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Comparative Study between the Corneal Volume in Mild and Severe Keratoconic Eyes Using Pentacam Tomography

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ABSTRACT

Background: Keratoconus is the most common corneal ectasia. It usually appears in the second decade of the life and affects both genders and all ethnicities. Tomographic-based data have added significantly more information to the screening of corneal ectasia. In addition to anterior corneal analysis, tomography also provides information about the posterior cornea and the pachymetric distribution, which can increase our ability to identify early and subtle corneal changes.

Aim of the Work: The main aim is to determine how the corneal volume measurement changes in different diameters of corneal tissue, in the central 3 mm and 5 mm in mild and severe cases of keratoconus; in an attempt to quantify the loss of corneal tissue in keratoconus.

Patients and methods: This cross-sectional study included 20 eyes of keratoconic patients, from 15 to 36 years old. They were divided into 2 groups, each group included 10 eyes: Group A: mild keratoconic cases with steepest keratometry reading lower than 45 D. Group B: severe cases with steepest keratometry greater than 52 D, All cases were diagnosed as keratoconus using pentacam parameters.

Results: Corneal volume at 3 and 5 mm diameter was significantly lower in the severe keratoconic cases than in mild cases ($P<0.01$).

Conclusion: based on the data in our study, we think the effect of keratoconus is not limited to corneal thickness. Rather, it affects all anterior segment parameters of the eye and results in significant alternations with the progression of the disease. There is a clear reduction of corneal volume in early keratoconus, and such reduction increases significantly with the severity of the disease. Measurement of corneal volume could prove to be a useful tool to monitor the progression of the disease and in other applications, such as assessing the effect of treatments including corneal collagen crosslinking and implatation of Intacs.

Recommendations: Further studies on a larger scale of patients are needed to confirm the results obtained by this work.

Keywords: corneal volume, keratoconus, pentacam tomography.

INTRODUCTION

Keratoconus is a chronic, bilateral, usually asymmetrical, non-inflammatory, ectatic disorder, being characterized by progressive steepening, thinning and apical scarring of the cornea [(1)]. As the cornea steepens, the amount of astigmatism increases, causing a distortion of the image which reduces visual acuity of affected patients [(2)].

Keratoconus is a complex condition that involves both external factors, such as allergies and eye rubbing, and genetics factors [(3)]. Severity of the disease has been shown to be associated with family history and ethnic origin [(4)].

Histological studies have described how, in the advanced stages of keratoconus, the basal cells of the epithelial layer eventually disappear, leaving the epithelium with only one or two layers of superficial flattened cells [(5)].

In the advanced stages of keratoconus, Bowman's layer may present prominent fracture lines [(6)] that are thought to occur in weak areas due to the inability to withstand normal intraocular pressure or physical stress, such as that caused by eye rubbing, leading to breaks [(7)]. The collagen lamellae in the keratoconic stroma slides resulting in loss of their natural arrangement and corneal thinning.

The basic diagnostic examinations for keratoconus include placido disk–based corneal topography, Orbscan I and II slit topography, Pentacam Scheimpflug imaging [(8)].

Corneal tomography provides 3-dimensional reconstruction of the cornea, enabling evaluation of the anterior and posterior corneal surfaces and creation of a pachymetric map [(9)]. Corneal thickness spatial profile, corneal volume (CV) distribution, percentage increase in thickness, and percentage increase in volume were studied, and it was reported that these parameters could serve as indices to diagnose keratoconus and screen refractive candidates [(10)].

Among the numerous morphologic parameters that can be measured by modern examination techniques is the CV, it reflects topographical and pachymetric changes and characterizes corneal morphometric changes with a single value [(11)].

CV was recently identified as an additional screening factor for keratoconus [(12)]. Significant differences in CV have been reported between normal and moderate keratoconic eyes, suggesting

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the potential role for CV as a diagnostic factor for corneal ectatic disorders [(10)].

AIM OF THE WORK

The main aim is to determine how the corneal volume measurement changes in different diameters of corneal tissue, in the central 3 mm and 5 mm in mild and severe cases of keratoconus,
in attempt to quantify the loss of corneal tissue in keratoconus.

PATIENTS AND METHODS

This study was a cross sectional study. It included 20 eyes of keratoconic patients, from 15 to 36 years old .They were divided into 2 groups, each group included10 eyes:

- Group A: mild keratoconic cases with steepest keratometry reading lower than 45 D.
- Group B: severe cases with steepest keratometry greater than 52 D. All cases were diagnosed as keratoconus using pentacam parameters.

Exclusion criteria were:

1. Any history of systemic or ocular disease (other than keratoconus).
2. Systemic or ocular medications.
3. Previous ocular surgery or trauma.
4. Pregnancy or nursing.
5. Severe corneal scarring or opacification

The study was done according to the standards of the ethical committee of the Faculty of Medicine, Ain Shams University and informed consent was obtained from every patient.

A complete ophthalmic history and full ophthalmic examination were done for each patient including:

1. **History taking** including previous ocular trauma, medications or surgeries.
2. **Visual acuity** assessment (best corrected visual acuity).
3. **Ophthalmological examination** using slit lamp biomicroscopy for assessment of the anterior segment and fundus examination.

Pentacam tomography was done for each patient, the subjects Placed their chin on the chin rest and were asked to fixate on the black ring that is situated in the center of the blue LED slit emitted from the head unit. Three scans were obtained for each subject under reduced room illumination to avoid unwanted corneal reflections.

The Oculus Pentacam software provides a quality specification index for the data obtained. Using this index, the best quality image/map for each subject was identified and used for the analysis. The Pentacam software constructs the 3-dimensional image of the anterior segment and calculates the total corneal volume.

