The Role of Corneal Volume Distribution and Percentage Increase in Volume in Detection of Mild and Moderate Keratoconus

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Abstract

***Purpose*:** To investigate the validity of Pentacam derived parameters like corneal volume distribution and percentage increase in volume in differentiation of mild to moderate keratoconus from normal corneas

***Methods*:** Forty eyes with mild to moderate keratoconus and 200 normal eyes were studied by Pentacam. Corneal volume was calculated within diameters from 1.0 to 7.0 mm with 0.5 mm steps centered on the thinnest point to create the corneal volume distribution. The percentage increase in volume was calculated for each position of the corneal volume distribution from their first value. Statistical analysis was done using the Mann-Whitney test to compare mean levels of two groups and the Wilcoxon test for two consecutive measurements.

***Results*:** Statistically significant differences were observed between the keratoconic and normal corneas ($P<0.01$) in all positions of corneal volume distribution and in the percentage increase in volume. The differences between the curves of the two groups were more significant in 3 mm diameter and further.

***Conclusion*:** There are significant difference between corneal volume distribution and percentage increase in volume in keratoconic and normal corneas and could serve as valid indices to diagnose mild and moderate forms of keratoconus.

***Keywords*:** Corneal Volume Distribution, Keratoconus

Iranian Journal of Ophthalmology 2010;22(4):49-58 © 2010 by the Iranian Society of Ophthalmology

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Received: June 29, 2010
Accepted: November 4, 2010

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Published by Otagh-e-Chap Inc.

Introduction

Refractive surgeons often encounter patients with corneal topographic features that are suspicious for keratoconus.[1] In advanced stages, the diagnosis is easily made by slit-lamp and keratometric findings[2] however; the identification of subclinical forms of the disease in patients with normal best spectacle-corrected visual acuity (BSCVA) and minimal or no clinical signs is a challenging issue. It is sometimes difficult to decide whether these patients are candidates for ablative refractive surgery as topographic abnormalities occur in a wide range of severity and with great variation in pattern and patients with forme fruste keratoconus often have poor outcomes and may have progressive ectasia after refractive surgeries.[3-6] In these situations, it is useful to have additional information that can confirm or rule out the presence of early forms of keratoconus.

Determination of central corneal thickness is useful in identifying corneal thinning disorders such as keratoconus, contact lens-related complications, accurate measurement of intraocular pressure, preoperative assessment and both planning and follow-up of all corneal refractive procedures. The three-dimensional models of the cornea provided by tomographers are obtained from cross-sectional images. Commonly used varieties of this technology include three-dimensional topography (Astramax, LaserSight Technologies, Inc., Winter Park, Florida), slit scanning (Orbscan, Bausch & Lomb, Rochester, New York), Scheimpflug imaging (Pentacam, Oculus Inc., Dutenhofen, Germany); Precisio, (LIGI Tecnologie Medicali S.p.A., Taranto, Italy), very high frequency (VHF) ultrasound tomography (Artemis, Ultralink LLC, St Petersburg, Florida), and high-speed anterior segment optical coherence tomography (Visante, Carl Zeiss Meditech, Jena, Germany).[7] Although theoretically ultrasound (US) pachymetry is the gold standard for measurement of corneal thickness, but use of the topical anaesthesia and contact of the probe with cornea and the fact that this method could be influenced by fluctuations in corneal hydration, makes it important to use some alternative, robust and less invasive techniques.[8] Scheimpflug camera (Pentacam Oculus, Wetzlar, Germany) calculates thickness and curvature values for the entire cornea, determining its front and back surfaces. From the achieved images, data of the anterior and posterior corneal topography, corneal pachymetry, anterior chamber depth, angle and lens density can be measured quickly and noninvasively.[9]

In past studies, several methods like Modified Rabinowitz/McDonnell,[10] Maeda/Klyce[11] and KISA% indices[12] have been proposed to detect keratoconus.

In this study, we investigated another corneal tomography parameters derived from the Pentacam Comprehensive Eye Scanner to study corneal thickness spatial profile and corneal volume distribution in mild to moderate forms of keratoconic corneas and compared these parameters with those of normal eyes.

