scientific reports

Check for updates

OPEN

Comparison of a Scheimpflug imaging with other screening indices in diagnosing keratoconus and keratoconus suspect

Yan Huo[1,4], Ruisi Xie[1,4], Xuan Chen[1], Shuangcheng Li[1], Haohan Zou[2,3], Yutong Liu[1] & Yan Wang[1,2,3]✉

Keratoconus (KC) is an irreversible blinding eye disease; therefore, early screening of KC suspects (KCS) is crucial for protecting patients' quality of life. Scheimpflug imaging is a commonly used screening device in clinical practice. We aimed to evaluate the diagnostic ability of a Scheimpflug imaging device (Scansys) for KC and KCS and compared it with other Scheimpflug-based devices (Pentacam and Corvis ST). This prospective case-control study included 107 normal eyes, 72 KCS, and 57 KC. Scansys screening index Keratoconus probability (KCP) showed excellent performance in diagnosing KC at a cutoff value of 16.4 (area under the receiver operating characteristic [AUROC] = 1.000), with 100% sensitivity and 98.11% specificity. KCP had a better KCS diagnostic ability at a cutoff value of 8.9 (AUROC = 0.813) than Corvis biomechanical index (CBI, AUROC = 0.764), reaching 67.61% sensitivity and 85.85% specificity. Pentacam screening index Belin/Ambrósio enhanced ectasia display deviation (BAD-D) showed the best performance with 92.96% sensitivity and 89.62% specificity at a cutoff value of 1.525 (AUROC = 0.970) in diagnosing KCS. Scansys provides accurate KCP parameters in diagnosing KC; however, the efficiency of diagnosing KCS should be further optimized.

Keywords Scheimpflug imaging, Keratoconus, Keratoconus suspect, Corneal tomography, Corneal biomechanics

Keratoconus (KC) is an irreversible blinding eye disease and routine preoperative screening disease of refractive surgery[1]. Accurately screening for KC suspect (KCS) before refractive surgery is important to reduce iatrogenic ectasia and intervene promptly to protect the patient's vision[2–4]. Corneal tomography is an indispensable ophthalmic technology for preoperative examinations in refractive surgery and the diagnosis of KC[5]. Compared to traditional topography technology, which focuses on curvature analysis of the corneal anterior surface, corneal tomography can provide information about the entire anterior segment, generating a three-dimensional display of the cornea to provide the height and thickness of the anterior and posterior corneal surfaces[6]. Calculating corneal biological and diagnostic parameters aids in KCS screening[7].

Scheimpflug-based devices are representative corneal tomography devices that can help clinicians screen for KCS early[8]. Pentacam (Oculus, Wetzlar, Germany) is the first Scheimpflug-based tomographic device, and its repeatability and reliability have been validated through extensive research[9,10]. Its proprietary diagnostic parameters, such as Belin/Ambrósio enhanced ectasia total derivation value (BAD-D), have shown good diagnosing ability for KCS[7,11]. Corvis ST (Oculus, Wetzlar, Germany) is a functional biomechanical device based on Scheimpflug imaging. Previous studies have reported that its proprietary machine learning parameter, the Corvis biomechanical index (CBI), can effectively diagnose KC[12], whereas its effectiveness decreases when diagnosing KCS[7]. The tomographic biomechanical index (TBI) generated by combining the Corvis ST and Pentacam was used to diagnose KCS[7,13]. Therefore, we referenced the diagnostic parameters of the Corvis ST and Pentacam for a comprehensive evaluation.

Scansys (MediWorks, Shanghai, China) is a Scheimpflug-based tomographic device, which has Food and Drug Administration and Conformitee Europeenne approval[14]. Scansys has good repeatability[15,16], and its system has a self-implanted diagnostic parameter called keratoconus probability (KCP), which are calculated

[1]School of Medicine, Nankai University, Tianjin, China. [2]Tianjin Key Lab of Ophthalmology and Visual Science, Tianjin Eye Institute, Tianjin Eye Hospital, Nankai University Affiliated Eye Hospital, Tianjin, China. [3]Nankai Eye Institute, Nankai University, No. 4, Gansu Road, Heping District, Tianjin 300020, China. [4]These authors contributed equally: Yan Huo and Ruisi Xie. ✉email: wangyan7143@vip.sina.com

by artificial intelligence algorithms combined with corneal topographic 4 Maps Refractive. To date, no studies have evaluated the ability of KCP to diagnose suspected or clinical KC. In addition, Scansys and Pentacam are both Scheimpflug photography devices, and the agreement between important ocular biological parameters in measuring suspected and clinical KC remains unclear. Although this study focuses on the evaluation and comparison of diagnostic parameter efficacy, we also preliminarily propose to assess the agreement of important ocular parameters. The agreement of ocular biological parameters helps diagnose and assess disease progression between different devices[17–19].

This study aimed to evaluate the ability of the corneal tomographic device (Scansys) to diagnose KC and KCS and compare it with the Pentacam and Corvis ST. Clarifying the sensitivity, specificity, and cutoff value of each diagnostic parameter could further guide clinical practice. Simultaneously, we evaluated the agreement of important ocular biological parameters between Scansys and Pentacam when measuring KC and KCS, providing a reference for clinicians to diagnose, monitor, and treat KC using different corneal tomographic devices.

Methods

This prospective case-control study followed the principles of the Declaration of Helsinki, informed participants of the study's purpose, obtained signed informed consent for data use, obtained approval from the Tianjin Eye Hospital Ethics Committee (KY2023026), and was registered at ClinicalTrials.gov (NCT06119321).

Participants and inclusion criteria

A total of 236 eyes from 200 patients at Tianjin Eye Hospital were included. All patients underwent a complete examination including objective refraction, manifest refraction, slit-lamp, non-contact intraocular pressure test, corneal tomography (Pentacam and Scansys), and corneal biomechanical (Corvis ST) examinations. All patients stopped wearing corneal contact lenses (soft corneal contact lenses within 2 weeks or rigid gas-permeable contact lenses within 4 weeks) before the evaluation.

For the KC group, corneas meeting the following criteria were included in the cohort: corrected distance visual acuity (CDVA) < 20/20, with at least one clinical sign of KC (corneal stromal thinning, cone-shaped anterior protrusions, Fleischer's ring, Vogt's striae, epithelial or subepithelial scarring), and an abnormal corneal tomography scan (inferior–superior asymmetry on the anterior corneal surface, central or paracentral steep)[1].

