Comparing Pentacam HR Screening Indices in Different Normal Corneal Thicknesses among Refractive Surgery Candidates

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Abstract

Purpose: To compare Pentacam indices in normal eyes with different corneal thicknesses.

Methods: It is a retrospective observational study. Ninety-six normal eyes of 96 patients who were referred for refractive surgery in a tertiary university-based hospital from October 2015 to April 2019 were recruited consecutively. Corneal keratometry as well as Pentacam's software Belin-Ambrósio Enhanced Ectasia Display (BAD) parameters including pachymetry progression indices (PPIs), maximum Ambrosio's relational thickness (ART-max), corneal elevations, normalized deviations, BAD total deviation value (BAD-D), and anterior surface indices were measured by Pentacam HR (Type 70900). The included were classified as thin (26 eyes), average (45 eyes), and thick (25 eyes) corneas with the thinnest point thickness of ≤496 µm, 497–595 µm, and ≥596 µm, respectively. The specificities of all parameters were calculated based on routine cut-off values.

Results: The refraction, keratometry, and elevations were not different ($P > 0.05$). All PPIs (minimum, average, and maximum) of thick corneas were significantly lower than average and thin corneas ($P < 0.001$). ART-max increased by thickening of the cornea ($P < 0.001$). BAD-D score and normalized indices of pachymetric parameters decreased with the increase of thickness ($P < 0.001$), while specificities of all indices increased with corneal thickening. More than 96% of thick corneas were classified as normal PPI-max (24/25), ART-max (25/25), and BAD-D (25/25), while nearly <54% of thin corneas (14/26 for PPI-max, 9/26 for ART-max, and 12/26 for BAD-D) were normal.

Conclusions: The pachymetry-related indices and BAD-D were different among normal corneas with various thicknesses. The specificities of PPIs, ART-max, and BAD-D of thin corneas were lower than in thick corneas.

Keywords: Ambrosio's relational thickness, Corneal thickness, Pachymetry progression, Pentacam, Thin cornea

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Submitted: 12-Aug-2021; **Revised:** 30-Oct-2021; **Accepted:** 31-Oct-2021; **Published:** 26-Jul-2022

Introduction

Corneal topography and Scheimpflug imaging are frequently used to analyze the corneal surface. Pentacam is one of the most commonly used corneal tomographic technologies in clinical practice. It employs a rotating Scheimpflug camera that measures 138,000 elevation points in a maximum of 2 s and computes a three-dimensional map of the cornea and anterior chamber.[1-3]

Pentacam is capable of vast data output including a combination of tomographic, topometric, and pachymetric parameters.[4] This opens new horizons to create artificial intelligence indices for the diagnosis and classification of corneal ectasia. However, there is still controversy surrounding the refractive indices that should be used in patient evaluation.[4] The literature has identified neither specific protocols nor parameters that are capable of carrying out this process appropriately. Therefore, the considerable overlap of healthy subjects and early forms of corneal ectatic disorders occurs based on these indices.[4]

Access this article online

Quick Response Code:

Website: www.jcurrophthalmol.org

DOI: 10.4103/joco.joco_249_21

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How to cite this article: Ghiasian L, Abdolalizadeh P, Hadavandkhani A, Eshaghi A, Hadi Y, Nadjafi-Semnani F. Comparing Pentacam HR screening indices in different normal corneal thicknesses among refractive surgery candidates. J Curr Ophthalmol 2022;34:200-7.

There is a large variation in corneal thickness of the normal population.[5,6] Roshdy *et al*.[7] reported different back elevation and pachymetric-based measures including pachymetry progression indices (PPIs) and Ambrosio's relational thickness (ART) among thin, average, and thick healthy corneas, although they did not evaluate other parameters of Belin-Ambrósio Enhanced Ectasia Display (BAD) such as deviation indices and keratoconus indices as well as specificity of these indices based on routine cut-off values.[7] Indeed, it is predicted that various corneal thicknesses have different pachymetric-based indices, while the question remains unanswered whether they differ in terms of normalized indices as well. The specificities of Pentacam indices in various corneal thicknesses are another ambiguous issue by considering nonconsensual protocols, especially for subjects with preclinical keratoconus who have overlap with normal subjects in terms of corneal thickness.[4,8]

Therefore, in this study, we focused on the Pentacam HR indices in healthy corneas undergoing cornea refractive procedures. The aim was to evaluate the differences in crude values and specificities of Pentacam HR pachymetry, anterior surface, and normalized deviation indices among various corneal thicknesses.

