REVIEW

Scheimpflug-Derived Keratometric, Pachymetric and Pachymetric Progression Indices in the Diagnosis of Keratoconus: A Systematic Review and Meta-Analysis

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Abstract: Scheimpflug Pentacam Tomography is becoming crucial in the diagnosis and monitoring of keratoconus, as well as in preand post-corneal refractive care, but there are still some inconsistencies surrounding its evidence base diagnostic outcome. Therefore, this study aimed at employing meta-analysis to systematically evaluate the keratometric, pachymetric, and pachymetric progression indices used in the diagnosis of Keratoconus. The review protocol was registered with PROSPERO (Identifier: CRD4202310058) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. PubMed, MEDLINE, Web of Science, and EMBASE were used for data search, followed by a quality appraisal of the included studies using the revised tool for the quality assessment of diagnostic accuracy studies (QUADAS-2). Meta-analysis was conducted using the meta (6.5.0) and metafor (4.2.0) packages in R version 4.3.0, as well as Stata. A total of 32 studies were included in the analysis. All keratometry (K) readings (flattest meridian, K1; steepest meridian, K2, maximum, Kmax) were significantly steeper in keratoconic compared to normal eyes: [MD (95% CI)], K1 [2.67 (1.81; 3.52)], K1-back [-0.71 (-1.03; -0.39)], K1-front [4.06 (2.48; 5.63)], K2 [4.32 (2.89; 5.75)], K2-back [-1.25 (-1.68; -0.82)], K2-front [4.82 (1.88; 7.76)], Kmax [7.57 (4.80; 10.34)], and Kmean [2.80 (1.13; 4.47)]. Additionally, corneal thickness at the center, CCT [-61.19, (-73.79; -48.60)] and apex, pachy-apex [-41.86, (-72.64; -11.08)] were significantly thinner in keratoconic eyes compared to normal eyes. The pooled estimates for pachymetric progression index (PPI): PPImin [0.66 (0.43; 0.90)], PPImax [1.26 (0.87; 1.64)], PPIavg [0.90 (0.68; 1.12)], and Ambrosio relational thickness (ART): ARTmax [-242.77 (-288.86; -196.69)], and ARTavg [-251.08 (-308.76; -195.39)] revealed significantly more rapid pachymetric progression in keratoconic eves than in normal eyes. The Pentacam Scheimpflug-derived keratometric, pachymetric, and pachymetric progression indices are good predictors in discriminating KC from normal eyes.

Keywords: corneal topography, keratometric readings, central corneal thickness, keratoconus, pachymetric progression

Introduction

Keratoconus (KC) remains an important ocular disorder with enormous implications for affected persons' quality of life.^{1,2} It is known to be characterised with progressive corneal asymmetry, steepening and alteration, apical thinning and central corneal scarring.³ There have been variations in the reported onset of the disease, including adolescence, early adulthood and childhood.⁴

As a disease of the cornea, the use of tomographic techniques for the diagnosis and progression of keratoconus is very crucial. In the advanced stages of the disease, it is easy to diagnose using the slit lamp assessment technique; however, in the early stages, its diagnosis can be tricky and easily missed.⁵

© 2023 Owusu et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs A2 and 5 of our Terms (https://www.dovepress.com/terms.php). Posterior corneal and pachymetric measures have proven useful in the early-stage diagnosis of this corneal ectasia.^{6,7} The Scheimpflug system has incorporated a spectrum of indices for the objective diagnosis and staging of Keratoconus.^{8,9} The system characterizes the anterior corneal curvature-based topometric measures together with the posterior corneal and thickness-oriented Belin/Ambrosio Enhanced Ectasia Display (BAD) and Ambrosio's related thickness maximum.^{10,11}

The quest for refractive surgical interventions has brought to the fore the need for tests with high sensitivity and reliability, including non-tomographic techniques. The Scheimpflug imaging system, unlike others, allows for the visualization and measurement of corneal defects under standardized air puff indentation. The quality of published data on KC evaluation is often low due to various factors. Some studies had small sample sizes, which limited the generalizability of their findings. Other studies used different criteria in the classification of KC, leading to inconsistencies in the results. These limitations highlight the need for more rigorous research using standardized methods and larger sample sizes. The present study, therefore, investigated the use of the Scheimpflug -derived keratometric, pachymetric, and pachymetric progression indices in the diagnosis of Keratoconus.

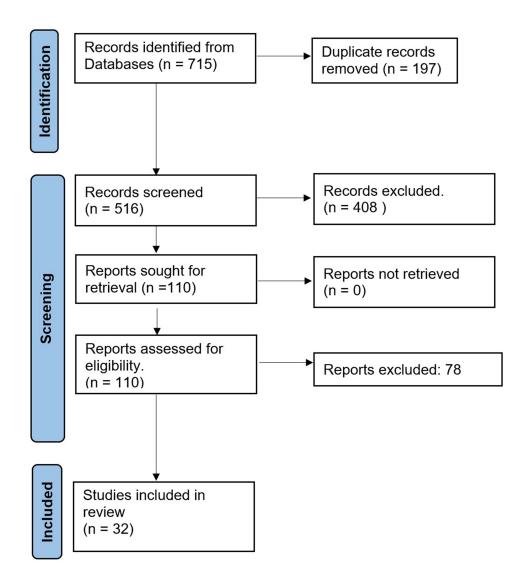


Figure I PRISMA flow chart of study selection.

Notes: PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;29;n71. Creative Commons.¹³

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Study, Year (Reference)	Country	Setting	Subjects Analysed	Age (KC, NE)	Definition	Instrument, Method	Funding Source
Thulasidas And Teotia, 2020 ¹⁴	India	Out-patients	49	26.4, 25.22	The case study included patients with unilateral keratoconus (KC) while the control group were candidates for refractive surgery with normal corneas.	Pentacam	Nil
Galleti et al, 2014 ¹⁵	Turkey	Out-patients	190	32, 32	Healthy controls consisted of patients with unremarkable Scheimpflug tomography in both eyes, defined as showing normal values (less than 1.6) in the standardised indices (back elevation, corneal thickness progression, relational thickness, and overall indices) and for the Ambrosio's maximum relational thickness index (339 or greater). Patients with at least one abnormal value in any of the aforementioned indices (2.6 or greater for the standardised index or maximum relational thickness less than 339) were diagnosed as having keratoconus.	Pentacam HR, Placido disk	Not stated

 Table I Summary of the Key Characteristics of the Studies That Were Analyzed

(Continued)

Table I (Continued).

Study, Year (Reference)	Country	Setting	Subjects Analysed	Age (KC, NE)	Definition	Instrument, Method	Funding Source
Guo et al, 2021 ¹⁶	China		675	23.08, 22.56	The control group was made up of volunteers with normal eye (their right eyes were used), while the study group consisted of patients with keratoconus in both eyes.	Pentacam, Corvis ST	National Natural Science Foundation of China (31,600,758); the Beijing Nova Program (Z181100006218099); the Open Research Fund from Beijing Advanced Innovation Center for Big Data- Based Precision Medicine, Beijing Tongren Hospital, Beihang University & Capital Medical University (BHTR-KFJJ-202001); Beijing Nova Program [Z181100006218099];
Reddy et al, 2014 ¹⁷	USA	Out-patients	141	34, 31	The keratoconus group comprised patients with keratoconus diagnosed by a corneal specialist on the basis of clinical and topographic signs. The normal group comprised normal eyes of patients evaluated for refractive surgery.	Rotating Scheimpflug imaging system	Nil
Hashem et al, 2022 ¹⁸	Egypt	Out-patients	480	13.5, 15.3	The study group comprised normal paediatric right eyes while the study group comprised eyes of paediatric keratoconus	Rotating Scheimpflug Camera (Oculyzer II, Pentacam HR)	The Science and Innovation Funding in cooperation with The Egyptian Knowledge Bank
Bae et al, 2014 ¹⁹	South Korea	Out-patients	48	28, 25.08	Patients who had advanced KC in one eye and a normal fellow eye were considered unilateral KC. The normal control patients were candidates for refractive surgery with clinically normal corneas.	Pentacam rotating Scheimpflug camera (Oculus, Wetzlar, Germany).	Not stated
Chan et al, 2017 ²⁰	Hong Kong	Out-patients	42	33.6, 34.9	Patients with clinically evident KC were recruited as the study group while an age-matched with normal corneas were recruited as control group.	Pentacam (Oculus Optikgeräte, Wetzlar, Germany) and Corvis (Oculus Optikgeräte)	Not stated