Methods

Forty eyes of 27 patients (12 women) diagnosed with mild to moderate keratoconus based on keratoconus severity score (KSS)[13] and 200 normal eyes of 100 consecutive healthy patients (54 women) were studied using the rotating Scheimpflug camera [Pentacam (Oculus, Wetzlar, Germany)]. Mild and moderate forms of keratoconus were defined by features in Table 1.

Table 1. Keratoconus severity score

Mild disease	***Required features:*** Axial topgraphic pattern consistent with KCN May have positive slit-lamp signs No corneal scarring consistent with keratoconus ***Additional features:*** Apical Corneal Power ≤52.00 D
Moderate disease	***Required features:*** Axial pattern consistent with KCN Must have positive slit-lamp signs ***Additional features:*** Apical Corneal Power >52.00 D, ≤56.00 D

Eyes with previous acute corneal hydrops or a history of corneal surgery were excluded from the study. The protocol of measurement by Pentacam Eye Camera was similar to previously published studies.[14,15]

Corneal volume was calculated within diameters from 1.0 to 7.0 mm with 0.5 mm steps centered on the thinnest point to create the corneal volume distribution. Corneal volume was calculated for each position from the 1.0 mm volume using the formula:

Corneal volume in diameter y=[average corneal thickness in 360◦ from thinnest point to diameter y] × [corneal area from thinnest point to diameter y].

And so the distribution of corneal volume was yielded.

The percentage increase in volume was calculated for each position from the 1.0 mm volume using the formula:

(CV@y_CV@ 1:0mm) /CV@ 1:0 mm

Where CV is the corneal volume at each diameter and y represents the calculated diameters of corneal volume from 1.0 to 7.0 mm with 0.5 mm steps.

After completion of data extraction, they imported into a Microsoft Excel spreadsheet. Data from the Excel spreadsheet were exported to SPSS software (SPSS mInc, Chicago, version 12) for statistical analysis. Statistical analysis was done using the Mann-Whitney test to compare mean levels of two groups and the wilcoxon test for two consecutive measurements.

Results

Significant differences were found in all positions of the corneal volume distribution and percentage volume increase between normal eyes and keratoconic eyes ($P \le 0.01$). The keratoconic corneas had much less volume and more percentage volume increases.

In keratoconus eyes, the mean volume within the 1.0 mm diameter was 0.33±0.04 mm^3 (95% CI limits, 0.32 to 0.35; range 0.22 to 0.38 mm^3). In normal eyes, the mean was 0.41±0.02 mm^3 (95% CI limits, 0.41 to 0.42; range 0.37 to 0.45 mm^3).

For the 4.0 mm diameter, the mean volume of the keratoconic corneas was 6.06±0.53 mm^3 (95% CI limits, 5.89 to 6.23; range 4.91 to 6.84 mm^3). In normal eyes, the mean was 7.06±0.33 mm^3 (95% CI limits, 6.98 to 7.14; range 6.45 to 7.46 mm^3).

For the 7.0 mm diameter, the mean volume of the normal corneas was 24.99±1.14 mm^3 (95% CI limits, 24.67 to 25.32; range 21.85 to 26.29 mm^3). In keratoconic eyes, the mean was 22.49±1.49 mm^3 (95% CI limits, 22.01 to 22.97; range 17.80 to 25.57 mm^3).

Table 2 shows the mean, standard deviation, 95% CI limits, and the minimal and maximal values for the corneal volume in normal eyes and keratoconic eyes and Figure 1 shows the corneal volume distribution in normal eyes and keratoconic eyes.

In keratoconus eyes within the 3.0 mm diameter, the mean percentage increase in volume was 905.24±53.51% (95% CI limits, 888.13% to 922.35%; range 845.95% to 1127.27%). In normal eyes, the mean was 843.77±17.1% (95% CI limits, %838.91 to 848.63%; range 805.44% to 913.51%).

For the 5.0 mm diameter, the mean percentage increase in volume in keratoconic eyes was 2965.72±238.58% (95% CI limits, 2889.42%to 3042.02%; range 2659.46% to 3900%). In normal eyes, the mean was 2717.27±62.52% (95% CI limits, 2699.51% to 2735.04%; range 2593.33% to 2905.41%).

In normal eyes within the 7.0 mm diameter, the mean percentage increase in volume was 5990.96±141.67% (95% CI limits, 5950.69% to 6031.22%; range 5726.67% to 6489.19%). In keratoconic eyes, the mean was 6710.53±669.29% (95% CI limits, 6496.48% to 6924.58%; range 5813.15% to 9284%).