Methods

This study is a retrospective observational study on patients referred to refractive surgery clinics from October 2015 to April 2019. Informed consent and ethics committee approval (IUMS.1398.83) were obtained, and the study adhered to the tenets of the Declaration of Helsinki. Myopic and hyperopic patients with unremarkable slit-lamp examination, and patients with corrected distance visual acuity of 20/20 or better, and who were seeking refractive surgery were included in the study. All subjects were Caucasian within a normal range of topography and tomography parameters (Keratoconus Severity Score 0,[9] normal topography pattern, and average and maximum corneal power ≤47.75 D) in both eyes, which was assessed by a senior corneal specialist. Such strict criteria were used to restrict the sample to subjects without suspicious clinical and topographical findings. Patients with previous eye surgery, any eye disease such as ectatic disorders, corneal opacities, chronic use of topical medications, or contact lens wear within the previous 3 weeks were excluded. Only the right eye of each patient was considered in this study. In corneas thicker than 600 μm, specular microscopy was done to assess the Fuchs endothelial corneal dystrophy. The eyes were grouped into thin, average, and thick cornea according to the quartiles of thickness of the thinnest point. Each quartile comprises 25% of the cornea. Corneas with thickness less than the first quartile, between the first and third quartile, and more than the third quartile were classified as thin, average, and thick corneas, respectively.

Both eyes for each patient were scanned by Pentacam HR (Type 70900, Pentacam, Oculus GmbH, Wetzlar, Germany) according to the recommendations of the device manual. All measurements were performed by an experienced operator in a darkened room within a 15-min period, and the subjects were told to blink immediately before each examination. Only good-quality automatic Scheimpflug scans that passed the Pentacam software's quality check were accepted.

Parameters of corneal keratometry (K) (including flat-K, steep-K, mean-K, astigmatism, and quality [Q] score at back and front surfaces) and anterior chamber (including anterior chamber depth, volume, and angle) were investigated. In addition, the following corneal descriptors were obtained from the Pentacam's software Belin-Ambrósio Enhanced Ectasia Display: Thickness of the thinnest point and apex, PPIs (minimum, average, and maximum), ART maximum score, front and back corneal elevation at the thinnest point (from best-fit-sphere at 8 mm zone), normalized indices' including deviation of normality of the front elevation (Df), deviation of normality of the back elevation (Db), deviation of normality of pachymetric progression (Dp), deviation of normality of corneal thinnest point (Dt), deviation of normality of relational thickness (Da), and Belin-Ambrósio Enhanced Ectasia Display Total Deviation Value (BAD-D) indices. Anterior surface indices including keratoconus index (KI), central KI (CKI), index of height asymmetry (IHA), index of height decentration (IHD), index of surface variance (ISV), index of vertical asymmetry (IVA), and minimum radius of curvature (R-min) were also evaluated.[4,10,11] Table 1 presents the definition of the BAD indices. The PPI, ART maximum score, and anterior surface indices for each observation were categorized as normal, suspicious, and abnormal according to the cut-off values mentioned in Table 1.[4] The deviation indices are indicated by the software, in white (normal) if it is <1.6 standard deviation (SD), in yellow (suspicious) if it is ≥1.6 and <2.6 SD, and in red (abnormal) if it is ≥2.6 SD from the mean.[4,8] This scheme was followed throughout this work.

Statistical analysis

Statistical analyses were performed with SPSS for Windows software version 22.0 (SPSS Inc., Chicago IL, USA). Quantitative data were described with means ± SD and percentage in continuous and numerical data, respectively. One-way analysis of variance (for continuous variables with normal distribution), Kruskal–Wallis test (for continuous variables without normal distribution), and Chi-square test (for categorical variables) were used to evaluate the changes of the Pentacam HR parameters among corneas with different corneal thicknesses. $P < 0.05$ was considered statistically significant.