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Dienes et al, 2014 ²¹	Hungary	Out-patients	194	39.95, 36.98	Persons with mild to moderate keratoconus (KC group) and eyes		Hungarian Scientific Research Fund OTKA NN106649 research grant
					of refractive surgery candidates		OTRA INITIOOTY research grain
					(control group) were evaluated in		
					this study. Both eyes of each		
					patient in both groups were used.		
Henriquez et al, 2015	Peru	Out-patients	671		The study group were eyes with an	Scheimpflug Imaging Analyzer	Nil
$(KC)^{22}$	Teru	Out-patients	0/1		increased area of corneal power	(Pentacam; Oculus GmBH,	
					surrounded by concentric areas of	Wetzlar, Germany)	
					decreasing power while the	Wetziai, Germany)	
					control group were normal eyes		
					with no family history of ectasia.		
Henriquez et al, 2015	Peru	Out-patients	418		The study group consisted of eyes	Scheimpflug Imaging Analyzer	Nil
VEKC) ²²	reiu	Out-patients	017		with very early keratoconus while	(Pentacam; Oculus GmBH,	
VENC)					the control group were normal	`	
						Wetzlar, Germany)	
					eyes with no family history of ectasia.		
Huseynli et al, 2018 ²³	Azerbaijan	Out-patient	114	21.19, 21.75	The study group were patients	Pentacam HR	Nil
luseyilli et al, 2016	Azerbaijan	Out-patient	114	21.19, 21.75	with early stage of keratoconus		
					after complete ophthalmologic		
					evaluation also with minimal		
					pachymetry \leq 500µm while the		
					control group were normal		
					corneas.		
afarinasab et al,	Iran		210	28.6, 30.7	The study group consisted of eyes	Rotating Scheimpflug imaging	Nil
2013 ²⁴	11 d11		210	20.0, 50.7	with keratoconus on slit lamp	system	
2015					biomicroscopy as well as	system	
					asymmetric bowtie without SRAX		
					while the control group were eyes		
					without keratoconus.		

Table I (Continued).

Study, Year (Reference)	Country	Setting	Subjects Analysed	Age (KC, NE)	Definition	Instrument, Method	Funding Source
Kataria et al, 2018 ²⁵	India	Out-patients	300		The keratoconus group comprised of one eye of patients with bilateral keratoconus; the eye chosen had a mean simulated keratometry (K) value of less than 48.0 diopters while patients who had remained visually and topographically stable for at least two years after a laser refractive procedure with no evidence of post-refractive surgery ectasia constituted the normal control	Scheimpflug tomography (Pentacam HR, Oculus Optikger€ate GmbH), Corvis ST	Not stated
Kosekahya et al, 2018 ²⁶	Turkey	Out-patients	200	23.78, 26.06	group. The study group consisted of eyes with characteristic keratoconus signs in the anterior sagittal curvature maps while the normal group included eyes with a spherical equivalent less than 2.00 diopters (D) and a corrected distance visual acuity of 20/20 or better.	Pentacam HR	Not stated
Kovacs et al, 2010 ²⁷	Hungary	Out-patients	111	39.69, 35.25	The study evaluated eyes with mild to moderate keratoconus and eyes (study group) of refractive surgery candidates with normal corneas (control group).	Pentacam HR rotating Scheimpflug camera (version I.16 r:23, Oculus Optikgeräte GmbH)	Nil
Degirmenci et al, 2019 ²⁸	Turkey	Out-patients	61	32.33, 30.07	The study group were eyes with keratoconus while the control were the fellow eyes that were clinically and topographically normal.	Pentacam (Oculus Optikgerate GmbH, Wetzlar, Germany)	Nil

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Henriquez et al,	Peru	Out-patients	151	28.4, 29.29	The study group was defined as	Scheimpflug Imaging Analyzer	Not stated
2012 ²⁹					keratoconus in both eyes, with the	(Pentacam; Oculus GmBH,	
					presence of clinical signs and	Wetzlar, Germany)	
					topographic evaluation while the		
					control group were subjects who		
					had normal corneas in both eyes.		
Huseynova et al,	Azerbaijan	Out-patients	85	23.77, 26.06	The study group were eyes with	Pentacam HR (Oculus	Not stated
2016 ³⁰					keratoconus while the control	Optikgeräte GmbH, Wetzlar,	
					group were healthy corneas	Germany	
					diagnosed according to Amsler-		
					Krumeich criteria. ³¹		
Koc et al, 2020 ³²	Turkey	Out-patients	402	26, 24.8	The diagnosis of clinical	Pentacam HR rotating	Nil
,	,			,	keratoconus was defined by	Scheimpflug camera	
					characteristic keratoconus signs in		
					the anterior sagittal curvature		
					maps while the control group was		
					randomly selected from a database		
					of age-matched candidates' laser		
					in situ keratomileusis (LASIK) for		
					myopia (\leq 5.0 D) and myopic		
					astigmatism (≤ 3.0 D) who had		
					normal topographic, topometric		
					and tomographic analysis and did		
					not develop ectasia after at least		
					I-year follow-up.		
Kovacs et al, 2016 ¹²	Hungary	Out-patients	120	39.95, 33.17	The study group were patients	Scheimpflug camera	Nil
Rovaes et al, 2010	i iungai y	Out-patients	120	57.75, 55.17	with unilateral or bilateral mild to	(Pentacam HR, Oculus	
					moderate keratoconus while the	Optikgeräte GmbH)	
						Optikgerate Glibh)	
					control group were refractive		
					surgery candidates with normal		
					corneas.		

Table	I	(Continued).

Study, Year (Reference)	Country	Setting	Subjects Analysed	Age (KC, NE)	Definition	Instrument, Method	Funding Source
Lim et al, 2014 ³³	Singapore	Out-patients	70	31, 29.4	Cases in the study group were patients with eyes that met the Amsler-Krumeich criteria ³¹ for keratoconus while the group were control group were selected from a database of candidates for refractive surgery with normal corneas and myopia or myopic astigmatism.	Scheimpflug corneal tomography (Pentacam; Oculus. Wetzlar, Germany)	The Health Research Endowmen Fund of the Singapore Ministry of Health
Liu et al, 2021 ³⁴	China		110	24.87, 22	The study group were eyes with keratoconus based on slit-lamp findings and the presence of abnormal topographic patterns on the sagittal front curvature map while the control group was healthy eyes with no ectasia.	Rotating Scheimpflug corneal tomography (Pentacam HR), Corvis ST II	The Key Clinical Innovation Program of Peking University Third Hospital, category A (No. Y65495-05).
Mihaltz et al, 2009 ³⁵	Hungary	Out-patients	82	40.2, 38.7	The study group were patients with keratoconus diagnosed based on biomicroscopic and topographic findings in accordance with the criteria established by the Collaborative Longitudinal Evaluation of Keratoconus Study while the control group were refractive surgery candidates with healthy corneas.	Pentacam HR (version 1.16. r:23)	Not stated
Naderan et al, 2017 ³⁶	Iran	Out-patients	738	25.3, 26.1	Patients with bilateral keratoconus (both eyes with KISA% >100) were assigned to the KC group and those with bilateral normal eyes (both eyes with KISA% <60) were assigned to the normal group.	Pentacam Scheimpflug analyser (OCULUS Optikgeräte, Wetzlar, Germany)	Not stated