The KCS group included patients with bilateral suspect tomography or contralateral eye of unilateral KC[7,20]. In cases of bilateral suspect tomography, one eye was randomly selected[20]. For unilateral KC, the contralateral suspect cornea was included in the KCS, whereas clinical KC was included in the KC group[21]. The suspect criteria were as follows: no clinical evidence of disease, no KC slit-lamp signs, and a CDVA of 20/20 or better. All patients in this group had suspect corneal tomography (bow-tie pattern with skewed radial axes and/or inferior-superior asymmetry in corneal tomography or a posterior surface elevation at the thinnest point greater than 11 µm [using Pentacam AXL, best fit sphere 8-mm zone fitting])[7,22–24]. To evaluate the diagnostic performance of each parameter, we did not use diagnostic parameters for grouping (such as BAD-D, IS-value, and KISA%); and selected the central corneal thickness (CCT), the thinnest corneal thickness (TCT), the anterior corneal maximum keratometry (Kmax), and posterior elevation at the thinnest point (PTE) for agreement analysis[25–28].

In the normal controls (NL) groups, individuals had the CDVA ≥ 20/20, and both eyes showed normal clinical signs and tomography, with no abnormal findings suggestive of KC, as mentioned earlier. Moreover, no family history of KC was noted. The right eye was selected for analysis.

Devices and parameters

Scansys (model TA517, Shanghai MediWorks company, China) was based on 360° rotating Scheimpflug slit-image photography. This was a non-invasive anterior segment tomography using a 470 nm blue diode slit light. The device obtained 28 high-definition anterior segment cross-sectional images within 1 s, containing 107,520 data points ranging from 9 to 12 mm. Detailed tomography of the anterior and posterior corneal surfaces and ocular biological parameters were also calculated.

The Pentacam AXL (model 70100, version 1.25r.15, Oculus, Germany) principle was the same as that of Scansys. The Pentacam used a 475 nm light source to calculate a three-dimensional model of the cornea. It captured 25 images within 2 s, with each image consisting of 25,000 points. It generated detailed information on the anterior and posterior surfaces of the cornea and provided disease diagnostic parameters.

Corvis ST (model 72100, version 1.6b2507, Oculus, Germany) used an ultra-high-speed Scheimpflug camera to record corneal deformation using an air puff. The device automatically identified corneal deformation and captured 140 images within 31 ms, obtaining a corneal dynamic deformation video and dynamic response parameters to characterise the corneal biomechanics.

For the diagnostic parameters, the Scansys machine learning parameter KCP was selected for evaluation. KCP was a diagnostic parameter introduced using support vector machine algorithms and refractive topography from more than 2000 normal corneas and 500 KC samples. The parameter scale ranged from 0 to 100, and a higher KCP value suggested a greater likelihood of KC. Pentacam included the BAD-D, IS-value, KISA%, index of height asymmetry (IHA), keratoconus index (KI), index of surface variance (ISV), index of vertical asymmetry (IVA), index of height decentration (IHD), and central keratoconus index (CKI)[7,24,29]. Corvis ST selected diagnostic parameters with strong clinical applicability, TBI, CBI, stiffness parameter at first applanation (SP-A1), calculus of the radius of the reverse concavity (integrated radius), and corneal deformation ratio between the corneal apex and corneal apex within 2 mm (DA ratio 2 mm)[7,30–32]. TBI is the early ectasia diagnostic parameter introduced by artificial intelligence (random forest algorithm) using the biomechanical and tomographic parameters provided by Corvis ST and Pentacam. CBI is the KC diagnostic parameter introduced by the logistic regression algorithm using the biomechanical parameters provided by Corvis ST.

All examinations of the same patient were completed within 30 min, with each device undergoing at least two examinations in a consistent environment. The average value of multiple examinations with a quality of "OK" was analysed.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation for normal distribution and median (25%, 75%) for non-normal distribution. Categorical variables were expressed as frequencies and percentages. The Kolmogorov-Smirnov test was used to test the normality of the data. The Kruskal–Wallis test was used to compare the differences in diagnostic parameters among the three groups, the Bonferroni correction was used for post hoc corrections, and the statistical significance level was set at $P < 0.016$. The receiver operating characteristic (ROC) curve was used to analyse the diagnostic parameter performance that differentiated the three groups and to calculate the cutoff value, sensitivity, specificity, and area under the ROC curve (AUROC) of the parameters. An AUROC close to 1 indicated excellent performance. The Delong test was used to compare the AUROC of different parameters' performance. Paired t-tests, Pearson's r, and Bland–Altman plots were used to evaluate the agreement between devices, with 95% limits of agreement (LoA). Statistical significance was set at $P < 0.05$. The sample size was calculated by PASS (NCSS, LLC, Kaysville, UT) according to previous studies[19,24], considering an alpha error of 0.05 (two-sided) and statistical power of 80%. Each group included at least 50 eyes. All statistical analyses were performed using MedCalc Software (version 20.0.4, MedCalc Software, Ostend, Belgium) and SPSS 26.0 (IBM Corp., Armonk, NY, USA).

Results

The KCS group comprised 72 eyes (35 right eyes, 37 left eyes) with ages averaging 26.04 ± 8.31 (range, 16–51), including 28 males and 44 females. The KC group consisted of 57 eyes (25 right eyes, 32 left eyes) with ages averaging 23.61 ± 8.34 (range, 13–40), including 22 males (7 with unilateral KC) and 14 females (8 with unilateral KC). The NL group included 107 eyes (107 right eyes) with ages averaging 26.48 ± 5.70 (range, 18–41), including 54 males and 53 females.

Diagnosis parameters in three devices

Fifteen diagnostic parameters were included from the three devices, and Table 1 shows the differences in all diagnostic parameters between the groups. The Scansys diagnostic parameter KCP showed significant differences among the three groups ($P < 0.001$). All diagnostic parameters in Pentacam showed significant differences between NL and KC, and KCS and KC ($P < 0.001$), and 66.67% (6/9) of the parameters showed differences between NL and KCS ($P < 0.016$). All diagnostic parameters in Corvis ST showed significant differences among the three groups ($P < 0.016$).