Results

A total of 96 eyes of 96 patients were included. Mean age of patients was 30.67 ± 7.04 years ranging from 20 to 57 years. More than half of the patients were female (63.2%, 60/95). The mean and median corneal thicknesses at the thinnest point were 541.04 ± 52.15 μm and 523.50 (interquartile range = 496.00–596.00) μm, respectively. By considering 496 μm and 596 μm as the first and third quartiles of the

Table 1: Definition and abnormality ranges of anterior surface, pachymetric, and deviation indices provided by the Pentacam HR System

Variables	Definition	Cut-off values		
		Normal	Suspicious	Abnormal
PPI				
PPI-min	Percentage in corneal thickness increase along each meridian starting from the thinnest corneal point, reported as the minimum, average and maximum values[4]	<0.80	0.80-0.86	>0.86
PPI-avg		<1.08	1.08-1.17	>1.17
PPI-max		<1.40	1.40-1.52	>1.52
ART-max	Ratio of the thinnest pachymetry and PPI-max[4]	>368	357-368	<357
Anterior surface indices				
KI	Ratio of mean radius of curvature values in the upper and lower corneal segments[9]	≤1.07	-	>1.07
CKI	Ratio of the mean radius of curvature values in a periphery divided by a central ring[9]	<1.03	-	≥1.03
IHA	Level of elevation symmetry data with respect to the horizontal meridian[10]	<19	19-21	>21
IHD	Degree of centration in the vertical direction, on a ring with a radius of 3 mm[10]	<0.014	0.014-0.016	>0.016
ISV	Deviation of the corneal radius with respect to the mean value[10]	<37	37-40	>40
IVA	Level of curvature symmetry with respect to the horizontal meridian[10]	<0.28	0.28-0.31	>0.31
R-min	Point of maximum anterior curvature[9]	≥6.71	-	<6.71
Normalized indices				
Df	Standard deviation toward disease by considering the mean of normal population as a zero value[4]	<1.6	1.6-2.5	≥2.6
Db		<1.6	1.6-2.5	≥2.6
Dp		<1.6	1.6-2.5	≥2.6
Dt		<1.6	1.6-2.5	≥2.6
Da		<1.6	1.6-2.5	≥2.6
BAD-D	A multivariate index which is calculated based on regression analysis of 9 indices including Df, Db, Dt, Da, Dp, displacement of thinnest point along the vertical meridian, anterior elevation at the thinnest point, posterior elevation at the thinnest point, and K-max[4]	<1.6	1.6-2.5	≥2.6

PPI: Pachymetric progression index, PPI-min: Minimum PPI, PPI-avg: Average PPI, PPI-max: Maximum PPI, ART-max: Maximum Ambrósio relational thickness, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index of height asymmetry, IHD: Index of height decentration, ISV: Index of surface variance, IVA: Index of vertical asymmetry, R-min: Minimum radius of curvature, Df: Deviation of normality of the front elevation, Db: Deviation of normality of the back elevation, Dp: Deviation of normality of pachymetric progression, Dt: Deviation of normality of corneal thinnest point, Da: Deviation of normality of relational thickness, BAD-D: Belin-Ambrósio Enhanced Ectasia Display Total Deviation Value

thinnest point thicknesses, corneas with thickness ≤496 μm, 497–595 μm, and ≥596 μm were classified as thin, average, and thick corneas, respectively. There were 20 eyes with corneal thickness ≥600 μm. None of them was excluded due to low endothelial cell count. The total mean spherical equivalent was −3.02 ± 1.65 diopter (D) ranging from −6.50 D to 2.38 D. The refractive status of three groups is presented in Table 2.

The baseline clinical characteristics, keratometry, and anterior chamber indices of corneal groups are summarized in Table 2. Three groups did not differ in terms of age (P = 0.14), sex (P = 0.27), sphere (P = 0.87), and cylinder (P = 0.49) of refractive errors as well as volume (P = 0.67) and depth (P = 0.92) of anterior chamber. The amount of anterior chamber angle of the thick corneas was significantly higher than average corneas (P = 0.004) [Table 2]. All front and back keratometry values including maximum K, flat K, steep K, astigmatism, and Q-value were similar between the groups (all P > 0.05) [Table 2].

All pachymetry-based indices were different among three groups (all $P \leq 0.001$) [Table 3]. There was a significant difference between three groups in terms of the apex thickness (P < 0.001) (corneas with thicker thinnest point had thicker apex), although the distance between apex and thinnest point did not change (P = 0.15). All PPIs (minimum, average, and maximum) of thick corneas were significantly lower than average and thin corneas (all $P \leq 0.03$). The PPIs of average corneas were also less than thin corneas except for minimum PPI (P = 0.50) [Table 3]. Moreover, ART-max rose with the increase in corneal thickness (P < 0.001). More than 90% of eyes with thick cornea were classified as normal PPIs (minimum, average, maximum) and ART-max while nearly half to one-third of the eyes with thin cornea had normal PPIs (minimum, average, maximum) and ART-max [Table 4]. The percentage of normal PPIs and ART-max in average corneas were approximately 60%–78% [Table 4].