Table 3 shows the mean, standard deviation, 95% CI limits, and the minimal and maximal values for the percentage increase in volume in normal eyes and keratoconic eyes and Figure 2 shows the percentage increase in volume in normal eyes and keratoconic eyes. Figure 3 shows Pentacam screen of the corneal thickness and progression of corneal thickness. Figure 4 shows corneal volume distributions in normal and keratoconic eyes. Figure 5 shows percentage increase in thickness in normal and keratoconic eyes, y-axis shows percentage volume increase.

Table 2. Distribution of measured volume in keratoconus and control group

Number	Mean±SD in control	Mean±SD in KCN	Minimum in control	Minimum in KCN	Maximum in control	Maximum in KCN
Vol 1.0	0.41±0.02	0.33±0.04	0.37	0.22	0.45	0.38
Vol 1.5	0.92±0.04	0.77±0.08	0.84	0.54	0.99	0.88
Vol 2.0	1.69±0.07	1.4±0.14	1.51	1.03	1.8	1.59
Vol 2.5	2.67±0.12	2.25±0.19	2.39	1.74	2.87	2.54
Vol 3.0	3.87±0.15	3.34±0.29	3.56	2.7	4.1	3.75
Vol 3.5	5.42±0.2	4.67±0.4	4.98	3.78	5.74	5.25
Vol 4.0	7.06±0.27	6.06±0.53	6.45	4.91	7.46	6.84
Vol 4.5	9.33±0.35	8.04±0.74	8.54	6.48	9.89	9.02
Vol 5.0	11.56±0.53	10.15±0.75	10.11	7.91	12.3	11.56
Vol 5.5	14.13±0.63	12.56±0.91	12.55	9.8	14.85	14.31
Vol 6.0	17.32±0.77	15.35±1.17	15.4	12.02	18.27	17.55
Vol 6.5	21.13±0.95	18.76±1.37	18.73	14.63	22.19	21.36
Vol 7.0	24.99±1.14	22.49±1.49	21.85	17.8	26.29	25.57

All comparisons in each volume between control and KCN were statistically significant (P<0.01). Comparison of two consecutive measurements in control and KCN was also statistically significant (P<0.01).
All values are in mm^3
SD: Standard deviation
KCN: Keratoconus

Table 3. Percentage of thickness increase in normal and keratoconic corneas

Number	Mean±SD in control	Mean±SD in KCN	Minimum in control	Minimum in KCN	Maximum in control	Maximum in KCN
Vol 1.5	125.07±5.6	131.86±5.51	109.52	117.86	134.21	145.45
Vol 2.0	311.36±6.99	320.73±13.44	300	294.74	331.71	368.18
Vol 2.5	549.77±9.24	579.79±38.73	536.59	543.24	578.05	748
Vol 3.0	843.77±17.1	905.24±53.51	804.44	845.95	913.51	1127.27
Vol 3.5	1220.84±24.2	1306.57±76.79	1164.44	1224.32	1321.62	1618.18
Vol 4.0	1621.08±31.2	1727.78±97.98	1548.89	1618.92	1751.35	2131.82
Vol 4.5	2173.5±43.88	2321.44±126.54	2075.56	2172.97	2340.54	2845.45
Vol 5.0	2717.27±62.52	2965.72±238.58	2593.33	2659.46	2905.41	3900
Vol 5.5	3342.86±71.66	3695.94±295.79	3191.11	3318.92	3572.97	4872
Vol 6.0	4121.77±87.56	4533.8±298.96	3922.22	4083.78	4400	5382.14
Vol 6.5	5048.86±102.71	5571.11±451.01	4813.33	5008.11	5375.68	7376
Vol 7.0	5990.96±141.67	6710.53±669.29	5726.67	5813.51	6489.19	9284

All comparisons in each volume between control and KCN were statistically significant (P<0.01). Comparison of two consecutive measurements in both control and KCN was also statistically significant (P<0.01).
Values are the percentage from the 1.0 mm diameter
SD: Standard deviation
KCN: Keratoconus