Receiver operating characteristic analysis of diagnosis parameters

Tables 2, 3, and 4 show the diagnostic performances of the 15 diagnostic parameters for distinguishing each group. In distinguishing between NL and KC (Table 2), all diagnostic parameters had good diagnostic

Parameters	NL	KCS	KC	[a]*P*-value (NL vs. KCS)	[a]*P*-value (NL vs. KC)	[a]*P*-value (KCS vs. KC)
Scansys, median (25%, 75%)						
KCP	5.6 (3.6, 7.125)	12.5 (6.9, 26.6)	99 (98.3, 99)	< 0.001[a]	< 0.001[a]	< 0.001[a]
Pentacam, median (25%, 75%)						
BAD-D	0.96 (0.55, 1.28)	2.24 (1.83, 2.61)	8.31 (6.09, 11.54)	< 0.001[a]	< 0.001[a]	< 0.001[a]
IS-value	0.27 (-0.21, 0.57)	0.59 (0.05, 1.33)	3.96 (2.5, 6.82)	0.007[a]	< 0.001[a]	< 0.001[a]
KISA	4.42 (1.60, 7.90)	6.16 (3.09, 11.5)	759.59 (141.47, 2953.15)	0.168	< 0.001[a]	< 0.001[a]
ISV	17 (14, 20)	24 (18, 29)	90 (54, 117)	< 0.001[a]	< 0.001[a]	< 0.001[a]
IVA	0.11 (0.08, 0.15)	0.16 (0.12, 0.22)	0.9 (0.55, 1.16)	< 0.001[a]	< 0.001[a]	< 0.001[a]
KI	1.03 (1.03, 1.04)	1.05 (1.03, 1.07)	1.19 (1.13, 1.27)	< 0.001[a]	< 0.001[a]	< 0.001[a]
CKI	1.01 (1.00, 1.01)	1.01 (1.01, 1.01)	1.06 (1.03, 1.12)	0.027	< 0.001[a]	< 0.001[a]
IHA	5.4 (2.1, 7.6)	6.5 (3.2, 13.8)	23.5 (12.5, 41.8)	0.053	< 0.001[a]	< 0.001[a]
IHD	0.009 (0.007, 0.014)	0.016 (0.009, 0.023)	0.129 (0.074, 0.169)	0.001[a]	< 0.001[a]	< 0.001[a]
Corvis ST, median (25%, 75%)						
CBI	0.001 (0, 0.014)	0.04 (0.003, 0.191)	1 (0.993, 1)	< 0.001[a]	< 0.001[a]	< 0.001[a]
TBI	0.04 (0.008, 0.256)	0.497 (0.298, 1)	1 (1, 1)	< 0.001[a]	< 0.001[a]	< 0.001[a]
SPA1	108.28 (98.12, 119.14)	101.68 (88.31, 111.85)	65.002 (53.383, 79.923)	0.015[a]	< 0.001[a]	< 0.001[a]
DA ratio (2 mm)	4.27 (4.03, 4.55)	4.52 (4.27, 4.81)	5.66 (5.05, 6.33)	0.007[a]	< 0.001[a]	< 0.001[a]
Integrated radius	8.05 (7.38, 8.69)	8.54 (7.84, 9.27)	10.96 (10.11, 12.81)	0.014[a]	< 0.001[a]	< 0.001[a]

Table 1. Comparison of the parameters between each group. Data are shown as median (25%, 75%). *NL* normal controls, *KCS* keratoconus suspects, *KC* keratoconus. [a]P-values for comparison of the NL, KCS, and KC groups with post hoc corrections ($P < 0.016$ indicates a statistically significant difference after Bonferroni correction).

	AUROC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)
Scansys					
KCP	1.000	0.976–1.000	> 16.4	100	98.11
Pentacam					
BAD-D	1.000	0.977–1.000	> 3.12	100	100
IS-value	0.986	0.962–1.000	> 1.455	96.08	100
KISA	0.992	0.980–1.000	> 44.11	94.12	99.06
ISV	1.000	0.977–1.000	> 35.5	100	100
IVA	1.000	0.977–1.000	> 0.255	100	100
KI	1.000	0.977–1.000	> 1.075	100	99.06
CKI	0.974	0.947–1.000	> 1.025	90.2	100
IHA	0.912	0.855–0.969	> 11.5	82.35	90.57
IHD	1.000	0.977–1.000	> 0.027	100	100
Corvis ST					
CBI	0.998	0.971–1.000	> 0.566	98.04	99.06
TBI	1.000	0.977–1.000	> 0.938	100	100
SPA1	0.945	0.907–0.983	≤ 86.953	88.24	94.34
DA ratio (2 mm)	0.926	0.873–0.979	> 4.755	86.27	90.57
Integrated radius	0.964	0.934–0.994	> 9.546	84.31	96.23

Table 2. Receiver operating characteristic analysis for each parameter in differentiating NL from KC. *NL* normal controls, *KC* keratoconus, *AUROC* area under the receiver operating characteristic curve, *CI* confidence interval.

	AUROC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)
Scansys					
KCP	0.813	0.745–0.881	> 8.9	67.61	85.85
Pentacam					
BAD-D	0.970	0.950–0.990	> 1.525	92.96	89.62
IS-value	0.669	0.582–0.755	> 0.665	47.89	84.91
KISA	0.604	0.518–0.690	> 6.21	49.30	71.70
ISV	0.756	0.681–0.830	> 21.5	54.93	87.74
IVA	0.756	0.681–0.831	> 0.195	42.25	96.23
KI	0.724	0.641–0.806	> 1.045	56.34	83.96
CKI	0.633	0.548–0.717	> 1.015	22.54	95.28
IHA	0.611	0.522–0.699	> 8.45	43.66	81.13
IHD	0.716	0.635–0.797	> 0.0155	52.11	85.85
Corvis ST					
CBI	0.764	0.693–0.834	> 0.0055	71.83	66.98
TBI	0.892	0.846–0.938	> 0.234	92.96	74.53
SPA1	0.652	0.568–0.736	≤ 95.77	46.48	83.96
DA ratio (2 mm)	0.659	0.576–0.743	> 4.4042	64.79	63.21
Integrated radius	0.651	0.567–0.735	> 8.893	40.85	87.74

Table 3. Receiver operating characteristic analysis for each parameter in differentiating NL from KCS. *NL* normal controls, *KCS* keratoconus suspect, *AUROC* area under the receiver operating characteristic curve, *CI* confidence interval.

ability (AUROC > 0.900), and KCP (AUROC = 1.000) had a sensitivity and specificity of 100% and 98.11%, respectively, for diagnosing KC at a cutoff value of 16.4. In distinguishing between NL and KCS (Table 3), the top three diagnostic parameters were BAD-D (Pentacam, AUROC = 0.970), TBI (Corvis ST and Pentacam, AUROC = 0.892), and KCP (Scansys, AUROC = 0.813). KCP had the best diagnostic performance at a cutoff value of 8.9, with a sensitivity and specificity of 67.61% and 85.85%, respectively. To distinguish between the KCS and KC groups (Table 4), the best diagnostic parameters for the three devices were BAD-D (Pentacam, 0.999), CBI (Corvis ST, AUROC = 0.984) and KCP (Scansys, AUROC = 0.983).