There was an inverse correlation between BAD-D score and normalized indices related to pachymetric parameters including Dp, Dt, and Da and the corneal thickness (all P < 0.001) while normalized indices related to elevation parameters (Df [P = 0.18] and Db [P = 0.85]) were similar in three groups [Table 3]. The frequency of patients with normal BAD-D and normalized indices increased with the rise in the corneal thickness except Db (P = 0.44) and

Table 2: The baseline characteristics, keratometry, and anterior chamber Pentacam parameters in patients with thin (≤496 μm), average (497-595 μm), and thick (≥596 μm) corneas

Variable	Mean±SD (minimum-maximum)			*P**			
	Thin cornea	Average cornea	Thick cornea	To compare groups thin and average	To compare groups thin and thick	To compare groups average and thick	For overall comparison
Number of eyes	26	45	25	-	-	-	-
Age (years)	32.81±8.13 (22 - 51)	31.20±7.63 (22 - 57)	29.76±4.72 (21 - 39)	0.73	0.13	0.24	0.14
Sex (percentage of female)	61.5 (16/26)	71.1 (32/45)	52 (13/25)	0.41‡	0.49‡	0.11‡	0.27‡
Refractive error							
Sphere (D)	−2.81±0.94 (−3.75 - −2.00)	−2.31±1.78 (−5.5 - 2.5)	−2.44±2.13 (−6.25–0)	0.61	0.74	0.86	0.87
Cylinder (D)	−0.81±0.24 (−1.00 - 0.50)	−1.21±0.98 (−3.75 - 0)	−1.59±1.67 (−5.00 - 0.50)	0.51	0.26	0.39	0.49
Spherical equivalent (D)	−3.22±0.83 (−4.00 - −2.50)	−2.94±1.76 (−6.00 - 2.38)	−3.23±1.62 (−6.50 - −1.63)	0.76	0.99	0.67	0.89
Corneal front keratometry							
Maximum K (D)	45.15±1.37 (42.50 - 47.70)	44.65±1.44 (41.5 - 47.3)	44.34±1.06 (42.5 - 45.8)	0.13	0.03	0.36	0.09
Flat K (D)	43.25±1.37 (39.2 - 45.5)	42.94±1.27 (40.4 - 45.6)	42.38±1.39 (39.7 - 44.5)	0.33	0.02	0.10	0.07
Steep K (D)	44.72±1.60 (39.6 - 47.2)	44.20±1.44 (41.3 - 46.8)	43.96±1.05 (42.3 - 45.5)	0.14	0.05	0.48	0.14
Mean K (D)	44.00±1.38 (39.4 - 45.8)	43.52±1.27 (41.1 - 46.1)	43.15±1.07 (41.5 - 44.6)	0.16	0.02	0.23	0.07
Astigmatism (D)	1.46±1.13 (0.20 - 4.00)	1.27±0.77 (0.1 - 3.50)	1.58±1.26 (0.10 - 4.00)	0.45†	0.69†	0.23†	0.46†
Q value	−0.30±0.11 (−0.51 - −0.17)	−0.30±0.10 (−0.55 - −0.05)	−0.29±0.11 (−0.51 - −0.14)	0.89	0.76	0.84	0.95
Corneal back keratometry							
Flat K (D)	−6.15±0.18 (−6.5 - −5.7)	−6.14±0.18 (−6.5 - −5.8)	−6.14±0.24 (−6.5 - −5.6)	0.87	0.80	0.90	0.97
Steep K (D)	−6.50±0.21 (−7.0 - −6.0)	−6.35±0.90 (−7.0 - −0.6)	−6.56±0.22 (−7.0 - −6.2)	0.34	0.74	0.19	0.37
Mean K (D)	−6.32±0.17 (−6.7 - −5.8)	−6.30±0.20 (7.0 - −0.6)	−6.34±0.19 (−6.7 - −5.9)	0.65	0.76	0.43	0.72
Astigmatism (D)	0.35±0.22 (0 - 0.8)	0.33±0.14 (0 - 0.6)	0.42±0.24 (0 - 0.9)	0.66†	0.20†	0.06†	0.17†
Q value	−0.29±0.13 (−0.57 - −0.08)	−0.30±0.14 (−0.63 - −0.01)	−0.32±0.16 (−0.62 - −0.08)	0.87	0.53	0.59	0.80
Anterior chamber indices							
Anterior chamber volume (mm^2)	201.46±36.83 (108 - 266)	203.64±36.98 (108 - 290)	196.04±24.35 (147 - 239)	0.71	0.64	0.37	0.67
Anterior chamber depth (mm)	3.26±0.44 (2.34 - 4.55)	3.26±0.34 (2.35 - 4.22)	3.22±0.27 (2.73 - 3.75)	0.99	0.74	0.69	0.92
Anterior chamber angle (°)	35.98±7.76 (23.0 - 50.0)	39.93±10.08 (15.70 - 65.90)	33.51±6.63 (21.30 - 44.80)	0.07	0.31	0.004	0.01