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Nicula et al, 2022 ³⁷	Romania	Out-patients	252	30, 31	Patients diagnosed with KCN	Pentacam R (HR Premium;	Not stated
					confirmed by slit-lamp	Oculus Optikgeräte GmbH,	
					examination keratometry and	Wetzlar, Germany)	
					corneal topography, and		
					tomography were included in the		
					KCN group while the control		
					group comprises subjects selected		
					from the candidates for refractive		
					corneal surgery with myopia		
					(<-8.5D) and/or myopic		
					astigmatism (<3.5D) and a normal		
					corneal tomography and healthy		
					eyes.		
Ucakhan et al, 2011 ³⁸	Turkey	Out-patients	111	29.1, 26.1	Patients with clinically evident	Pentacam Comprehensive Eye	Not stated
					keratoconus were recruited as the	Scanner (Oculus Optikgeräte	
					study group while the control	GmbH)	
					group consisted of normal eyes		
					with myopic astigmatism (sphere		
					7.00 diopters [D] and cylinder 4.00		
					D) and normal corneal and ocular		
					findings.		
Orucoglu and Toker,	Turkey	Out-patient	1169	32.99, 31.18	The study group were eyes with	Rotating Scheimpflug camera	Not stated
2015 ³⁹					keratoconus diagnosed mainly on	(Pentacam, Oculus	
					the basis of clinical slit-lamp	Optikgeräte GmbH, Wetzlar,	
					findings, keratometry, and	Germany)	
					associated characteristic		
					topographic patterns while the		
					control group were normal eyes		
					with no ocular pathology, no		
					previous ocular surgery, and no		
					irregular corneal pattern.		

(Continued)

Table I (Continued).

Study, Year (Reference)	Country	Setting	Subjects Analysed	Age (KC, NE)	Definition	Instrument, Method	Funding Source
Shen et al, 2021 ⁴⁰	China	Out-patient	335	25.1, 22.8	The study group were eyes with keratoconus, diagnosed according to the Global Consensus on Keratoconus Diagnosis from 2015 ⁴¹ while the control were persons with healthy corneas.	Scheimpflug camera	National Natural Science Foundation of China (Grant No. 82101183) (Grant No. 81770955); Joint research project of new Frontier technology in municipal hospitals (SHDC12018103); Project of Shanghai Science and Technology (Grant No.20410710100), (Grant No. 21Y11909800); Clinical Research Plan of SHDC (SHDC2020CR1043B); Project of Shanghai Xuhui District Science and Technology (2020–015).
Shetty et al, 2017 ⁴²	India	Out-patients	130	25.5, 24.25	The study group were eyes with keratoconus diagnosed mainly on the basis of clinical findings, while the control group were normal eyes with no ocular pathology.	Pentacam, Galilei and Sirius	Nil
Steinberg et al, 2015 ⁴³	Germany and Austria	Out-patients	635	33, 34	The control group were normal eyes (both eyes KISA% <60); while the study group were clinical manifest keratoconus eyes (KISA% >100).	Rotating Scheimpflug imaging system (Pentacam, Oculus Inc	Not stated
Vazquez et al, 2014 ⁴⁴	Argentina	Out-patients	281	32.3, 32.5	The study group were eyes with keratoconus diagnosed mainly on the basis of clinical slit-lamp findings, keratometry, and associated characteristic topographic patterns while the control group were normal eyes.	Placido disk topography and aberrometry (iTrace, Tracey Technologies, Houston, TX, USA) and Scheimpflug camera (Pentacam, Oculus Optikgeräte GmbH, Wetzlar, Germany)	Nil

Parameter	COVARIATE	в	95% CI	Р
Average pachymetric progression index	Sample Size	0.00	-0.00, 0.00	0.36
	Publication Year	-0.01	-0.08, 0.06	0.73
Maximum Ambrosio relational thickness	Sample Size	-0.02	-0.16, 0.12	0.77
	Publication Year	0.92	-28.91, 30.75	0.95
Average Ambrosio relational thickness	Sample Size	-0.05	-0.40, 0.30	0.79
	Publication Year	1.82	-24.83, 28.46	0.89
Central corneal thickness	Sample Size	-0.07	-0.12, -0.01	0.02
	Publication Year	-2.89	-6.62, 0.84	0.13
Posterior corneal elevation	Sample Size	-0.09	-0.46, 0.28	0.63
	Publication Year	-27.79	-50.59, -5.00	0.02
КІ	Sample Size	-0.00	-0.01, 0.01	0.49
	Publication Year	-0.10	-0.36, 0.17	0.48
К2	Sample Size	-0.00	-0.01, 0.01	0.43
	Publication Year	-0.07	-0.53, 0.38	0.75
Maximum keratometric power	Sample Size	0.00	-0.00, 0.01	0.4
	Publication Year	0.99	-0.36, 2.36	0.16
Maximum pachymetric progression index	Sample Size	0.00	-0.00, 0.00	0.99
	Publication Year	0.03	-0.12, 0.19	0.69

Table 2 Meta-Regression

Methods

The review protocol was registered with PROSPERO (Identifier: CRD42023410058), and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed.

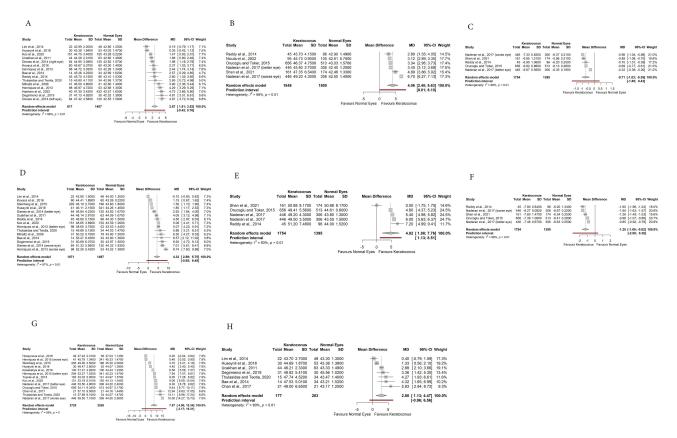


Figure 2 Forest Plots of keratometric readings in keratoconic and normal eyes (A-H) for K1, K1f, K1b, K2, K2f, K2b, Kmax and Kmean respectively.

٨	Study	Total		toconus SD	Total		nal Eyes SD	Mean Differe	nce MD	95%-CI	Weight
А	Nicula et al., 2022	95	464.13	1.3000	105	579.44	0.5000		-115.31	[-115.59; -115.03]	4.9%
	Naderan et al., 2017 (worse eye)	446	442.00	41.0000	306	548.00	35.0000	+	-106.00	[-111.46; -100.54]	4.9%
	Dienes et al., 2014 (worse eye)	64	463.60	33.5300	130	557.31	27.1800	+	-93.71	[-103.16; -84.26]	4.8%
	Toprak et al., 2015	183	481.08	39.9600	131	566.23	35.3800	+-	-85.15	[-93.53; -76.77]	4.8%
	Naderan et al., 2017 (better eye)	446	471.00	30.0000	306	552.00	31.0000	+	-81.00	[-85.45; -76.55]	4.9%
	Shen et al., 2021	161	469.50	53.7000	174	546.60	33.4000		-77.10	[-86.77; -67.43]	4.8%
	Henriquez et al. 2012 (worse eye)	98	468.89	39.0300	53	543.34	33.8300	****	-74.45	[-86.39; -62.51]	4.8%
	Mihaltz et al., 2009	41	491.30	43.4000	41	555.80	27.9000	-	-64.50	[-80.29; -48.71]	4.7%
	Kovacs et al., 2010	41	491.00	43.0000	70	555.00	28.0000	-	-64.00	[-78.71; -49.29]	4.7%
	Reddy et al., 2014	45	502.70	50.0000	96	565.20	27.0000		-62.50	[-78.08; -46.92]	4.7%
	Dienes et al., 2014 (better eye)			26.0400			26.9800	-+-	-60.89	[-68.78; -53.00]	4.8%
	Henriquez et al., 2012 (better eye)	98	487.14	35.6800	53	547.66	34.5900		-60.52	[-72.21; -48.83]	4.8%
	Wahba et al., 2016			35.3000			35.4000	+	-54.10	[-64.70; -43.50]	4.8%
	Kataria et al., 2018			31.8700			35.0400	+	-54.08	[-63.36; -44.80]	4.8%
	Ucakhan et al., 2011			41.4300			36.5200	<u> </u>	-51.50	[-66.70; -36.30]	4.7%
	Galleti et al., 2014 (left eye)			38.0000			30.0000	-	-46.00	[-59.28; -32.72]	4.7%
	Galleti et al., 2014 (right eye)			32.0000			30.0000		-43.00	[-52.08; -33.92]	4.8%
	Steinberg et al., 2015			43.5000			35.4000		-36.60	[-43.63; -29.57]	4.8%
	Huseynova et al., 2016			38.9600			27.2200		-25.36	[-39.43; -11.29]	4.7%
	Kovacs et al., 2016			43.1800			29.8900		-24.74	[-39.70; -9.78]	4.7%
	Lim et al., 2014	22	535.90	39.8700	48	534.10	28.0200		1.80	[-16.65; 20.25]	4.6%
	Random effects model Prediction interval Heterogeneity: $l^2 = 99\%$, $p = 0$	2525			2388			÷		[-73.79; -48.60] [-139.19; 16.80]	100.0%
	,							-100 -50 0 5	50 100		
							Favou	rs Keratoconus Fav	ours Normal Eyes		