	AUROC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)
Scansys					
KCP	0.983	0.940–0.998	> 69.25	96.08	95.77
Pentacam					
BAD-D	0.999	0.969–1.000	> 4.195	98.04	100
IS-value	0.967	0.918–0.991	> 1.935	92.16	95.77
KISA	0.981	0.938–0.997	> 42.642	94.12	94.37
ISV	0.995	0.961–1.000	> 37	100	95.77
IVA	0.994	0.960–1.000	> 0.315	96.08	95.77
KI	0.986	0.946–0.999	> 1.095	94.12	94.37
CKI	0.955	0.902–0.984	> 1.025	90.20	97.18
IHA	0.823	0.748–0.899	> 11.55	82.35	71.83
IHD	0.996	0.962–1.000	> 0.0425	96.08	98.59
Corvis ST					
CBI	0.984	0.942–0.998	> 0.69	98.04	92.96
TBI	0.861	0.794–0.927	> 0.999	94.12	74.65
SPA1	0.903	0.846–0.959	≤ 82.846	86.27	85.92
DA ratio (2 mm)	0.868	0.798–0.939	> 5.039	76.47	88.73
Integrated radius	0.906	0.852–0.959	> 10.074	80.39	88.73

Table 4. Receiver operating characteristic analysis for each parameter in differentiating KCS from KC. *KCS* keratoconus suspect, *KC* keratoconus, *AUROC* area under the receiver operating characteristic curve, *CI* confidence interval.

Groups	Parameters (AUROC)	KCP	CBI	TBI	BAD-D
NL vs. KCS	KCP (0.813)	–	0.3237	0.0403[a]	< 0.0001[a]
	CBI (0.764)	–	–	0.0003[a]	< 0.0001[a]
	TBI (0.892)	–	–	–	< 0.0001[a]
	BAD-D (0.970)	–	–	–	–
NL vs. KC	KCP (1.000)	–	0.3493	0.4135	0.4135
	CBI (0.998)	–	–	0.2385	0.2385
	TBI (1.000)	–	–	–	1.0000
	BAD-D (1.000)	–	–	–	–
KCS vs. KC	KCP (0.983)	–	0.9269	< 0.0001[a]	0.0798
	CBI (0.984)	–	–	< 0.0001[a]	0.0654
	TBI (0.861)	–	–	–	< 0.0001[a]
	BAD-D (0.999)	–	–	–	–

Table 5. Comparison between the AUROC of parameters for differentiating NL, KCS, and KC. *NL* normal controls, *KCS* keratoconus suspects, *KC* keratoconus, *AUROC* area under the receiver operating characteristic curve. [a]P-values using the Delong test ($P < 0.05$ indicates a statistically significant difference).

Diagnostic performance comparison

We further compared the diagnostic ability of the BAD-D, CBI, TBI, and KCP among the three groups (Fig. 1; Table 5). All parameters performed well in diagnosing KC (AUROC > 0.900, $P > 0.05$). For the diagnosis of KCS, the diagnostic ability of BAD-D (AUROC = 0.970) was significantly better than that of the other parameters ($P < 0.0001$), followed by TBI (AUROC = 0.892), which was better than KCP (AUROC = 0.813) and CBI (AUROC = 0.764). No difference was observed in the diagnostic ability of KCP and CBI in diagnosing KCS ($P = 0.3237$). In distinguishing between KC and KCS, BAD-D (AUROC = 0.999), CBI (AUROC = 0.984) and KCP (AUROC = 0.983) exhibited good diagnostic ability and were superior to TBI (AUROC = 0.861, $P < 0.05$).

Agreement between Scansys and Pentacam

Table 6 shows the differences and agreement of the ocular biological parameters measured by Scansys and Pentacam among the three groups. The CCT, TCT, and Kmax of the two devices had a high correlation among the three groups ($r > 0.900$), whereas the PTE had a weak correlation among the NL ($r = 0.615$), KCS ($r = 0.742$), and KC ($r = 0.874$) groups. No significant differences were observed in Kmax ($P = 0.125$) and PTE ($P = 0.595$) in the NL group, PTE ($P = 0.658$) in the KCS group, or CCT ($P = 0.335$) and Kmax ($P = 0.908$) between the two

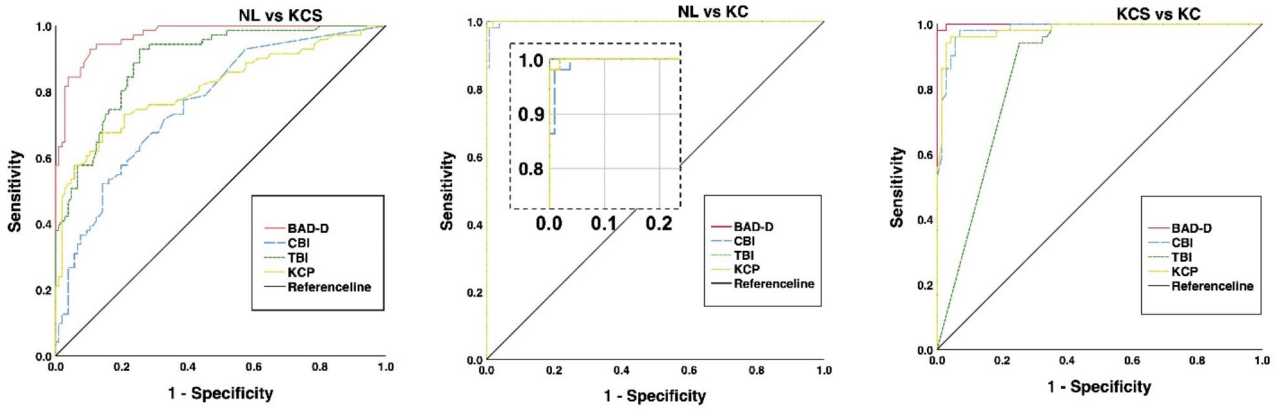

Fig. 1. Comparison of best distinguishing parameters in each group. *NL* normal controls, *KCS* keratoconus suspects, *KC* keratoconus, *BAD-D* Belin–Ambrósio enhanced ectasia total derivation value, *TBI* tomographic biomechanical index, *CBI* Corvis biomechanical index.