*One-way analysis of variance and least significant difference *post hoc* test for multiple comparison, †Kruskal-Wallis test, ‡Chi-square test. K: Keratometry, SD: Standard deviation, D: Diopter

Table 3: The corneal indices of Pentacam's software Belin-Ambrósio Enhanced Ectasia Display in patients with thin (≤496 μm), average (497-595 μm), and thick (≥596 μm) corneas

Variable	Mean±SD (minimum-maximum)			*P**			
	Thin cornea	Average cornea	Thick cornea	To compare groups thin and average	To compare groups thin and thick	To compare groups average and thick	For overall comparison
Pachymetry based indices							
Thickness of thinnest point (μm)	484.15±9.03 (461 - 496)	533.89±31.31 (497 - 592)	612.04±12.40 (596 - 644)	<0.001	<0.001	<0.001	<0.001
Thickness of pachy apex (μm)	488.54±9.24 (463 - 500)	537.20±32.16 (499 - 595)	616.52±11.44 (597 - 648)	<0.001	<0.001	<0.001	<0.001
Apex to thinnest point distance (mm)	0.61±0.22 (0.05 - 1.05)	0.60±0.22 (0.21 - 1.35)	0.71±0.21 (0.24 - 1.04)	0.89	0.12	0.06	0.15
PPI-min	0.78±0.22 (0.07 - 1.38)	0.74±0.12 (0.50 - 1.01)	0.65±0.10 (0.50 - 0.85)	0.50	0.004	0.009	0.008
PPI-avg	1.12±0.15 (0.89 - 1.57)	1.03±0.15 (0.74 - 1.32)	0.92±0.08 (0.70 - 1.13)	0.008	<0.001	0.003	<0.001
PPI-max	1.39±0.20 (1.05 - 1.86)	1.28±0.21 (0.84 - 1.65)	1.18±0.12 (0.94 - 1.42)	0.03	<0.001	0.03	0.001
ART-max (μm)	357.23±54.25 (248 - 460)	433.42±86.21 (305 - 630)	522.37±65.27 (436 - 630)	<0.001	<0.001	<0.001	<0.001
Elevation based indices							
Front elevation at the thinnest point (μm)	2.42±1.58 (−2 - 5)	2.01±1.35 (−3 - 5)	2.04±1.52 (−1 - 5)	0.26	0.36	0.94	0.49
Back elevation at the thinnest point (μm)	5.38±4.03 (−1 - 14)	4.93±2.97 (−2 - 12)	5.71±2.44 (0 - 10)	0.57	0.72	0.34	0.61
Anterior surface indices							
KI	1.02±0.02 (0.99 - 1.06)	1.09±0.45 (0.97 - 4.01)	1.01±0.02 (0.97 - 1.04)	0.37	0.94	0.32	0.51
CKI	1.00±0.01 (0.98 - 1.02)	1.00±0.01 (0.99 - 1.01)	1.00±0.01 (1.00 - 1.01)	0.52	0.83	0.68	0.79
IHA	4.88±3.67 (0 - 11.8)	4.34±3.79 (0.1 - 16.6)	4.40±2.88 (0.4 - 11.1)	0.55	0.64	0.94	0.83
IHD	0.008±0.004 (0.001 - 0.016)	0.011±0.019 (0.001 - 0.130)	0.008±0.003 (0.004 - 0.016)	0.50	0.91	0.41	0.65
ISV	17.35±8.28 (6 - 34)	15.58±4.94 (7 - 29)	17.64±8.54 (8 - 34)	0.32	0.88	0.24	0.41
IVA	0.09±0.03 (0.03 - 0.16)	0.09±0.04 (0.03 - 21)	0.09±0.03 (0.04 - 0.15)	0.85	0.73	0.55	0.84
R-min (mm)	7.45±0.21 (7.07 - 7.91)	7.57±0.24 (7.13 - 8.13)	7.62±0.18 (7.37 - 7.94)	0.03	0.009	0.38	0.02
Horizontal Q	−0.25±0.17 (−0.48 - 0.34)	−0.29±0.09 (−0.55 - 0.09)	−0.27±0.14 (−0.46 - 0.25)	0.23	0.64	0.48	0.46
Vertical Q	−0.27±0.20 (−0.65 - 0.42)	−0.30±0.13 (−0.65 - 0.06)	−0.26±0.22 (−0.56 - 0.19)	0.50	0.71	0.26	0.51
Normalized indices							
Dp	1.45±1.04 (−0.13 - 4.48)	0.83±1.03 (−1.09 - 2.80)	0.14±0.50 (−1.07 - 1.53)	0.008	<0.001	0.004	<0.001
Dt	1.68±0.32 (1.29 - 2.57)	0.16±0.89 (−1.42 - 1.27)	−1.71±0.76 (−2.55 - 1.50)	<0.001	<0.001	<0.001	<0.001
Da	1.19±0.50 (0.25 - 2.20)	0.50±0.79 (−1.29 - 1.67)	−0.30±0.50 (−1.29 - 0.47)	<0.001	<0.001	<0.001	<0.001
Df	0.40±1.21 (−1.61 - 4.55)	0.03±0.92 (−1.78 - 1.55)	−0.10±0.93 (−1.54 - 2.15)	0.14	0.08	0.60	0.18
Db	−0.09±1.08 (−1.49 - 3.93)	−0.21±0.77 (−1.39 - 1.71)	−0.20±0.76 (−1.03 - 1.34)	0.59	0.65	0.98	0.85
BAD-D	1.67±0.54 (0.66 - 2.62)	0.95±0.66 (−0.23 - 2.26)	0.25±0.36 (−0.23 - 1.21)	<0.001	<0.001	<0.001	<0.001