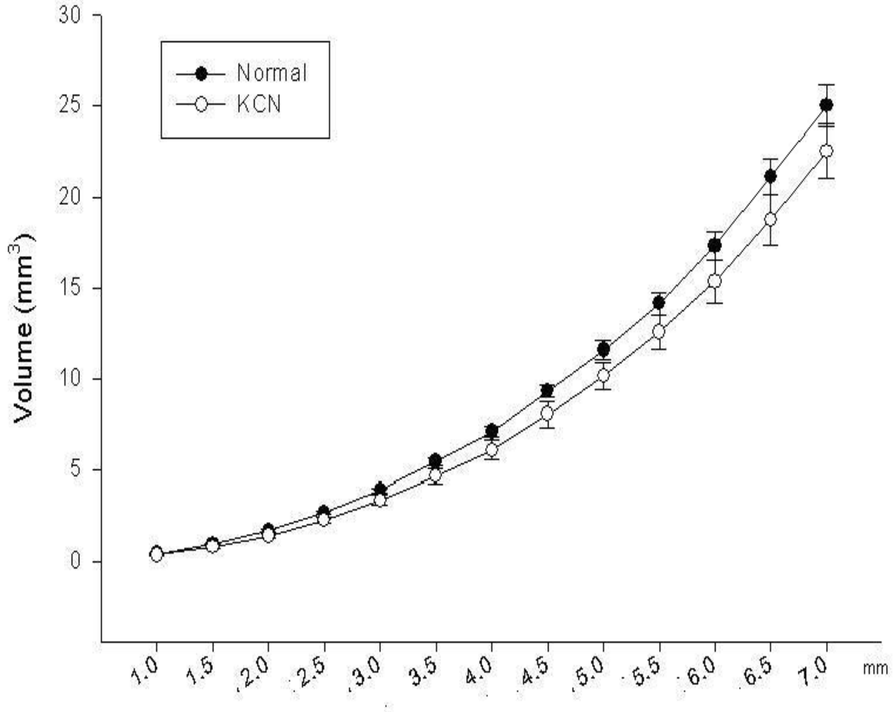


Figure 1. Shows corneal volume distribution in normal and keratoconus patient

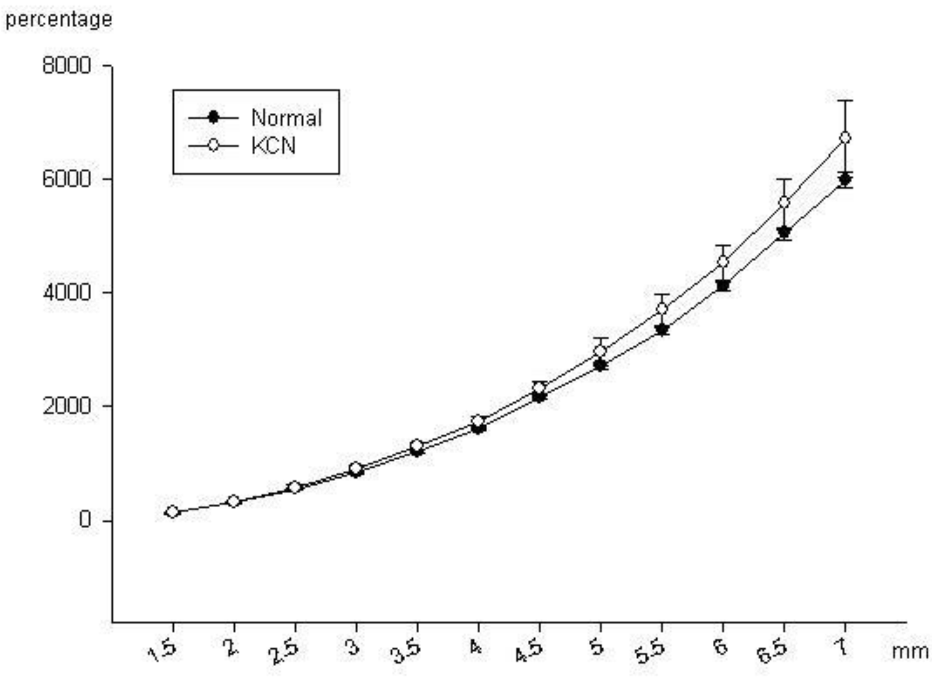
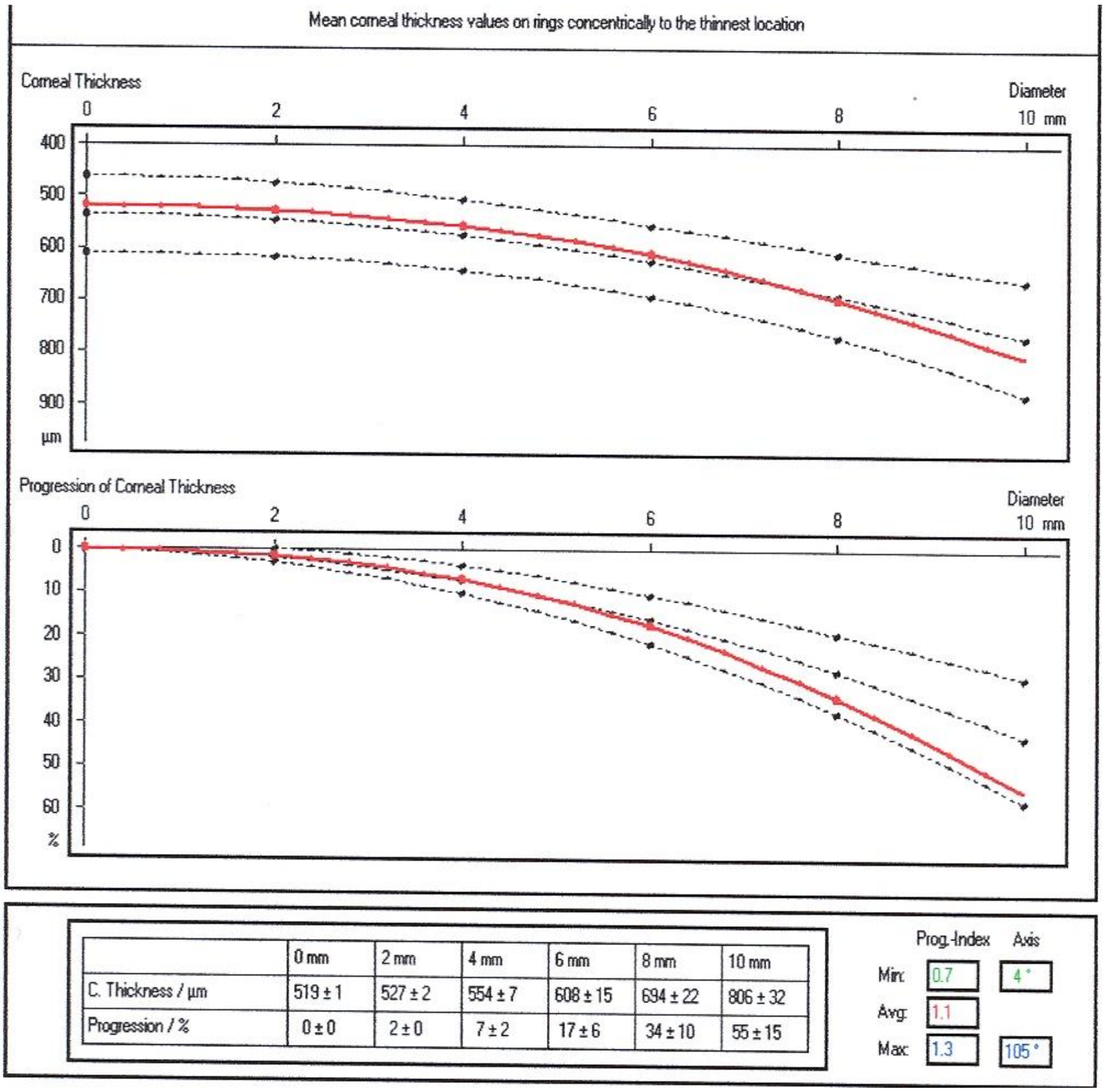


Figure 2. Percentage volume increase from 1 mm diameter in normal and keratoconus patient



	0 mm	2 mm	4 mm	6 mm	8 mm	10 mm
C. Thickness / µm	519 ± 1	527 ± 2	554 ± 7	608 ± 15	694 ± 22	806 ± 32
Progression / %	0 ± 0	2 ± 0	7 ± 2	17 ± 6	34 ± 10	55 ± 15

Figure 3. Pentacam screen of the corneal thickness and progression of corneal thickness