Group	Parameters	Mean ± SD		P-value[a]	r	95% LoA
		Scansys	Pentacam			
NL	CCT	547.73 ± 29.94	552.20 ± 29.19	< 0.001[a]	0.915[b]	− 19.43 to 28.36
	TCT	542.39 ± 29.01	549.29 ± 29.17	< 0.001[a]	0.920[b]	− 15.91 to 29.70
	Kmax	44.29 ± 1.56	44.19 ± 1.55	0.125	0.915[b]	− 1.35 to 1.16
	PTE	4.85 ± 4.34	4.67 ± 2.49	0.595	0.615[b]	− 6.89 to 6.53
KCS	CCT	527.38 ± 30.41	533.44 ± 31.95	< 0.001[a]	0.971[b]	− 8.99 to 21.10
	TCT	520.31 ± 30.92	527.82 ± 32.09	< 0.001[a]	0.972[b]	− 7.28 to 22.29
	Kmax	45.82 ± 2.08	45.61 ± 2.16	0.007[a]	0.958[b]	− 1.413 to 1.01
	PTE	12.155 ± 5.98	12.37 ± 4.24	0.658	0.742[b]	− 7.65 to 8.07
KC	CCT	464.61 ± 47.86	462.55 ± 44.09	0.335	0.949[b]	− 31.67 to 27.56
	TCT	450.94 ± 47.178	455.04 ± 42.59	0.042[a]	0.956[b]	− 23.42 to 31.62
	Kmax	58.81 ± 11.75	58.86 ± 10.32	0.908	0.983[b]	− 4.83 to 4.91
	PTE	62.30 ± 36.98	51.63 ± 24.56	< 0.001[a]	0.874[b]	− 48.99 to 27.65

Table 6. Agreement of parameters measured using the scansys and pentacam. Data are shown as mean ± SD. *NL* normal controls, *KCS* keratoconus suspects, *KC* keratoconus, *CCT* central corneal thickness, *TCT* thinnest corneal thickness, *Kmax* maximum keratometry, *PTE* posterior elevation at the thinnest point, *LoA* limits of agreement, *SD* standard deviation. The [a]P-values are for the comparison of the Scansys and Pentacam parameters (paired t-test, $^{a}P < 0.05$ indicates a statistically significant difference); r, Pearson's correlation coefficient; $^{b}P < 0.05$ indicates a statistically significant correlation.

devices in the KC group. Figure 2 shows that the 95% LoAs of all ocular biological parameters were wide in the KCS and KC groups.

Discussion

To the best of our knowledge, this study is the first to evaluate the performance of the Scheimpflug imaging (Scansys) in distinguishing KC and KCS and compare it with the clinically applicable Scheimpflug devices (Pentacam and Corvis ST). The diagnostic parameter KCP of Scansys had excellent diagnostic performance in distinguishing KC (AUROC = 1.000), with sensitivity and specificity reaching 100% and 98.11%, respectively, at a cutoff value of 16.4. KCP (AUROC = 0.813) had a lower diagnostic performance than the Pentacam diagnostic parameter BAD-D (AUROC = 0.970) in diagnosing KCS, with a sensitivity and specificity of 67.61% and 85.85%, respectively, at the cutoff value of 8.9. The price of Scansys is 50–70% of Pentacam, and its low price may have certain benefits for KC diagnosis and primary health care services in low- and middle-income countries. However, the performance of Scansys (at least currently) is not a useful screening tool in KCS.

Our study identified differences in 15 diagnostic parameters among the three groups: normal cornea, KCS, and KC (Table 1). A significant difference ($P < 0.001$) was observed in all diagnostic parameters between normal corneas and KCS compared to KC, as clinical KC exhibits significant tomographic changes compared to KCS and normal corneas[1], and its biomechanical properties are significantly weakened[33]. However, no significant difference was observed in the Pentacam diagnostic parameters KISA%, CKI, and IHA between normal corneas

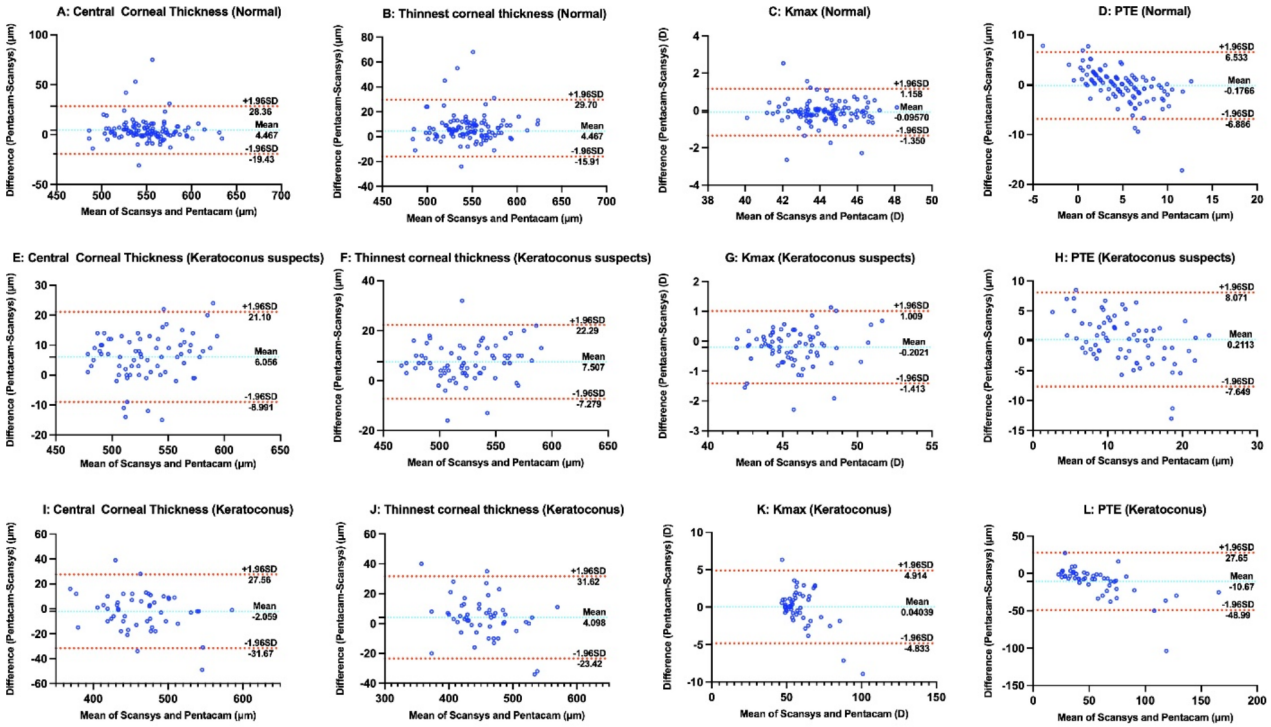

Fig. 2. Bland–Altman plots with LoAs for the different biometric parameters measured with the Scansys and Pentacam. *Kmax* anterior corneal maximum keratometry, *PTE* posterior elevation at the thinnest point.

and KCS ($P > 0.016$). Our results are consistent with those of Shetty et al[24]. and Steinberg et al[34]., which may be due to slight changes in the KCS corneal tomography. Nevertheless, the differences in the parameters between the groups suggest that the diagnostic parameters can be used to assess and screen for diseases. Therefore, we calculated the diagnostic performance of all the diagnostic parameters among the three devices.