*One-way analysis of variance and least significant difference *post hoc* test for multiple comparison, SD: Standard deviation, PPI-min: Minimum pachymetric progression index, PPI-avg: Average pachymetric progression index, PPI-max: Maximum pachymetric progression index, ART-max: Maximum ambrósio relational thickness, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index of height asymmetry, IHD: Index of height decentration, ISV: Index of surface variance, IVA: Index of vertical asymmetry, R-min: Minimum radius of curvature, Dp: Deviation of normality of pachymetric progression, Dt: Deviation of normality of corneal thinnest point, Da: Deviation of normality of relational thickness, Df: Deviation of normality of the front elevation, Db: Deviation of normality of the back elevation, BAD-D: Belin-Ambrósio Enhanced Ectasia Display Total Deviation Value

Table 4: The specificity of Pentacam's software Belin-Ambrósio Enhanced Ectasia Display in patients with thin (≤496 μm), average (497-595 μm), and thick (≥596 μm) corneas

Variable	Thin cornea			Average cornea			Thick cornea			*P**
	Normal	Suspicious	Abnormal	Normal	Suspicious	Abnormal	Normal	Suspicious	Abnormal	
Pachymetry based indices										
PPI-min	65.4% (17/26)	3.8% (1/26)	30.8% (8/26)	60% (27/45)	22.2% (10/45)	17.8% (8/45)	96% (24/25)	4% (1/25)	0% (0/25)	0.002
PPI-avg	34.6% (9/26)	34.6% (9/26)	30.8% (8/26)	62.2% (28/45)	17.8% (8/45)	20% (9/45)	96% (24/25)	4% (1/25)	0% (0/25)	<0.001
PPI-max	53.8% (14/26)	23.1% (6/26)	23.1% (6/26)	71.1% (32/45)	13.3% (6/45)	15.6% (7/45)	96% (24/25)	4% (1/25)	0% (0/25)	0.02
ART-max	34.6% (9/26)	11.5% (3/26)	53.8% (14/26)	77.8% (35/45)	6.7% (3/45)	15.6% (7/45)	100% (25/25)	0% (0/25)	0% (0/25)	<0.001
Anterior surface indices										
KI	100% (26/26)	0% (0/26)	0% (0/26)	95.6% (43/45)	0% (0/45)	4.4% (2/45)	100% (25/25)	0% (0/25)	0% (0/25)	0.35
CKI	100% (26/26)	0% (0/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	NA
IHA	100% (26/26)	0% (0/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	NA
IHD	92.3% (24/26)	7.7% (2/26)	0% (0/26)	86.7% (39/45)	4.4% (2/45)	8.9% (4/45)	92% (23/25)	8% (2/25)	0% (0/25)	0.30
ISV	100% (26/26)	0% (0/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	NA
IVA	100% (26/26)	0% (0/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	NA
R-min	100% (26/26)	0% (0/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	NA
Normalized indices										
Dp	57.7% (15/26)	30.8% (8/26)	11.5% (3/26)	80% (36/45)	15.6% (7/45)	4.4% (2/45)	100% (25/25)	0% (0/25)	0% (0/25)	0.009
Dt	50% (13/26)	50% (13/26)	0% (0/26)	100% (45/45)	0% (0/45)	0% (0/45)	28% (7/25)	72% (18/25)	0% (0/25)	<0.001
Da	76.9% (20/26)	23.1% (6/26)	0% (0/26)	88.9% (40/45)	11.1% (5/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	0.04
Df	84.6% (22/26)	11.5% (3/26)	3.8% (1/26)	97.8% (44/45)	2.2% (1/45)	0% (0/45)	96% (24/25)	4% (1/25)	0% (0/25)	0.22
Db	96.2% (25/26)	0% (0/26)	3.8% (1/26)	97.8% (44/45)	2.2% (1/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	0.44