			Kera	toconus		Norn	nal Eyes				
	Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	Weight
В	Toprak et al., 2015 Degirmenci et al., 2019 Wahba et al., 2016 Bae et al., 2014 Huseynova et al. 2016 Huseynli et al., 2018 Lim et al., 2014	31 183 14 49 30	491.63 482.50 511.14 505.92 483.00	43.3600 38.9500 39.4000 50.1500 38.7300 15.4000 38.9000	30 131 34 36 53	558.37 545.30 549.06 530.06 491.40	35.0900 31.9800 35.4000 30.2400 27.7100 10.2000 28.2000	*	-62.80 -37.92	[-84.60; -48.88] [-71.13; -54.47] [-66.09; -9.75] [-38.27; -10.01] [-14.56; -2.24]	14.7% 14.1% 14.7% 13.1% 14.4% 14.8% 14.1%
	Random effects model Prediction interval Heterogeneity: $l^2 = 98\%$, p				463		Favou	-100 -50 0 50 100 rs Keratoconus Favours No		[-72.64; -11.08] [-148.53; 64.80]	100.0%

Figure 3 Forest Plots of CCT and Pachy-apex (A and B respectively) in keratoconic and normal eyes.

Literature Search Strategy and Study Selection

We conducted a thorough literature search in PubMed, MEDLINE, Web of Science, and EMBASE to discover relevant articles, and the latest search was conducted on June 30, 2023. The search strategy was based on combinations of medical subject headings and free text words, and the search terms used included "Scheimpflug", "Pentacam", "keratoconus", "ectatic cornea", "diagnostic efficacy", "tomography", "topography", "outcome", "efficacy" "topographic", "tomographic", and "topometric" in varying combinations. The search was defined using the Boolean operators "AND" and "OR" and truncations. Figure 1 illustrates the PRISMA flowchart outlining the processes for obtaining the articles used in this review. The initial literature search turned up one hundred and ten (110) plausibly relevant articles, out of which thirty-seven¹² were included. Full-text articles that seemed relevant were retrieved after three reviewers (A.J.B.V., S.A., and S.O.) independently evaluated the titles and abstracts for possible eligibility. The three reviewers then independently evaluated these full-text articles to determine their suitability for inclusion. We reached a consensus on how to classify

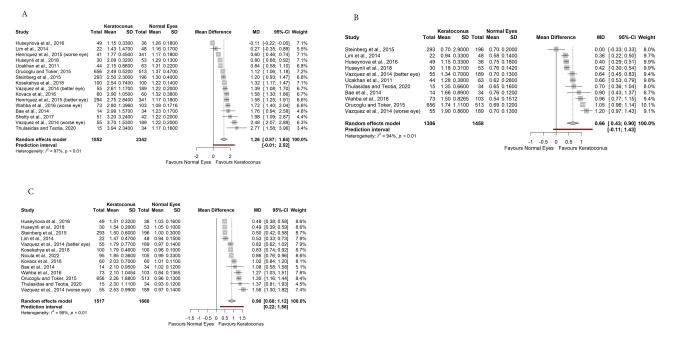


Figure 4 Forest Plots for the Pachymetric Progression indices in keratoconic and normal eyes (A-C) for PPImax, PPImin and PPIavg respectively.

the eligibility differences of the full-text articles through discussions, and where necessary, three other reviewers (S.K., M.A.K., and E.Z.) adjudicated the issue.

Published studies were considered eligible if they met the following criteria: Pentacam Scheimpflug Tomography was used in evaluating the cornea and compared any of the keratometry readings, pachymetric indices and/or pachymetric progression indices amongst participants with keratoconus and a control group (participants without keratoconus). Conference abstracts were included if they contained all relevant data. Review papers, studies without control groups, studies with no pertinent data, case reports, correspondence, and studies with missing or unidentifiable data were excluded from this review.

Study Appraisal and Data Extraction

Quality appraisal of the included studies was done using the revised tool for the quality assessment of diagnostic accuracy studies (QUADAS-2). The QUADAS-2 tool is commonly used in systematic reviews of diagnostic test accuracy studies to assess individual studies' risk of bias and applicability. It comprises seven categories of bias which are classified as "high", "low", or "unclear", but does not produce a single overall numerical score. For our study, two authors (S.O. and E.Z.) used the QUADAS-2 tool independently to evaluate the studies, and any disagreements were resolved by group discussion involving a third author (S.K.). This approach ensured a reliable and consistent assessment of the studies. Two authors (S.O. and A.J.B.V.) independently extracted data from each included study. Demographic characteristics of study subjects and means and standard deviations of the Scheimpflug Pentacam parameters were extracted using Microsoft Excel Spreadsheet, with accuracy confirmed by a third author (E.Z.). The parameters included in this review were keratometry readings (keratometric powers of the flat meridian [K1, K1-back, K1-front]; keratometric powers of the steep meridian [K2, K2-back, K2-front]; mean keratometric power, Kmean; keratometric power of the steepest point of the front surface, Kmax), pachymetric indices (central corneal thickness, CCT; corneal thickness at the apex, pachy-apex), and pachymetric progression indices (minimum pachymetric progression index, PPImin; maximum pachymetric progression index, PPImax, average pachymetric progression index, PPIavg; maximum Ambrosio relational thickness, ARTmax; average Ambrosio relational thickness, ARTavg).