When diagnosing frank KC (Table 2), all diagnostic parameters showed good diagnostic performance (AUROC > 0.900), indicating that each device could diagnose KC independently. Previous studies have shown that other clinical Scheimpflug devices' diagnostic parameters, such as Keratoconus Prediction Index (Galilei, AUROC = 0.993) and 4.5 mm RMS/A back (Sirius, AUROC = 0.983) can also effectively diagnose KC[7,35,36]. This indicates that the Scheimpflug-based devices currently used in clinical practice all have high accuracy in diagnosing KC, further clarifying the importance of Scheimpflug devices in screening clinical KC.

This study further evaluated the ability of each diagnostic parameter to screen for KCS (Table 3) and found that the performance of all the parameters decreased to some extent. The parameter with the best diagnostic performance was BAD-D (AUROC = 0.970), at a cutoff value of 1.525, with sensitivity and specificity of 92.96% and 89.62%, respectively. The performance of the BAD-D in diagnosing KCS has been evaluated in many studies[8]. TBI ranks second in diagnostic performance (AUROC = 0.892) and is fitted using CBI and BAD-D[13]. In diagnosing KCS, the performance of the CBI was poor (AUROC = 0.764). CBI is a machine learning parameter trained from KC and normal corneal data[12]; therefore, the performance of CBI decreases in diagnosing KCS, leading to a lower diagnostic performance for TBI than for BAD-D. The performance of KCP in diagnosing KCS is second only to BAD-D and TBI, with the best diagnostic performance at a cutoff value of 8.9 (AUROC = 0.813), with sensitivity and specificity of 67.61% and 85.85%, respectively. The KCP was fitted from a database of more than 2000 normal corneas and more than 500 frank KC, making it more suitable for diagnosing KC, which explains the decreased performance of the KCP in diagnosing KCS. The performance of the remaining parameters in diagnosing KCS is low (AUROC < 0.800), which is consistent with our previous research[31,37].

According to a recent report by the American Academy of Ophthalmology, KCS Scheimpflug-based diagnostic parameters detection performance(AUROC) ranged from 0.66 to 0.99[7]. Shetty et al. found Pentacam's BAD-D (AUROC = 0.887) was a strong parameter to distinguish KCS from normal eyes[24]. Asroui et al. reported that Corvis ST's TBI had the best ability (AUROC = 0.946) in distinguishing normal controls from early ectasia[30]. In consensus with previous studies, the two parameters with the best diagnostic efficacy for KCS in our study are BAD-D (AUROC = 0.970) and TBI (AUROC = 0.892). However, our study additionally compared the new Scheimpflug-based Scansys with other commonly used clinical diagnostic indices. By contributing empirical evidence on the diagnostic performance of Scansys, this study catalyzes advancements in corneal imaging technologies and provides a reference for researchers using Scansys in the future.

Compared to previous studies[7], we calculated the cutoff values of each parameter to distinguish KCS from KC, which provides a reference for clinicians in assessing the severity of the disease. Interestingly, the

diagnostic performance of the comprehensive diagnostic parameter, TBI (AUROC = 0.861), was weaker than that of BAD-D (AUROC = 0.999) and CBI (AUROC = 0.984). Therefore, we drew a dotted plot to explain this phenomenon (Fig. 3). As TBI was originally designed to detect early KC, it has evaluated and calculated most KCS as a disease state, which resulted in an overlap between most patients when distinguishing KCS from frank KC; thus, affecting the diagnostic performance of TBI.

After clarifying the performance of each diagnostic parameter, we compared the performance of four sensitive diagnostic parameters, BAD-D, TBI, CBI, and KCP, using the Delong test (Table 5). The four parameters performed well in diagnosing KC and did not exhibit significant differences ($P > 0.05$). When diagnosing KCS, BAD-D showed the best diagnostic performance ($P < 0.0001$), and TBI had certain diagnostic advantages over CBI and KCP ($P < 0.05$). No difference was observed in diagnostic performance between the CBI and KCP ($P = 0.3237$). This may be because the databases of the CBI and KCP training parameters do not include KCS, and the diagnostic performance of the parameters is highly correlated with the clinical environment. This emphasises that machine learning parameters should be used for applicable populations, and the cutoff values should be adjusted based on actual clinical environments to assist clinicians in diagnosing diseases more accurately. Scansys currently has only one self-diagnostic parameter, KCP, and its ability to diagnose KCS and its parameters remains to be developed.

Previous studies have shown that Scansys and Pentacam have good repeatability[9,15,16]; however, they have not evaluated the agreement of Scansys and Pentacam parameters in disease states, especially in diagnosing and screening KC. Therefore, we analysed the agreement between Pentacam and Scansys in measuring important ocular biological parameters of KC and KCS (Table 6)[25–27]. Regarding corneal thickness, a significant difference was observed in CCT between the NL and KCS groups ($P < 0.001$), and statistical differences were observed in the TCT among the three groups ($P < 0.05$). The mean thickness measured using Scansys was lower than that measured using Pentacam, although a strong correlation was observed between the two devices ($r > 0.9$). However, Scansys may underestimate the patient's thickness, suggesting that the same device should be used to