BAD-D	46.1% (12/26)	50% (13/26)	3.9% (1/26)	80% (36/45)	20% (9/45)	0% (0/45)	100% (25/25)	0% (0/25)	0% (0/25)	<0.001

*Chi-square test. NA: Not applicable due to 100% specificity in all categories. PPI-min: Minimum pachymetric progression index, PPI-avg: Average pachymetric progression index, PPI-max: Maximum pachymetric progression index, ART-max: Maximum Ambrósio relational thickness, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index of height asymmetry, IHD: Index of height decentration, ISV: Index of surface variance, IVA: Index of vertical asymmetry, R-min: Minimum radius of curvature, Dp: Deviation of normality of pachymetric progression, Dt: Deviation of normality of corneal thinnest point, Da: Deviation of normality of relational thickness, Df: Deviation of normality of the front elevation, Db: Deviation of normality of the back elevation, BAD-D: Belin-Ambrósio Enhanced Ectasia Display Total Deviation Value

Df (P = 0.22) [Table 4]. The specificity of BAD-D score was 46.1% (12/26) in thin, 80% (36/45) in average, and 100% (25/25) in thick corneas (P < 0.001). Moreover, three groups did not differ in terms of anterior surface indices including ISV (P = 0.41), IVA (P = 0.84), KI (P = 0.51), CKI (P = 0.79), IHA (P = 0.83) and IHD (P = 0.65). Horizontal (P = 0.46) and vertical (P = 0.51) Q-scores of three groups were also similar [Table 3].

Discussion

Pentacam has become a widely employed technique providing a three-dimensional reconstruction of the entire anterior segment from anterior surface of the cornea to the posterior surface of the lens.[2] Several indices and artificial intelligence methods have been developed to help screening the presence of the risk of the future ectatic corneal diseases.[4] These indices have to have a high degree of sensitivity to detect any risk of ectasia.[12] However, false positive could occur in normal cases because most of the systems were calibrated for keratoconus.

The current study assessed the Pentacam measures in normal corneas with various thicknesses, which had similar refractive errors, anterior chamber, and front and back keratometry [Table 2]. Although thin, average, and thick corneas differ in terms of the pachymetry-based parameters, pachymetry-related normalized indices, and BAD-D, three groups had similar elevation-based and anterior surface indices [Table 3]. Moreover, this study showed that the specificity of all Pentacam pachymetry and normalized screening parameters increased with thickening of the cornea in normal eyes. The specificity of PPIs and pachymetry-related normalized indices (Dp, Dt, Da, and BAD-D) ranged between 46% and 77% in thin corneas while they were 100% in thick corneas [Table 4]. Conversely, the specificity of anterior surface indices and anterior surface-related normalized parameters (Df and Db) was more than 84% in thin corneas without any significant difference between average and thick corneas.

