values demonstrated exceptional discriminatory capability (AUC > 0.95) to discriminate between early KCN and normal have been demonstrated by earlier study.[48] The biomechanical parameters based on Corvis ST showed good performance in discriminating early KCN in corneas with normal and HA.

Limitation

Although this research utilised a limited number of participants, it provided adequate data for comprehensive analysis. To enhance future investigations, it is recommended to incorporate residual ocular astigmatism and ORA as additional independent variables. Furthermore, including a subclinical KCN group would allow for a more in-depth examination of Scheimpflug biomechanics' diagnostic capabilities.

Conclusion

While additional research is essential, biomechanical analysis can enhance the diagnostic capabilities of other modalities to identify sub-clinical KCN. Use of TBI and BAD parameters can improve the sensitivity and specificity of ectasia risk detection. Screening for ectasia risk among individuals with HA and asymmetrical curvature is one of the most vital steps in the early detection of KCN.

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Competing interests

The author reported that they received funding from the Faculty of Medicine, National University of Malaysia, which may be affected by the research reported in the enclosed publication. The author has disclosed those interests fully and has implemented an approved plan for managing any potential conflicts arising from their involvement. The terms of these funding arrangements have been reviewed and approved by the affiliated university in accordance with its policy on objectivity in research.

Authors' contributions

N.R., W.H.W.A.H. and B.M-.A. made a significant contribution to the work reported, in the conception, study design, execution, acquisition of data, analysis and interpretation. N.R., W.H.W.A.H. and B.M-.A. contributed towards drafting, revising, critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted and agree to be accountable for all aspects of the work.

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Data availability

The data that support the findings of this study are available on request from the corresponding author, N.R. upon reasonable request. The data are not publicly available because of restrictions containing information that could compromise the privacy of research participants.