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	Keratoconus		Normal Eyes								
Study	Total	Mean	SD	Total	Mean	SD	Mean Di	fference	MD	95%-CI	Weight
Wahba et al., 2016	70	276 60	138.2000	102	677 60	131,4000		I	401.00	[-441.61; -360.39]	10.0%
Vazquez et al., 2014 (worse eye)		209.00	99.0000		555.00					[-375.66; -316.34]	10.4%
Koc et al., 2020	151	259.60	98.0000	150	540.70	67.0000	+			[-300.05; -262.15]	10.7%
Chan et al., 2017	21	264.87	140.7300	21	545.43	84.4800			-280.56	[-350.76; -210.36]	8.6%
Bae et al., 2014	14	281.13	12.3000	34	541.97	67.6700	-+		-260.84	[-284.48; -237.20]	10.5%
Vazquez et al., 2014 (better eye)	55	318.00	142.0000	189	555.00	98.0000			-237.00	[-277.04; -196.96]	10.0%
Steinberg et al., 2015	293	347.10	145.9000	196	548.20	116.8000	-+-		-201.10	[-224.48; -177.72]	10.5%
Lim et al., 2014	22	390.60	134.5000	48	576.00	1 11.7000			-185.40	[-249.88; -120.92]	8.9%
Huseynova et al., 2016	49	346.83	94.2900	36	523.43	80.3700			-176.60	[-213.83; -139.37]	10.1%
Huseynli et al., 2018	30	319.40	76.1000	53	468.90	46.9100			-149.50	[-179.52; -119.48]	10.4%
Random effects model Prediction interval Heterogeneity: $I^2 = 95\%$, $p < 0.01$	763			1019					-252.08	[-308.76; -195.39] [-421.07; -83.08]	100.0%
							-400 -200 (rs Keratoconus) 200 4 Favours Nori	00 mal Eyes		

В

2		Keratoconus		Normal Eyes							
Study	Total	Mean	SD	Total	Mean	SD	Mean Di	fference	MD	95%-CI	Weight
Kovacs et al., 2016	60	73.27	64.1800	60	464 55	127.7000	—	I	-391 28	[-427.44; -355.12]	8.2%
Wahba et al., 2016			100.6000		517.80	90.6000				[-339.66; -281.74]	8.5%
Vazquez et al., 2014 (worse eye)		145.00	73.0000		445.00	87.0000				[-322.94; -277.06]	8.7%
Orucoglu and Toker, 2015		145.00			457.83	86.4400				[-280.31; -259.87]	9.0%
Chan et al., 2017			100.6300		436.81	82.9500				[-314.72; -203.16]	7.4%
Kosekahya et al., 2018		199.20	64.4000		452.30	70.7000	÷			[-271.84; -234.36]	8.8%
Bae et al., 2014		204.15			452.97	69.4900				[-301.82; -195.82]	7.5%
Vazquez et al., 2014 (better eye)			109.0000		445.00	87.0000	- 10 A			[-253.36; -190.64]	8.4%
Steinberg et al., 2015			121.9000			100.1000				[-206.28; -166.72]	8.8%
Huseynova et al., 2016		248.74			427.72	70.1000	-			[-200.20; -100.72]	8.4%
Huseynli et al., 2018		232.80			381.80	44.0700				[-170.32; -127.68]	8.7%
Lim et al., 2014			106.9000		418.90		-			[-192.05; -87.15]	7.5%
Lilli et al., 2014	22	279.30	100.9000	40	410.90	97.2000			-139.00	[-192.05, -67.15]	7.5%
Random effects model	1428			1542			\diamond		-242.77	[-288.86; -196.69]	100.0%
Prediction interval									_	[-381.80; -103.74]	
Heterogeneity: / ² = 96%, <i>p</i> < 0.01							1 1	1 1	1		
						-	400 -200	0 200 4	400		
	Favours Keratoconus Favours Normal Eyes										

Figure 5 Forest Plots of the Ambrosio Relational Thickness (A and B respectively) for ARTavg and ARTmax in keratoconic and normal eyes.

Data Analysis

The meta-analysis (inverse variance random-effect model) was conducted using the meta (6.5.0) and metafor (4.2.0) packages in R version 4.3.0 (R Foundation) as well as Stata (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.). We reported the estimates of effect size as mean differences (MD) with a 95% confidence interval (CI). A meta-regression was conducted for parameters with at least 10 studies to examine whether potential effect modifiers, such as sample size and publication year, could account for any variation in effect sizes. A sensitivity analysis was performed to ensure the robustness of the pooled estimates using a leave-one-out meta-analysis approach, wherein the impact of a particular study on the final combined estimate was assessed by systematically excluding each study in turn. Additionally, we evaluated publication bias for parameters with at least 10 studies by visually inspecting funnel plots and addressed any potential bias using the Trim and Fill method developed by Duval and Tweedie.

Results

Table 1 presents a summary of the key characteristics of the studies that were analyzed in the review. All the studies included in the meta-analysis were published within the period spanning from 2009 to 2022. Table 2 presents the meta-regression conducted for parameters with at least 10 studies.

		with 95% CI	p-value
Galleti et al., 2014 (right eye)	•	-62.26 [-74.58, -49.95]	0.000
Galleti et al., 2014 (left eye)		-62.09 [-74.44, -49.74]	0.000
Reddy et al., 2014		-61.27 [-73.72, -48.81]	0.000
Dienes et al., 2014 (better eye)		-61.35 [-73.82, -48.87]	0.000
Dienes et al., 2014 (worse eye)	•	59.71 [-71.73, -47.69]	0.000
Kataria et al., 2018		-61.69 [-74.14, -49.25]	0.000
Kovacs et al., 2010		-61.19 [-73.64, -48.74]	0.000
Henriquez et al., 2012 (better eye)		-61.36 [-73.82, -48.91]	0.000
Henriquez et al. 2012 (worse eye)		60.68 [-73.07, -48.29]	0.000
Huseynova et al., 2016 -	•	-63.10 [-75.01, -51.20]	0.000
Kovacs et al., 2016 -	•	-63.16 [-75.03, -51.28]	0.000
Lim et al., 2014 -	•	-64.44 [-75.23, -53.65]	0.000
Mihaltz et al., 2009		-61.17 [-73.61, -48.74]	0.000
Naderan et al., 2017 (better eye)	•	60.31 [-72.63, -48.00]	0.000
Naderan et al., 2017 (worse eye)			0.000
Nicula et al., 2022	•		0.000
Ucakhan et al., 2011		-61.80 [-74.20, -49.40]	0.000
Shen et al., 2021	•	60.53 [-72.90, -48.17]	0.000
Steinberg et al., 2015	•	-62.61 [-74.80, -50.42]	0.000
Toprak et al., 2015	•	60.13 [-72.36, -47.90]	0.000
Wahba et al., 2016		-61.69 [-74.13, -49.25] 	0.000

Random-effects REML model

Figure 6 Leave-one-out meta-analysis for central corneal thickness (CCT).

As shown in Figure 2, all keratometry readings were significantly steeper in eyes with keratoconus than in normal eyes, [MD (95% CI)], K1 [2.67 (1.81; 3.52)], K1-back [-0.71 (-1.03; -0.39)], K1-front [4.06 (2.48; 5.63)], K2 [4.32 (2.89; 5.75)], K2-back [-1.25 (-1.68; -0.82)], K2-front [4.82 (1.88; 7.76)], Kmax [7.57 (4.80; 10.34)], and Kmean [2.80 (1.13; 4.47)]. Further, CCT [-61.19 (-73.79; -48.60)] and pachy-apex [-41.86 (-72.64; -11.08)] were significantly thinner in keratoconic eyes compared to normal eyes (Figure 3). The pooled estimates for PPImin [0.66 (0.43; 0.90)], PPImax [1.26 (0.87; 1.64)], PPIavg [0.90 (0.68; 1.12)], ARTmax [-242.77 (-288.86; -196.69)], and ARTavg [-251.08 (-308.76; -195.39)] showed significantly more rapid pachymetric progression in keratoconic eves than in normal eves (Figures 4 and 5). Notably, we observed significant heterogeneity in the meta-analysis for all the parameters (I²>50%); however, the results of the leave-one-out sensitivity analysis indicated that the exclusion of any single study did not substantially alter the pooled effect size estimate for all parameters, suggesting that the overall findings were robust as the pooled effect size estimate remained relatively stable (Figures 6-9). The contour-enhanced funnel plots showed evidence of non-random publication bias for K2, CCT, PPImax, and PPIavg, with an excess of studies in the lower-right corners of the plots, implying that smaller studies with non-significant results may not have been published, and this might have over-estimated the treatment effects (Figures 10-13). Publication bias adjustments with Duval and Tweedie's trim and fill are shown in Figure 14. Publication-bias-corrected estimates of the true effect sizes were [2.53 (0.78; 4.27); outliers removed: 2.80 (1.10; 4.54)], [-104.82 (-128.69; -80.96); outliers removed: -106.19 (-128.68; [-83.69], [0.94 (0.52; 1.36); outliers removed: 1.08 (0.73; 1.42)], and [0.64 (0.38; 0.89); outliers removed: 0.64 (0.40; 0.87)] for K2, CCT, PPImax, and PPIavg, respectively. The adjusted effect sizes were relatively smaller for K2, PPImax, and PPIavg and relatively larger for CCT, than the unadjusted estimates, suggesting that there may have been publication bias favoring studies with larger effect sizes; however, the effect sizes remained statistically