In general, the Pentacam indices can be divided into pachymetric-based, curvature-based, and combined subgroups. The pachymetric-based measures reflect the corneal thickness whose robust role has been confirmed as a determinant of corneal properties.[13] It is considered an important screening parameter of corneal ectatic disorders and a major risk factor for postoperative ectasia development.[13-15] Several pachymetric-related indices have been introduced, which excel single-point pachymetry in the identification of keratoconus.[16] These indices are calculated based on the values of corneal thickness [Table 1]. Therefore, it is speculated that pachymetric-based indices would differ in various corneal thicknesses. Roshdy *et al*.[7] showed that thinner corneas had a PPI-max greater than that of thicker corneas. On the contrary, ART-max increased with the increase in thickness. These were in agreement with the current study [Table 3]. Indeed, the decrease in relational thickness indices in thin cornea and their rising in thick cornea is an anticipated finding as relational thickness indices are calculated by division of corneal thickness into progression indices. Among the pachymetric-derived indices, the ART values provide validated accuracy in identifying ectasia even in relatively normal central corneal thickness.[16,17] However, no consensus exists regarding the cut-off point of ART, which is recommended between 300 µm and 400 µm.[4,18-20] Belin and Ambrósio reported 95.6% specificity for ART-max based on a 339 micrometer (µm) threshold.[19] It was significantly higher than our observation in thin corneas with 35% specificity although we reported 100% specificity in thick and 78% specificity in average corneas. Our finding highlights the possible low accuracy of this value in normal thin corneas.

The second subgroup of Pentacam indices was curvature-based. The relationship between corneal curvature and corneal thickness is unclear. Some studies did not find a significant relationship between the corneal curvature and thickness.[21,22] Similarly, three corneal groups of the current study did not differ in terms of keratometry values and elevation measures at both anterior and posterior surfaces. Similarity of anterior surface indices (such as KI, CKI, IHA, etc.) of our three corneal groups could be attributed to similar keratometry and elevation values [Table 3]. On the other hand, Nangia *et al*. reported a trend of reduction in corneal thickness for an increase in keratometry, while the correlation between central corneal thickness and cylinder was not significant.[23] Mimouni *et al*. also observed that thinner corneas were associated with an increase in mean keratometry readings.[24] Roshdy *et al*.[7] reported higher back elevation of the thinnest point in thick corneas than thin and average ones. It contradicts our result without a significant difference between groups in terms of back and front elevations. Additionally, by considering the overlap between normal and ectatic corneas, especially in lower thicknesses and the probably increased back elevation in early stages of ectasia,[25] the higher value of back elevation should be observed in thinner corneas instead of thicker ones if any, which again disagrees with Roshdy *et al*.'s study.

Specificity describes the ability of an index or test to identify the proportion of patients without diseases (true-negatives).[26] If the specificity of a screening index is 100%, then the false-positive rate is zero. Sensitivity and specificity are inversely proportional, meaning that as the sensitivity increases, the specificity decreases and vice versa.[26] In screening, the cut-off values for indices have usually been set in a manner to provide better sensitivity (to detect a particular disease) instead of specificity.[26] This may lead to more false positives of some indices in the current study. On the other hand, the lowest specificities in the current study were observed for PPIs, ART value, and BAD-D. These indices have lower thresholds to corneal ectasia and are the most effective parameters to detect pre-keratoconus. It may be another justification for their lower specificity in our study.[4]

This study has some limitations. Although we compared three corneal groups with each other, the relatively high mean corneal thickness in the average group may not be parallel with the routine definition of the average cornea and it skewed toward thicker values in the current study that can affect the specificities in this group. Selection of patients only from refractive surgery candidates was another limitation of this study. Moreover, we did not adjust the results with corneal diameter which might affect them.[27]

In conclusion, our study showed thin, average, and thick corneas had different pachymetric-based Pentacam indices while their curvature-based parameters were similar. Lower specificity of some Pentacam intelligent indices in thin corneas emphasized that the clinician should never solely rely on one index in clinical decision-making. Rather, Pentacam data should be interpreted in combination, with clinical judgment and patient demographics.

Acknowledgment

The authors thank Somayeh Akrad for her contribution to data grading.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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