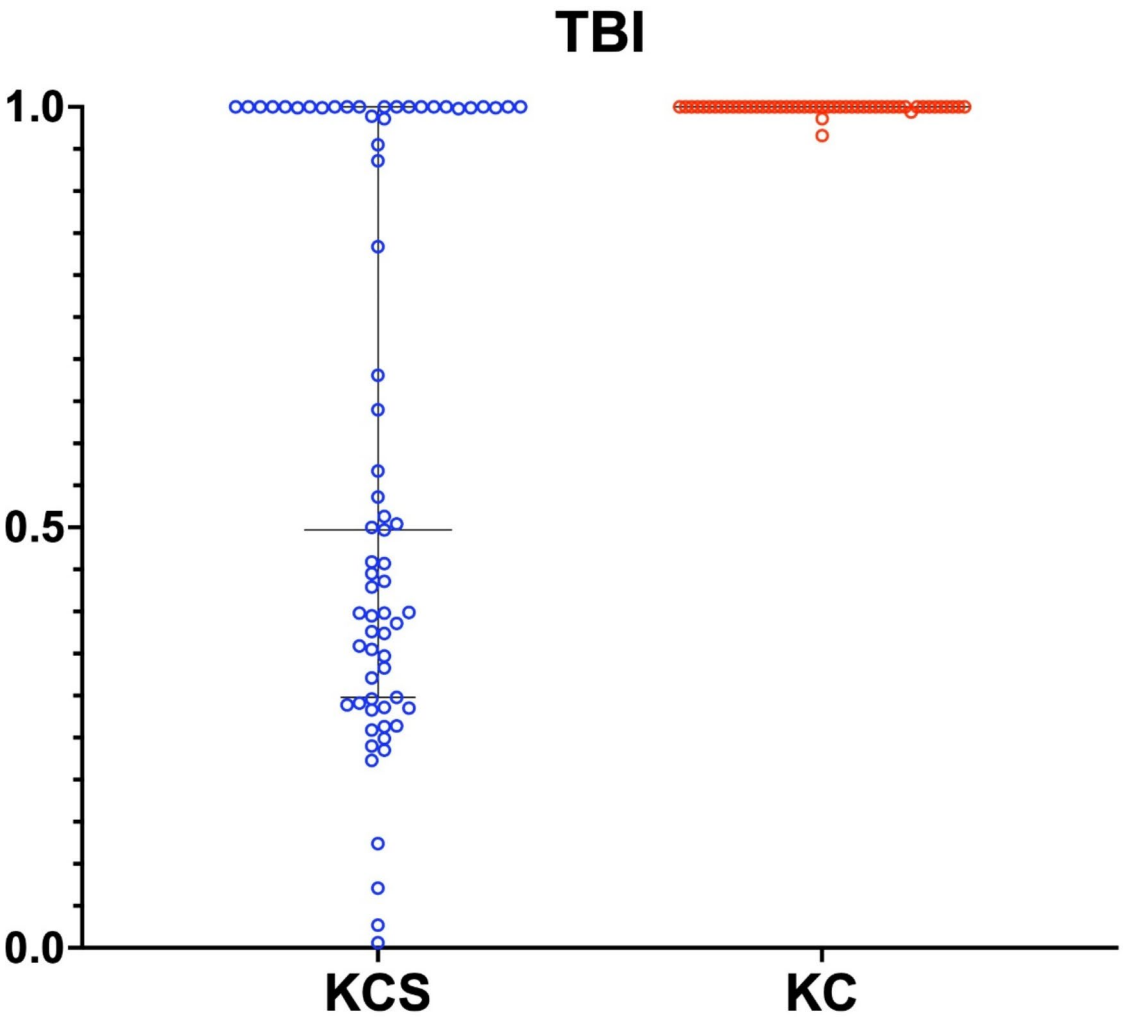

Fig. 3. The distribution of TBI in KCS and KC groups. *KCS* keratoconus suspects, *KC* keratoconus; error bar as median (25%, 75%).

accurately assess changes in the patient's thickness when evaluating corneal thickness. Elevation of the posterior corneal surface is a sensitive indicator for diagnosing KCS[23]. No significant difference was observed between the PTE of the two devices in NL and KCS; however, the 95% LoA was wide and increased with the severity of NL, KCS, and KC, indicating that the agreement between the two devices decreased as the disease progressed. As the severity of KC increases, the repeatability and reliability of the device itself decrease[38,39], necessitating caution when exchanging ocular biological parameters under disease conditions. Therefore, we believe that in the KC and KCS populations, the ocular biological parameters of the two devices cannot be replaced with each other, and the same device should be used for follow-up of the same patient.

Our study had some limitations. Different grades of KC can affect the reliability and repeatability of device measurements and agreement between devices[32]. As the focus of this study was to evaluate the diagnostic performance of Scansys, we only conducted a preliminary study on the agreement of important biological parameters between the devices. In the future, we will refine the clinical severity of KC and evaluate the repeatability and agreement of more parameters, as well as the diagnostic performance of different parameters.

In conclusion, our study found that the Scheimpflug imaging Scansys can effectively screen for KC using the Scansys diagnostic parameter KCP, with sensitivity and specificity of 100% and 98.11%, respectively, for diagnosing KC. Currently, Scansys diagnostic parameter KCP does not perform adequately in diagnosing KCS. Therefore, further optimisation of the performance of KCP for diagnosing KCS is needed. The 95% LoAs of Scansys and Pentacam measurements of ocular biological parameters in suspected and clinical KC were wide. To achieve an accurate diagnosis and assess the progression of KC, the ocular biological parameters of Scansys and Pentacam cannot be used interchangeably. In clinical practice, the same device should be used for follow-up and assessment of the same patient.

Data availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Received: 27 June 2024; Accepted: 26 September 2024
Published online: 05 October 2024

References

1. Santodomingo-Rubido, J. et al. Keratoconus: an updated review. *Cont. Lens Anterior Eye*. **45**, 101559. https://doi.org/10.1016/j.clae.2021.101559 (2022).
2. McMonnies, C. W. Screening for keratoconus suspects among candidates for refractive surgery. *Clin. Exp. Optom.***97**, 492–498 (2014).
3. Moshirfar, M. et al. Ectasia after corneal refractive surgery: a systematic review. *Ophthalmol. Ther.***10**, 753–776 (2021).
4. Randleman, J. B., Woodward, M., Lynn, M. J. & Stulting, R. D. Risk assessment for ectasia after corneal refractive surgery. *Ophthalmology*. **115**, 37–50 (2008).
5. Kong, A. W. et al. Trends in corneal topography and tomography imaging for keratoconus management. *Clin. Ophthalmol.***16**, 1357–1363 (2022).
6. de Sanctis, U., Missolungi, A., Mutani, B., Richiardi, L. & Grignolo, F. M. Reproducibility and repeatability of central corneal thickness measurement in keratoconus using the rotating Scheimpflug camera and ultrasound pachymetry. *Am. J. Ophthalmol.***144**, 712–718 (2007).
7. Kuo, A. N. et al. Advanced corneal imaging in keratoconus: a report by the American Academy of Ophthalmology. *Ophthalmology*. **131**, 107–121 (2024).
8. de Sanctis, U. et al. Sensitivity and specificity of posterior corneal elevation measured by Pentacam in discriminating keratoconus/subclinical keratoconus. *Ophthalmology*. **115**, 1534–1539 (2008).
9. McAlinden, C., Khadka, J. & Pesudovs, K. A comprehensive evaluation of the precision (repeatability and reproducibility) of the oculus Pentacam HR. *Invest. Ophthalmol. Vis. Sci.***52**, 7731–7737 (2011).
10. Zhao, Y. et al. The precision and agreement of corneal thickness and keratometry measurements with SS-OCT versus Scheimpflug imaging. *Eye Vis. (Lond)*. **7**, 32 (2020).
11. Ruiseñor Vázquez, P. R. et al. Pentacam Scheimpflug tomography findings in topographically normal patients and subclinical keratoconus cases. *Am. J. Ophthalmol.***158**, 32–40e2 (2014).
12. Vinciguerra, R. et al. Detection of keratoconus with a new biomechanical index. *J. Refract. Surg.***32**, 803–810 (2016).
13. Ambrósio, R. et al. Integration of Scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. *J. Refract. Surg.***33**, 434–443 (2017).
14. Kanclerz, P., Przewłócka, K., Toprak, I. & Alio, J. The prevalence of keratoconus in northern Poland: a cross-sectional study of patients from a primary healthcare practice. *Cont. Lens Anterior Eye*. **46**, 101846. https://doi.org/10.1016/j.clae.2023.101846 (2023).
15. Yu, A. Y. et al. Reliability and agreement of the central and mid-peripheral corneal thickness measured by a new Scheimpflug based imaging. *Ann. Transl Med.***9**, 1136. https://doi.org/10.21037/atm-20-7895 (2021).
16. Xu, W. et al. Repeatability and agreement between a reference Scheimpflug tomographer and a low-cost Scheimpflug system. *J. Cataract Refract. Surg.***49**, 614–619 (2023).
17. Seiler, T. G., Mueller, M. & Mendes Baiao, T. Repeatability and comparison of corneal tomography in mild to severe keratoconus between the anterior segment OCT MS-39 and Pentacam HR. *J. Refract. Surg.***38**, 250–255 (2022).
18. Gustafsson, I., Bergström, A., Myers, A. C., Ivarsen, A. & Hjortdal, J. Association between Keratoconus disease severity and repeatability in measurements of parameters for the assessment of progressive disease. *PLOS ONE*. **15**, e0228992. https://doi.org/10.1371/journal.pone.0228992 (2020).
19. Meyer, J. J., Gokul, A., Vellara, H. R., Prime, Z. & McGhee, C. N. J. Repeatability and agreement of Orbscan II, Pentacam HR, and Galilei tomography systems in corneas with keratoconus. *Am. J. Ophthalmol.***175**, 122–128 (2017).
20. Randleman, J. B. et al. Subclinical keratoconus detection and characterization using motion-tracking Brillouin microscopy. *Ophthalmology*. **131**, 310–321 (2024).
21. McAlinden, C., Khadka, J. & Pesudovs, K. Statistical methods for conducting agreement (comparison of clinical tests) and precision (repeatability or reproducibility) studies in optometry and ophthalmology. *Ophthalmic Physiol. Opt.***31**, 330–338 (2011).
22. Henriquez, M. A., Hadid, M. & Izquierdo, L. Jr. A systematic review of subclinical keratoconus and forme fruste keratoconus. *J. Refract. Surg.***36**, 270–279 (2020).
23. Gomes, J. A. P. et al. Global consensus on keratoconus and ectatic diseases. *Cornea*. **34**, 359–369 (2015).