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References

1. Santodomingo-Rubido J, Carracedo G, Suzaki A, Villa-Collar C, Vincent SJ, Wolffsohn JS. Keratoconus: An updated review. Cont Lens Anterior Eye. 2022;45(3):101559. https://doi.org/10.1016/j.clae.2021.101559
2. Rabinowitz YS, Galvis V, Tello A, Rueda D, García JD. Genetics vs chronic corneal mechanical trauma in the etiology of keratoconus. Exp Eye Res. 2021;202:108328. https://doi.org/10.1016/j.exer.2020.108328
3. Gatinel D, Galvis V, Tello A, et al. Obstructive sleep apnea-hypopnea syndrome and keratoconus: An epiphenomenon related to sleep position? Cornea. 2020;39(4):e11–e12. https://doi.org/10.1097/ICO.0000000000002219
4. Galvis V, Tello A, Barrera R, Niño CA. Inflammation in keratoconus. Cornea. 2015;34(8):e22–e23. https://doi.org/10.1097/ICO.0000000000000499
5. Galvis V, Tello A, Carreño NI, et al. Corneal cross-linking (with a partial deepithelization) in keratoconus with five years of follow-up. Ophthalmol Eye Dis. 2016;8:17–21. https://doi.org/10.4137/OED.S38364
6. Raiskup F, Herber R, Lenk J, et al. Corneal crosslinking with riboflavin and UVA light in progressive keratoconus: Fifteen-year results. Am J Ophthalmol. 2023;250: 95–102. https://doi.org/10.1016/j.ajo.2023.01.022
7. Deshmukh R, Ong ZZ, Rampat R, et al. Management of keratoconus: An updated review. Front Med (Lausanne). 2023;10:1212314. https://doi.org/10.3389/fmed.2023.1212314
8. Hwang S, Chung TY, Han J, Kim K, Lim DH. Corneal transplantation for keratoconus in South Korea. Sci Rep. 2021;11(1):12580. https://doi.org/10.1038/s41598-021-92133-y
9. Seiler T, Matallana M, Sendler S, Bende T. Does Bowman's layer determine the biomechanical properties of the cornea? Refract Corneal Surg. 1992;8(2): 139–142. https://doi.org/10.3928/1081-597X-19920301-08
10. Torres-Netto EA, Hafezi F, Spiru B, et al. Contribution of Bowman layer to corneal biomechanics. J Cataract Refract Surg. 2021;47(7):927–932. https://doi.org/10.1097/j.jcrs.0000000000000543
11. Wilson SE. The Cornea: No difference in the wound healing response to injury related to whether, or not, there's a Bowman's layer. Biomolecules. 2023;13(5):771. https://doi.org/10.3390/biom13050771
12. Loh IP, Sherwin T. Is keratoconus an inflammatory disease? The implication of inflammatory pathways. Ocul Immunol Inflamm. 2022;30(1):246–255. https://doi.org/10.1080/09273948.2020.1780271
13. Ambrósio R, Jr., Valbon BF, Faria-Correia F, Ramos I, Luz A. Scheimpflug imaging for laser refractive surgery. Curr Opin Ophthalmol. 2013;24(4):310–320. https://doi.org/10.1097/ICU.0b013e3283622a94
14. Alpins NA. New method of targeting vectors to treat astigmatism. J Cataract Refract Surg. 1997;23(1):65–75. https://doi.org/10.1016/S0886-3350(97)80153-8
15. Alpins NA. Treatment of irregular astigmatism. J Cataract Refract Surg. 1998;24(5):634–646. https://doi.org/10.1016/S0886-3350(97)80153-8
16. Alpins N. Astigmatism analysis by the Alpins method. J Cataract Refract Surg. 2001;27(1):31–49. https://doi.org/10.1016/S0886-3350(00)00798-7
17. Piñero DP, Pérez-Cambrodí RJ, Soto-Negro R, Ruiz-Fortes P, Artola A. Clinical utility of ocular residual astigmatism and topographic disparity vector indexes in subclinical and clinical keratoconus. Graefes Arch Clin Exp Ophthalmol. 2015;253(12):2229–2237. https://doi.org/10.1007/s00417-015-3169-x
18. Martínez-Abad A, Piñero DP, Ruiz-Fortes P, Artola A. Evaluation of the diagnostic ability of vector parameters characterizing the corneal astigmatism and regularity in clinical and subclinical keratoconus. Cont Lens Anterior Eye. 2017;40(2):88–96. https://doi.org/10.1016/j.clae.2016.11.008
19. Vinciguerra R, Ambrósio R, Jr., Elsheikh A, et al. Detection of keratoconus with a new biomechanical index. J Refract Surg. 2016;32(12):803–810. https://doi.org/10.3928/1081597X-20160629-01
20. Salouti R, Alishiri AA, Gharebaghi R, et al. Comparison among ocular response analyzer, Corvis ST and Goldmann applanation tonometry in healthy children. Int J Ophthalmol. 2018;11(8):1330–1336.
21. Ali NQ, Patel DV, McGhee CN. Biomechanical responses of healthy and keratoconic corneas measured using a noncontact scheimpflug-based tonometer. Invest Ophthalmol Vis Sci. 2014;55(6):3651–3659. https://doi.org/10.1167/iovs.13-13715
22. Ambrósio R.J. CDL, Ramos I., Luz A. Textbook on keratoconus new insights. A B, editor. New Delhi: Jaypee Brothers Medical Publishers; 2012. p. 70–90.
23. Tian L, Huang YF, Wang LQ, et al. Corneal biomechanical assessment using corneal visualization scheimpflug technology in keratoconic and normal eyes. J Ophthalmol. 2014;2014:147516. https://doi.org/10.1155/2014/147516
24. Lopes BT, Roberts CJ, Elsheikh A, et al. Repeatability and reproducibility of intraocular pressure and dynamic corneal response parameters assessed by the Corvis ST. J Ophthalmol. 2017;2017:8515742. https://doi.org/10.1155/2017/8515742
25. Herber R, Vinciguerra R, Lopes B, et al. Repeatability and reproducibility of corneal deformation response parameters of dynamic ultra-high-speed Scheimpflug imaging in keratoconus. J Cataract Refract Surg. 2020;46(1):86–94.