Owusu et al					Dovepress
A Omitted study	Mean diff. with 95% Cl p-value	B Omitted study			Mean diff. with 95% Cl p-value
Reddy et al., 2014	-0.71 [-1.00, -0.43] 0.000 -0.82 [-0.96, -0.67] 0.000 -0.64 [-0.88, -0.40] 0.000 -0.71 [-1.01, -0.42] 0.000 -0.66 [-0.93, -0.40] 0.000 864	Reddy et al., 2014 Naderan et al., 2017 (better eye) Naderan et al., 2017 (worse eye) Nicula et al., 2022 Orucoglu and Toker, 2015 Shen et al., 2021	3	4 5	 4.27 [2.93, 5.61] 0.000 4.17 [2.73, 5.61] 0.000 3.43 [2.93, 3.93] 0.000 4.23 [2.83, 5.63] 0.000 4.18 [2.75, 5.61] 0.000 3.88 [2.48, 5.28] 0.000
C Omitted study Reddy et al., 2014 Naderan et al., 2017 (better eye) Naderan et al., 2017 (worse eye) Orucoglu and Toker, 2015 Shen et al., 2021	Mean diff. with 95% Cl p-value -1.17 [-1.51, -0.84] 0.000 -1.34 [-1.65, -1.03] 0.000 -1.12 [-1.41, -0.83] 0.000 -1.31 [-1.67, -0.95] 0.000 -1.24 [-1.63, -0.84] 0.000	D Omitted study Reddy et al., 2014 Naderan et al., 2017 Naderan et al., 2017 Orucoglu and Toker, 2015	•		Mean diff. with 95% Cl p-value 4.16 [1.60, 6.71] 0.001 4.39 [1.49, 7.29] 0.003 -4.55 [1.56, 7.54] 0.003 -4.70 [1.68, 7.72] 0.002 5.67 [4.86, 6.47] 0.000
-1.6 Random-effects REML model	-1.4 -1.2 -18	Shen et al., 2021 2 Random-effects REML model	4	6	5.07 [4.80, 0.47] 0.000
E <u>Omitied study</u> Thulasidas and Taolia, 2020 Ohan et al., 2017 Henriquez et al., 2015 (better eye) Heurgyiet et al., 2015 (better eye) Heurgyiet et al., 2018 Kosetkattya et al., 2018 Koset et al., 2010 Naderan et al., 2017 (Wortse eye) Onucoglu and Tokex, 2015 Steinberg et al., 2015	Mean diff. with 95% C1 p-value 7.17 [4.64, 9.66] 0.000 7.22 [4.68, 9.77] 0.000 8.19 [5.81, 10.57] 0.000 7.65 [4.97, 10.28] 0.000 7.65 [4.97, 10.39] 0.000 7.65 [4.98, 10.37] 0.000 7.65 [4.98, 10.39] 0.000 7.64 [4.74, 10.15] 0.000 7.64 [4.74, 10.15] 0.000 7.64 [4.77, 10.15] 0.000 7.65 [4.61, 10.27] 0.000 7.67 [4.68, 10.27] 0.000 7.67 [4.68, 10.27] 0.000	F Omitted study Thulasidas and Teotia, 2020 — Bae et al., 2014 — Chan et al., 2017 — Huseynli et al., 2018 Degirmenci et al., 2019 — Lim et al., 2014 Ucakhan et al., 2011 —			Mean diff. with 95% Cl p-value 2.74 [1.27, 4.21] 0.000 2.74 [1.28, 4.21] 0.000 2.61 [1.32, 3.91] 0.000 2.81 [1.80, 4.76] 0.000 2.92 [1.37, 4.47] 0.000 3.01 [1.38, 4.64] 0.000
4 Random-effects REML model	4 6 8 10	1 Random-effects REML model	2	3 4	5

Figure 7 Leave-one-out meta-analyses for K1b, K1f, K2b, K2f, Kmax and Kmean (A-F respectively).

significant after adjustment. The results of the meta-regression analysis showed that sample size ($\beta = -0.07$, P =0.02) was a significant predictor of the effect size estimate for CCT. Specifically, studies with larger sample sizes tended to report larger effect sizes. None of the covariates was a significant predictor of the remaining parameters (Table 2 and Figures 15–18). The study further established transparency of evidence synthesis results and findings by assessing the risk of bias and quality of the studies (Figure 19).

Discussion

Corneal topography is generally a non-invasive probing technique that examines qualitatively and quantitatively the anatomical structure of the cornea. It allows for geometric classification and affords a discriminating typical pattern of normal corneas from pathological ectatic ones.^{10,45-48} Existing corneal topographers operates on either one or more of these principles; light reflection on the cornea, projection of a slit light onto the cornea, and asymmetric reflection of multicolor light-emitting diodes (LEDs).⁴⁹ Clinical characterization of the structure (shape) of the human cornea through topographic analysis is a common practice among eye care practitioners when the diagnosis of keratoconus is intended.

Recent technological advances such as Pentacam Scheimpflug tomography allow for the assessment of both the anterior and posterior surfaces of cornea at different points.^{41,49,50} Anteriorly, keratoconus is morphologically characterized by a cone-shaped protrusion of the cornea.^{49,51,52} This protrusion is typically eccentric but inferiortemporally positioned, read off as an area higher than the curve of the best adjustment surface in the elevation maps, and as an area more curved in the curvature map. The outcomes of the meta-analysis reveal evidence of significant mean differences in both anterior and posterior cornea keratometry readings between keratoconus and normal eyes. Specifically, the results indicate that the keratometry readings were significantly steeper in the keratoconus eyes compared to the normal eyes. Studies have suggested that early changes in eyes with

A Omitted study	Mean diff. with 95% Cl p-value	B Omitted study		Mean diff. with 95% Cl	p-value
Bae et al., 2014 Huseynli et al., 2018 Degirmenci et al., 2019 Huseynova et al. 2016 Lim et al., 2014 Toprak et al., 2015 Wahba et al., 2016 -80 -60 -40 -20	with 95% C1 p-value -42.38 [-71.40, -13.36] 0.004 -47.68 [-73.95, -21.40] 0.000 -37.75 [-65.50, -10.00] 0.008 -44.72 [-73.26, -16.18] 0.002 -48.51 [-73.49, -23.52] 0.000 -33.30 [-55.53, -11.08] 0.003 -38.17 [-66.46, -9.87] 0.008	Omitted study Bae et al., 2014 Chan et al., 2017 Huseynoit et al., 2018 Huseynova et al., 2016 Koc et al., 2020 Lim et al., 2014 Steinberg et al., 2015 Vazquez et al., 2014 Vazquez et al., 2014 Wahba et al., 2016		with 95% C1 .83 [-305,98, -195,68] .04 [-303,15, -194,92] .73 [-312,63, -214,82] .24 [-312,27, -208,20] .42 [-303,32, -193,51] .61 [-311,29, -205,92] .72 [-311,58, -203,87] .52 [-308,65, -198,40] .98 [-290,97, -190,99] .30 [-277,16, -193,43]	0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000
Random-effects REML model	0		-300 -250 -200		

Random-effects REML model

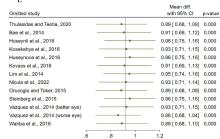
Random-effects REML model

		Mean diff.	
Omitted study		with 95% CI	p-value
Bae et al., 2014		-242.05 [-286.72, -197.38]	0.000
Chan et al., 2017		241.24 [-285.69, -196.79]	0.000
Huseynli et al., 2018 -	•	-251.49 [-292.21, -210.78]	0.000
Kosekahya et al., 2018		241.60 [-286.58, -196.62]	0.000
Huseynova et al., 2016	•	-248.39 [-291.50, -205.29]	0.000
Kovacs et al., 2016		229.41 [-263.89, -194.93]	0.000
Lim et al., 2014 -	•	-251.24 [-291.79, -210.68]	0.000
Orucoglu and Toker, 2015		239.96 [-284.68, -195.24]	0.000
Steinberg et al., 2015	•	-247.89 [-291.43, -204.36]	0.000
Vazquez et al., 2014 (better eye)	•	-244.50 [-289.25, -199.74]	0.000
Vazquez et al., 2014 (worse eye)		237.25 [-280.72, -193.77]	0.000
Wahba et al., 2016	•	236.31 [-279.16, -193.46]	0.000
-300	-250 -20		
Random-effects REML model			

Figure 8 Leave-one-out meta-analyses for Pachy-apex, ARTavg and ARTmax (A-C respectively).