24. Shetty, R. et al. Keratoconus screening indices and their diagnostic ability to distinguish normal from ectatic corneas. *Am. J. Ophthalmol.***181**, 140–148 (2017).
25. Ferdi, A. et al. Predictors of progression in untreated keratoconus: a Save Sight Keratoconus Registry study. *Br. J. Ophthalmol.***106**, 1206–1211 (2022).
26. Shajari, M. et al. Evaluation of keratoconus progression. *Br. J. Ophthalmol.***103**, 551–557 (2019).
27. Meyer, J. J., Gokul, A., Vellara, H. R. & McGhee, C. N. J. Progression of Keratoconus in children and adolescents. *Br. J. Ophthalmol.***107**, 176–180 (2023).
28. Chan, E. et al. Prevalence of keratoconus based on Scheimpflug imaging: the Raine study. *Ophthalmology*. **128**, 515–521 (2021).
29. Neuhann, S. et al. Comparison of variables measured with a Scheimpflug device for evaluation of progression and detection of keratoconus. *Sci. Rep.* **10**. https://doi.org/10.1038/s41598-020-76020-6 (2020).
30. Asroui, L. et al. Biomechanical evaluation of topographically and tomographically normal fellow eyes of patients with keratoconus. *J. Refract. Surg.***38**, 318–325 (2022).
31. Huo, Y. et al. Biomechanical properties analysis of forme fruste keratoconus and subclinical keratoconus. *Graefes Arch. Clin. Exp. Ophthalmol.***261**, 1311–1320 (2023).
32. Song, P., Ren, S., Liu, Y., Li, P. & Zeng, Q. Detection of subclinical keratoconus using a novel combined tomographic and biomechanical model based on an automated decision tree. *Sci. Rep.***12**, 5316. https://doi.org/10.1038/s41598-022-09160-6 (2022).
33. Padmanabhan, P. & Elsheikh, A. Keratoconus: a biomechanical perspective. *Curr. Eye Res.***48**, 121–129 (2023).
34. Steinberg, J. et al. Screening for keratoconus with new dynamic biomechanical in vivo scheimpflug analyses. *Cornea*. **34–1012**, 1404–1412 (2015).
35. Salman, A., Darwish, T., Ali, A., Ghabra, M. & Rafea, S. Sensitivity and specificity of Sirius indices in diagnosis of keratoconus and suspect keratoconus. *Eur. J. Ophthalmol.* 790–797 (2021).
36. Shetty, R. et al. Repeatability and agreement of three Scheimpflug-based imaging systems for measuring anterior segment parameters in keratoconus. *Invest. Ophthalmol. Vis. Sci.***55**, 5263–5268 (2014).
37. Chen, X. et al. Screening of sensitive in vivo characteristics for early keratoconus diagnosis: a multicenter study. *Front. Bioeng. Biotechnol.***11**, 1158299. https://doi.org/10.3389/fbioe.2023.1158299 (2023).
38. de Luis Eguileor, B., Argaluza, E., Pijoán, J., Zubizarreta, J. I. & Carro, S. Etxebarria Ecenarro, J. evaluation of the reliability and repeatability of Scheimpflug system measurement in keratoconus. *Cornea*. **37**, 177–181 (2018).
39. Kreps, E. O. et al. Repeatability of the Pentacam HR in various grades of keratoconus. *Am. J. Ophthalmol.***219**, 154–162 (2020).

Acknowledgements

This study was supported by The National Program on Key Research Project of China (2022YFC2404502), the National Natural Science Foundation of China (82271118), the Tianjin Diversified Investment Fund for Applied Basic Research (21JCZDJC01190), the Tianjin Health and Technology Project (TJWJ2022XK036), and the Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-016 A), and the Tianjin Natural Science Foundation (21JCQNJC01000).

Author contributions

Y.H., R.X., and Y.W. contributed to the conception and design of the study. Y.H., X.C., S.L., H.Z., and Y.L. organized the database. Y.H., and R.X. performed the analysis and interpretation of data. Y.H. wrote the first draft. Y.H., R.X., and X.C. commented on previous versions of the manuscript. Y.W. provided administrative, technical, or material support, as well as supervision. All authors contributed to the article and approved the submitted and revised version.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to Y.W.