26. Sedaghat MR, Momeni-Moghaddam H, et al. Diagnostic ability of corneal shape and biomechanical parameters for detecting Frank keratoconus. Cornea. 2018;37(8):1025–1034. https://doi.org/10.1097/ICO.0000000000001639
27. Roberts CJ, Mahmoud AM, Bons JP, et al. Introduction of two novel stiffness parameters and interpretation of air puff-induced biomechanical deformation parameters with a dynamic scheimpflug analyzer. J Refract Surg. 2017;33(4): 266–273. https://doi.org/10.3928/1081597X-20161221-03
28. Ambrósio R, Faria-Correia F, Ramos I, et al. Enhanced screening for ectasia susceptibility among refractive candidates: The role of corneal tomography and biomechanics. . Curr Ophthalmol Rep. 2013;1:28–38. https://doi.org/10.1007/s40135-012-0003-z
29. Shakir AN, Alwan EH. Prevalence of keratoconus in patients with astigmatism more than two diopters: A cross-sectional study. Int J Med Invest. 2019;8(2):12–22.
30. Ibrahim M, kher A, Helaly H, Said A. Prevalence of keratoconus in Egyptian subjects with high corneal astigmatism. The Egyptian J Cataract Refract Surg. 2021;27(1):13–7.
31. Wu Y, Guo LL, Tian L, et al. Comparative analysis of the morphological and biomechanical properties of normal cornea and keratoconus at different stages. Int Ophthalmol. 2021;41(11):3699–36711. https://doi.org/10.1007/s10792-021-01929-4
32. Herber R, Pillunat LE, Raiskup F. Development of a classification system based on corneal biomechanical properties using artificial intelligence predicting keratoconus severity. Eye Vis (Lond). 2021;8(1):21. https://doi.org/10.1186/s40662-021-00244-4
33. Sharma SK, Mudgal SK, Thakur K, Gaur R. How to calculate sample size for observational and experimental nursing research studies? Natl J Physiol Pharm Pharmacol. 2020;10(1):1–8.
34. Piyacomn Y, Kasetsuwan N, Puangsricharern V, Reinprayoon U, Satitpitakul V, Chantaren P. Keratoconus in Thai population – A cross-sectional hospital-based study. Asian Biomed (Res Rev News). 2022;16(6):316–321.
35. Vellara HR, Patel DV. Biomechanical properties of the keratoconic cornea: A review. Clin Exp Optom. 2015;98(1):31–38. https://doi.org/10.1111/cxo.12211
36. Mercer RN, Waring GOt, Roberts CJ, et al. Comparison of corneal deformation parameters in keratoconic and normal eyes using a non-contact tonometer with a dynamic ultra-high-speed scheimpflug camera. J Refract Surg. 2017;33(9): 625–631. https://doi.org/10.3928/1081597X-20170621-03
37. Elham R, Jafarzadehpur E, Hashemi H, et al. Keratoconus diagnosis using Corvis ST measured biomechanical parameters. J Curr Ophthalmol. 2017;29(3):175–181. https://doi.org/10.1016/j.joco.2017.05.002
38. Andreassen TT, Simonsen AH, Oxlund H. Biomechanical properties of keratoconus and normal corneas. Exp Eye Res. 1980;31(4):435–441. https://doi.org/10.1016/S0014-4835(80)80027-3
39. Fontes BM, Ambrósio R, Jr., Jardim D, Velarde GC, Nosé W. Corneal biomechanical metrics and anterior segment parameters in mild keratoconus. Ophthalmology. 2010;117(4):673–679. https://doi.org/10.1016/j.ophtha.2009.09.023
40. Kataria P, Padmanabhan P, Gopalakrishnan A, Padmanaban V, Mahadik S, Ambrósio R, Jr. Accuracy of scheimpflug-derived corneal biomechanical and tomographic indices for detecting subclinical and mild keratectasia in a South Asian population. J Cataract Refract Surg. 2019;45(3):328–336. https://doi.org/10.1016/j.jcrs.2018.10.030
41. Kozobolis V, Sideroudi H, Giarmoukakis A, Gkika M, Labiris G. Corneal biomechanical properties and anterior segment parameters in forme fruste keratoconus. Eur J Ophthalmol. 2012;22(6):920–930. https://doi.org/10.5301/ejo.5000184
42. Vinciguerra R, Ambrósio R, Jr., Roberts CJ, Azzolini C, Vinciguerra P. Biomechanical characterization of subclinical keratoconus without topographic or tomographic abnormalities. J Refract Surg. 2017;33(6):399–407. https://doi.org/10.3928/1081597X-20170213-01
43. Ambrósio R, Lopes BT, Faria-Correia F, et al. Integration of scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg. 2017;33(7):434–443. https://doi.org/10.3928/1081597X-20170426-02
44. De Sanctis U, Loiacono C, Richiardi L, Turco D, Mutani B, Grignolo FM. Sensitivity and specificity of posterior corneal elevation measured by Pentacam in discriminating keratoconus/subclinical keratoconus. Ophthalmology. 2008;115(9): 1534–1539. https://doi.org/10.1016/j.ophtha.2008.02.020
45. Galletti JG, Pförtner T, Bonthoux FF. Improved keratoconus detection by ocular response analyzer testing after consideration of corneal thickness as a confounding factor. J Refract Surg. 2012;28(3):202–208. https://doi.org/10.3928/1081597X-20120103-03
46. Garcia-Porta N, Fernandes P, Queiros A, Salgado-Borges J, Parafita-Mato M, González-Méijome JM. Corneal biomechanical properties in different ocular conditions and new measurement techniques. ISRN Ophthalmol. 2014;2014:724546. https://doi.org/10.1155/2014/724546
47. Wu Y, Li XL, Yang SL, Yan XM, Li HL. [Examination and discriminant analysis of corneal biomechanics with CorVis ST in keratoconus and subclinical keratoconus]. Beijing Da Xue Xue Bao Yi Xue Ban. 2019;51(5):881–886.
48. Sedaghat MR, Momeni-Moghaddam H, Heravian J, Ansari A, Shayanfar H, Moshirfar M. Detection ability of corneal biomechanical parameters for early diagnosis of ectasia. Eye (Lond). 2023;37(8):1665–1672. https://doi.org/10.1038/s41433-022-02218-9