A Mean diff. Omitari datudy with 05% Cl p-value Tuluasidas and Teotia, 2020 2.67 [133, 3.51] 0.000 Red ydy call, 2014 2.69 [134, 3.54] 0.000 Hashen et al., 2022 2.61 [173, 3.28] 0.000 Dienes et al., 2014 (left etys) 2.65 [173, 3.28] 0.000 Dienes et al., 2014 (left etys) 2.55 [173, 3.38] 0.000 Diegement et al., 2014 2.55 [173, 3.38] 0.000 Diegement et al., 2014 2.55 [173, 3.38] 0.000 Horriquez et al., 2013 2.55 [173, 3.38] 0.000 Horriquez et al., 2014 2.55 [173, 3.38] 0.000 Mindtiz et al., 2020 2.57 [178, 3.48] 0.000 Context et al., 2014 2.56 [173, 3.38] 0.000 Minatiz et al., 2020 2.77 [136, 3.48] 0.000 Context et al., 2014 2.68 [173, 3.48] 0.000 Minatiz et al., 2020 2.76 [132, 3.59] 0.000 Minatiz et al., 2020 2.67 [178, 3.48] 0.000 Minatiz et al., 2020 2.67 [178, 3.48] 0.000	Omitated study with Thulaids and Footia, 2020 4.29 (2) Reddy et al., 2014 4.38 [2] Base et al., 2014 4.28 [2] Dienes et al., 2014 4.26 [2] Dienes et al., 2014 (better eye) 4.56 [2] Dienes et al., 2014 (better eye) 4.58 [2] Harriquez et al., 2019 (better eye) 4.38 [2] Henriquez et al., 2019 (better eye) 4.38 [2] Kora et al., 2016 (better eye) 4.38 [2] Kora et al., 2016 (better eye) 4.38 [2] Unn et al., 2016 (better eye) 4.36 [2] Unn et al., 2010 (better eye) 4.36 [2] Unr et al., 2010 (better eye) 4.36 [2] Unr et al., 2011 (better eye) 4.36 [2] Unr et al., 2010 (better eye) 4.36 [2] Unr et al., 2014 (better eye) 4.36 [2] Unr et al., 2014 (better et al., 2020 (better et al.,	Cl. P-value 9291, 6.67 0.000 2.89, 5.78 0.000 2.89, 5.78 0.000 2.89, 5.79 0.000 2.80, 5.63 0.000 2.80, 5.63 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.84, 5.74 0.000 2.85, 6.53 0.000 2.86, 5.63 0.000 2.84, 5.74 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.82 0.000 3.71, 5.83 0.000	ye)	Mean diff. with 95% CI p-value 1.21 [0.87, 1.65] 0.00 1.27 (0.88, 1.65] 0.00 1.28 (0.88, 1.66] 0.00 1.28 (0.88, 1.66] 0.00 1.28 (0.88, 1.66] 0.00 1.38 (0.85, 1.77] 0.00 1.28 (0.88, 1.66] 0.000 1.38 (0.85, 1.71] 0.000 1.38 (0.85, 1.71] 0.000 1.38 (0.85, 1.71] 0.000 1.38 (0.85, 1.71] 0.000 1.38 (0.85, 1.71] 0.000 1.29 (0.86, 1.68] 0.000 1.20 (0.86, 1.68] 0.000 1.20 (0.86, 1.54] 0.000 1.20 (0.86, 1.54] 0.000 1.20 (0.86, 1.54] 0.000 1.20 (0.86, 1.54] 0.000 1.20 (0.86, 1.54] 0.000 1.20 (0.86, 1.54) 0.000
D	E	Mara ##		

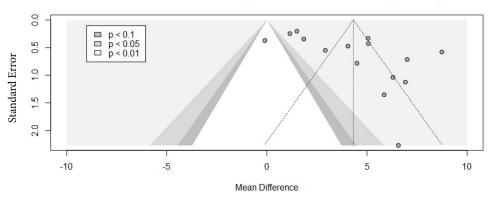
Omitted study					Mean diff. with 95% CI		p-value
Thulasidas and Teotia, 2020					0.67 [0.45, 0.8	91	0.000
Bae et al., 2014					0.65 [0.44, 0.8	7]	0.000
Huseynli et al., 2018					0.70 [0.49, 0.9	1]	0.000
Huseynova et al., 2016					0.70 [0.49, 0.9	1]	0.000
Lim et al., 2014					0.71 [0.50, 0.9	2]	0.000
Ucakhan et al., 2011			-		0.68 [0.45, 0.9	0]	0.000
Orucoglu and Toker, 2015	-				0.64 [0.43, 0.8	4]	0.000
Steinberg et al., 2015					0.72 [0.54, 0.9	1]	0.000
Vazquez et al., 2014 (better eye)			-		0.68 [0.46, 0.9	0]	0.000
Vazquez et al., 2014 (worse eye)				_	0.62 [0.44, 0.8	1]	0.000
Wahba et al., 2016	-				0.65 [0.43, 0.8	6]	0.000
	4	6	-	8			
andom-effects REML model	1	.0					



6

Random-effects REML model

Figure 9 Leave-one-out meta-analyses for K1, K2, PPImax, PPImin and PPIavg (A-E respectively).



Contour-Enhanced Funnel Plot (Keratometric Power of Steep Meridian)

Figure 10 Contour-Enhanced Funnel Plot for the keratometric power at the steep Meridian (K2).

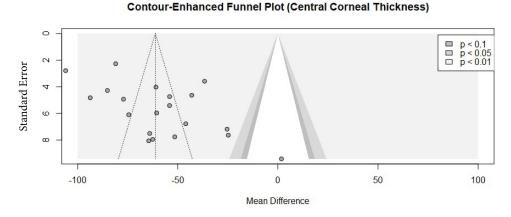
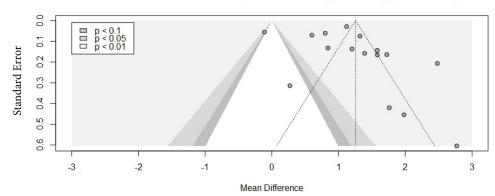
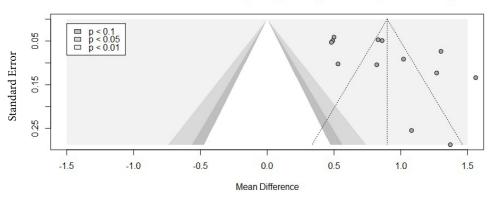


Figure 11 Contour-Enhanced Funnel Plot for the central corneal thickness (CCT).



Contour-Enhanced Funnel Plot (Maximum Pachymetric Progresion Index)

Figure 12 Contour-Enhanced Funnel Plot for the maximum pachymetric progression Indices (PPImax).



Contour-Enhanced Funnel Plot (Average Pachymetric Progresion Index)

Figure 13 Contour-Enhanced Funnel Plot for the average pachymetric progression Indices (PPlavg).