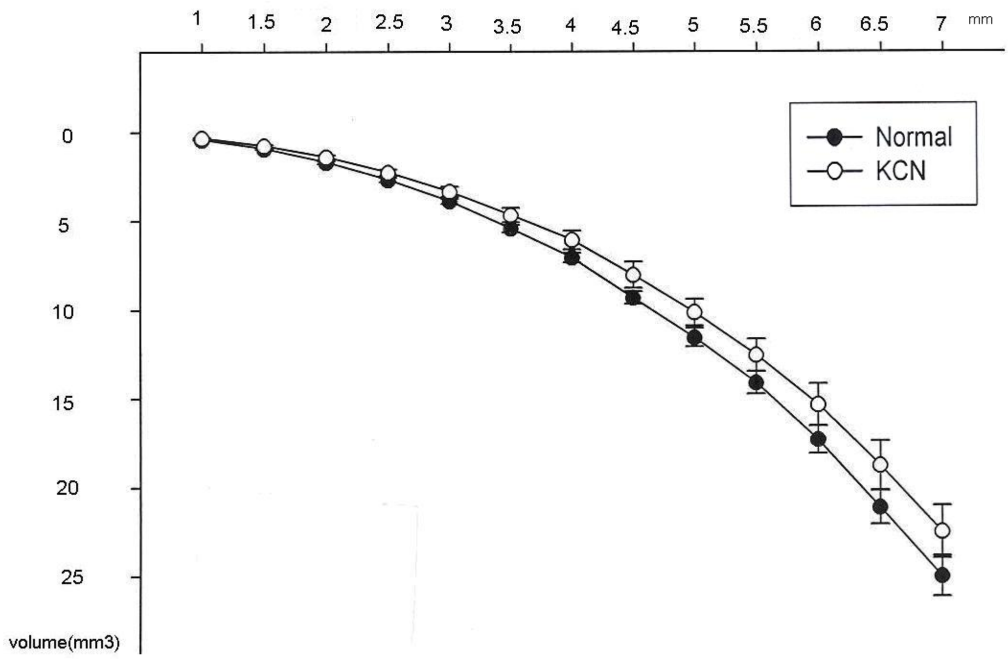


Figure 4. Corneal volume distributions in normal and keratoconic eyes

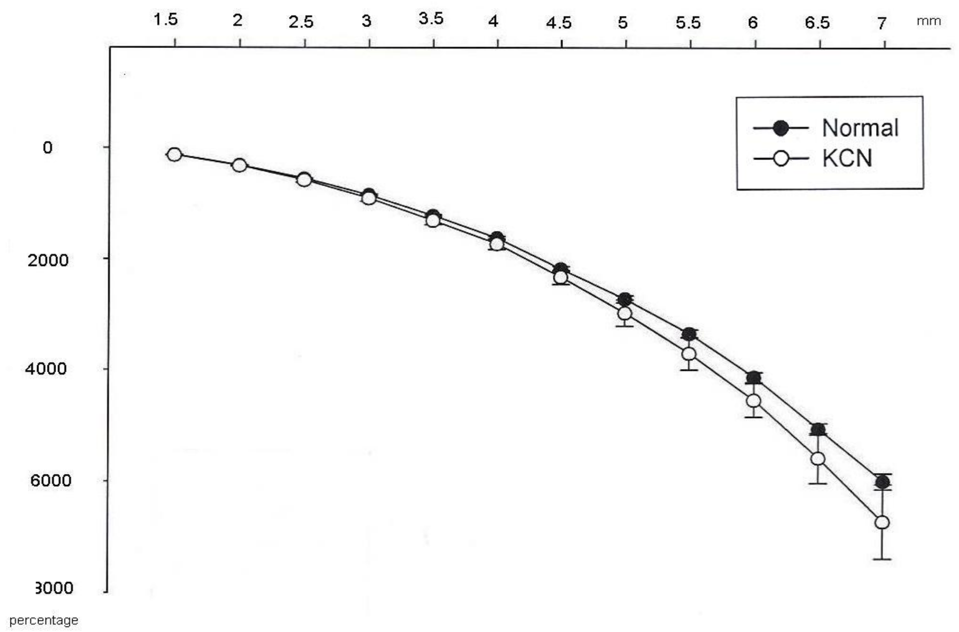


Figure 5. Percentage increase in thickness in normal and keratoconic eyes, y-axis shows percentage of volume increase

Discussion

The aim of this study was to investigate corneal tomography indices such as corneal volume distribution and percentage increase in volume derived from Pentacam Eye Camera for detection of keratoconus.