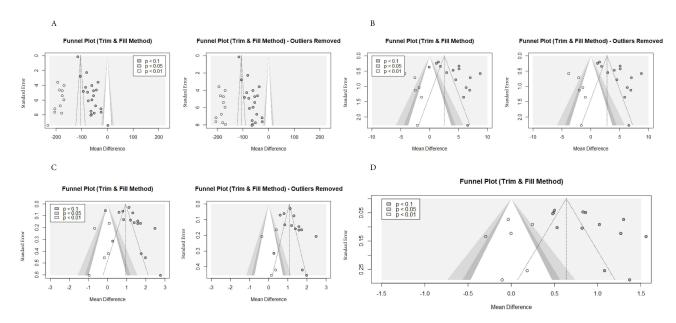


Figure 14 Tweedie's trim and fill for CCT, K2, PPImax and PPIavg (A-D respectively).

keratoconus are also present on the posterior corneal surface.⁵³ The geometric correlation between anterior and posterior cornea surfaces, have proven clinically useful in the discrimination of normal cornea from keratoconic corneas even at the subclinical stages.^{54–56} The disparities observed in keratometry readings provide valuable insights into the structural changes occurring in keratoconus, highlighting the complex nature of the condition. Understanding these differences can have important clinical implications, as they can aid in the accurate diagnosis and monitoring of keratoconus, as well as the development of targeted treatment approaches.

Also, this review highlights the significance of considering pachymetric and pachymetric progression indices in differentiating keratoconic eyes from normal ones. This study found that CCT and pachy-apex were significantly thinner in keratoconic eyes than normal ones. The pooled estimates for pachymetric progression indices also showed significantly more rapid pachymetric progression in keratoconic eyes than in normal eyes. These findings indicate that these indices provide valuable insights into discriminating KC from normal eyes considering the severity, and the progression of KC, aiding in its early detection and management. Several studies have used only the pachymetry indices in evaluating and diagnosing KC.^{57–59} Therefore, a comprehensive assessment of these factors is essential

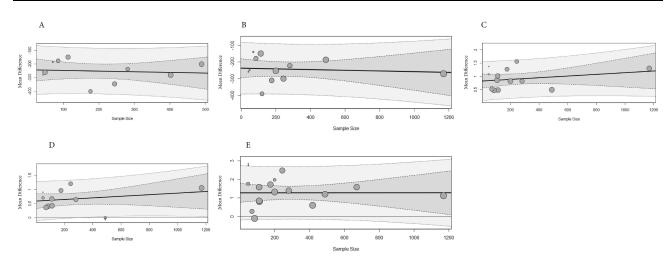


Figure 15 Bubble plots of meta-regression for the effect of sample sizes on ARTavg, ARTmax, PPlavg, PPlmin and PPlmax (A-E respectively).

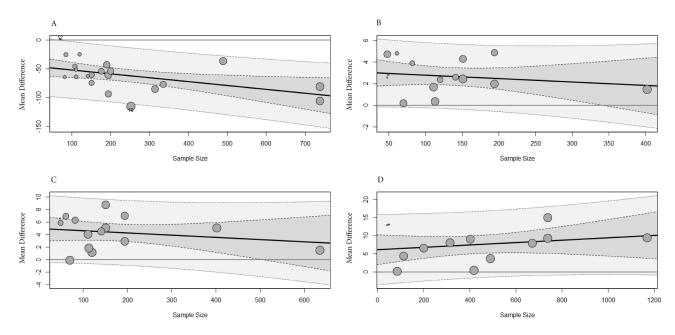


Figure 16 Bubble plots of meta-regression (A-D) for the effect of sample sizes on CCT, K1, K2 and Kmax respectively.

for an accurate diagnosis and personalised management of KC. In addition, using these indices can also help monitor the effectiveness of various treatment options for keratoconus. By regularly assessing these indices, healthcare professionals can make informed decisions with regards to the need for intervention or adjustment of treatment plans. This approach can potentially improve patient outcomes and minimise the risk of complications associated with advanced stages of keratoconus.

The results of the meta-regression analysis revealed sample size as a significant moderator of the effect size estimate for CCT, indicating that it plays a crucial role in explaining the heterogeneity observed among the studies. This finding suggests that the impact of sample size on CCT should be carefully considered when interpreting the results. However, other factors not accounted for in this analysis may also contribute to the between-study variation.

There is the need to acknowledge the limitations of this review study. Firstly, the included studies may have had variations in their methodologies and sample sizes, which introduced high heterogeneity in the pooled estimates. However, the leave-one-out sensitivity analysis results indicated that the pooled effect size estimate for all

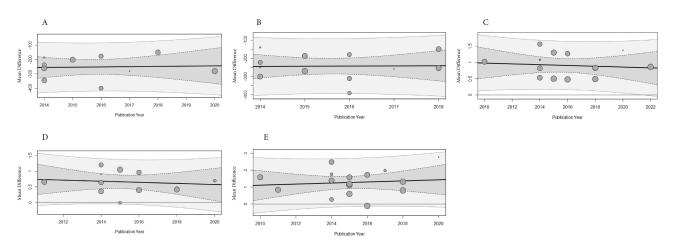


Figure 17 Bubble plots of meta-regression for the effect of publication year on ARTavg, ARTmax, PPlavg, PPlmin and PPlmax (A-E respectively).

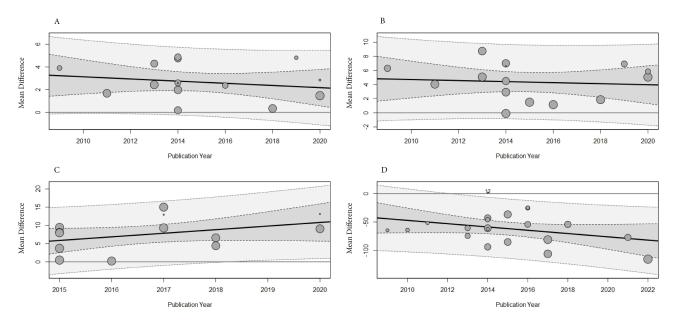


Figure 18 Bubble plots of meta-regression for the effect of publication year on K1, K2, Kmax and CCT (A-D respectively.

parameters was stable suggesting that the results were not heavily influenced by any single study or group of studies. Secondly, the review study focused primarily on keratometric, pachymetric and pachymetric progression indices, and other factors related to keratoconus were not explored. Future review studies should consider other elements used in diagnosing KC.

Conclusion

The Pentacam Scheimpflug-derived keratometric, pachymetric, and pachymetric progression indices are good predictors in discriminating KC from normal eyes. The findings of this review study have important implications for the diagnosis and management of keratoconus. By incorporating these indices into the diagnostic process, healthcare professionals can improve the accuracy of their assessments and provide personalised treatment plans.

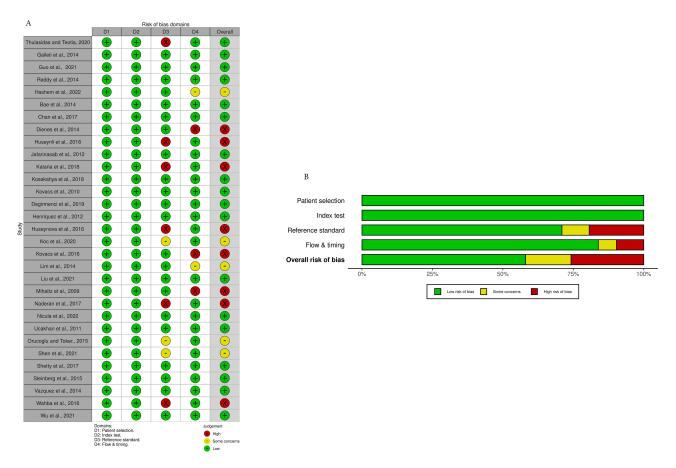


Figure 19 Traffic Light and Weighted Bar Plot for Risk of Bias Assessment using QUADAS-2 (A and B respectively).

Disclosure

The authors report no conflicts of interest in this work.

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