Keratoconus and forme fruste keratoconus should be regarded as contraindications to refractive surgeries specially LASIK because of developing postoperative ectasia.[4] Several topography based screening tools related to the corneal surface have been developed to detect eyes with keratoconus.[10-12] However, Ambrosio et al[16] firstly introduced new corneal tomography findings, corneal thickness spatial profile to determine characteristics which may help to detect keratoconus. Corneal thickness at the thinnest point was used for spatial thickness profiles and volume centered on the thinnest point. Significant differences were found in all positions of the spatial thickness profile and volume distributions, with lower values for each in keratoconic eyes.

Keratoconic corneas were thinner with less volume and a more abrupt increase as one moved outward from the thinnest point of the cornea than normal eyes.

The results of our study are in agreement with the result of Ambrósio et al.[16] Although in their study the percentage increase in volume was statistically significant only between 3.5 mm and 7.0 mm diameters, however, in our study the percentage increase in corneal volume was statistically higher in keratoconic corneas than normal corneas in all positions. However, attention to figure 2 reveals that the difference between two groups is more apparent from 3 mm toward periphery and the slope of the keratoconus patients curve is steeper than normal eyes. In agreement to our result, Luz et al[17] investigated the variation and progression of the pachymetric values from the thinnest point towards the limbus in normal and keratoconic corneas using the Orbscan. They found statistically significant different values for all circles and conclude that there is greater pachymetric variability in patients with keratoconus and also a faster progression of pachymetric values than healthy eyes.

In the support of the discriminative role of corneal thickness indices for distinguishing keratoconus from contact lens-induced corneal thinning, Pflugfelder et al[18] evaluated two indices generated from measurements obtained from the Orbscan Corneal Topography System. They used the corneal thickness index (CTI) and discriminant function 1 [DF1]. CTI in keratoconus patients (1.28±0.15) was significantly greater than in contact lens-wearing (1.10±0.03; P<0.001) and normal eyes (1.09±0.04; P<0.001). The CTI was not significantly different between normal and contact lens wearers (P=0.67). They stated that corneal thickness indices generated from the Orbscan CTS appear to be sensitive and specific for diagnosing keratoconus from contact lens-induced corneal thinning. Although this method did not become available, and not followed by other studies.

In previous studies, excellent correlation was reported between thickness measurements by the Pentacam and those by ultrasound pachmetry and other methods.[19,20] Recently, Sanctis et al[21] compared repeatability and reproducibility of rotating Scheimpflug camera and ultrasound pachymetry in measuring central thickness of keratoconic corneas and found that Scheimpflug camera provides measurements of central thickness that are more reproducible and repeatable than those obtained with ultrasound pachymetry. Ultrasound pachymetry was less reproducible and repeatable; importantly, when using ultrasound pachymetry in keratoconic corneas, different examiners and measurements repeated by the same examiner may record thickness values that are clinically different.[21]

Conclusion

This study was designed to provide guidance in evaluating spatial profile of corneal thickness and volume from topography for evidence of mild forms of keratoconus. This spatial profile of cornea together with the previous corneal surface features[22] could improve the sensitivity and specificity for the detection of very early forms of keratoconus. The Pentacam software could draw the graph of the corneal thickness of the patient and compare it with the normal population (Figure 3). If it is out of boundaries of standard deviation then it will be considered abnormal. Furthermore, the Pentacam could perform the same procedure for the percentage increase of corneal thickness from the thinnest point to periphery and draw normal and standard deviation graphs and using the normal and corneal progression index graphs, detects keratoconus cornea.

As keratoconus eyes have thinner cornea, there is a need for a reproducible, repeatable and accurate measurements of corneal thickness for diagnosis, staging, and follow-up of this disease, as well as planning surgical procedures. It seems that Pentacam derived parameters like corneal volume distribution and percentage increase in volume can be helpful in differentiation of mild and moderate forms of keratoconus from normal corneas. The difference between keratoconus from normal corneas is more apparent from 3 mm toward periphery and the slope of the keratoconus patients curve is steeper than normal eyes.

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