We calculated the corneal volume at 3 and 5 mm diameter using this 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].

- Eyes were assessed for the following **parameters**:
  - Corneal thickness at the apex (CTA)
  - Thinnest corneal thickness (TCT)
  - Anterior chamber depth (ACD)
  - Corneal volume (CV)
  - Corneal keratometry (K)
  - Corneal asphericity (Q)

After completion of data extraction, statistical analysis was done using SPSS.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**.** **(**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean and standard deviation. Values were considered significant if P value < 0.05.

The used tests were:

1 - Chi-square test

For categorical variables, to compare between different groups.

2 - Fisher's Exact

Correction for chi-square when more than 20% of the cells have expected count less than 5.

3 - Student t-test

For normally distributed quantitative variables, to compare between two studied groups.

RESULTS

Twenty eyes from 20 keratoconic subjects were included in the study, 10 in each group. Age ranged from 15 to 36 years.

No significant difference between the 2 groups as regards sex, age and the examined eye.

P values were (1.000, 0.678 and 0.650) respectively. (**Tables 1, 2)**

Table (1): Comparison between the two studied groups according to demographic data

	Group A (n= 10)		Group B (n= 10)		Test of sig.	p
	No.	%	No.	%		
Sex						
Male	5	50.0	6	60.0	□□= 0.202	1.000
Female	5	50.0	4	40.0		
Age (years)						
Min. – Max.	15.0 – 36.0		15.0 – 36.0		t= 0.421	0.678
Mean ± SD.	26.20 ± 7.76		24.80 ± 7.08			

Table (2): Comparison between the two studied groups according to eye

	Group A (n= 10)		Group B (n= 10)		FE	p
	No.	%	No.	%		
Eye						
Left	5	50.0	3	30.0	0.833	0.650
Right	5	50.0	7	70.0		

Table (3): Comparison between the two studied groups according to corneal thickness at the apex and thinnest corneal thickness

	Group A (n= 10)	Group B (n= 10)	T	P
Corneal thickness at the apex (micron)				
Min. – Max.	441.0 – 606.0	378.0 – 431.0	6.098*	<0.001*
Mean ± SD.	498.7 ± 47.37	400.9 ± 18.13		
Thinnest corneal thickness (micron)				
Min. – Max.	427.0 – 599.0	355.0 – 425.0	6.031	<0.001*
Mean ± SD.	487.1 ± 46.20	390.1 ± 21.27		

The mean corneal thickness at the apex in group A (498.7 ± 47.37) was statistically significantly greater than that of group B (400.9 ± 18.13), P < 0.001.

The mean thinnest corneal thickness in group A (487.1 ± 46.20) was statistically significantly greater than that of group B (390.1 ± 21.27), p < 0.001 **(table 3).**

Table (4): Comparison between the two studied groups according to anterior chamber depth (mm)

	Group A (n= 10)	Group B (n= 10)	T	P
Anterior chamber depth (mm)				
Min. – Max.	2.38 – 3.91	3.37 – 4.34	3.363*	0.003*
Mean ± SD.	3.20 ± 0.43	3.74 ± 0.26		

In group A, the mean anterior chamber depth was 3.20 ± 0.43. In group B, the mean was 3.74 ± 0.26, P value = 0.003. According to these values the anterior chamber was significantly deeper in group B. (**Figure 18)**

Table (5): Comparison between the two studied groups according to corneal keratometry

	Corneal keratometry	Group A (n= 10)	Group B (n= 10)	T	p
Front	**K1**			9.462*	<0.001*
	Min. – Max.	36.90 – 43.50	46.80 – 53.80		
	Mean ± SD.	41.71 ± 1.82	50.88 ± 2.46		
	K2			11.732	<0.001*
	Min. – Max.	42.10 – 45.10	53.30 – 61.40		
	Mean ± SD.	43.87 ± 1.10	56.29 ± 3.16		
Back	**K1**			8.312	<0.001*
	Min. – Max.	-6.50 – -5.50	-8.40 – -6.80		
	Mean ± SD.	-5.94 – 0.29	-7.65 ± 0.58		
	K2			9.193	<0.001*
	Min. – Max.	-7.20 – -5.90	-9.60 – -7.60		
	Mean ± SD.	-6.45 ± 0.39	-8.57 ± 0.61		

In group A the mean keratometry reading (K1) in corneal front was 41.71 ± 1.82, in group B was 50.88 ± 2.46. p <0.001. The mean K2 in corneal front was 43.87 ± 1.10 in group A, and was 56.29 ± 3.16 in group B. P <0.001.

Regarding the corneal back (group A) the mean K1 was -5.94 – 0.29 and the mean K2 was -6.45 ± 0.39.

In group B the corneal back, the mean K1 was -7.65 ± 0.58 and the mean K2 was -8.57 ± 0.61. p<0.001.

According to these values the corneal keratometry readings were statistically significantly greater in group B in the corneal front and back.

Table (6): Comparison between the two studied groups according to corneal volume

	Group A (n= 10)	Group B (n= 10)	T	P
Corneal volume (mm3)			1.799	0.089
Min. – Max.	52.60 – 66.0	49.0 – 57.90		
Mean ± SD.	56.97 ± 3.85	54.15 ± 3.12		
Corneal volume at 3 millimeter diameter (mm3)			6.588*	<0.001*
Min. – Max.	12.90 – 17.20	11.04 – 12.60		
Mean ± SD.	14.36 ± 1.18	11.65 ± 0.54		
Corneal volume at 5 millimeter diameter (mm3)			4.723*	<0.001*
Min. – Max.	24.60 – 31.02	20.60 – 24.60		
Mean ± SD.	26.27 ± 1.88	22.94 ± 1.19		

In group A: the mean corneal volume was 56.97 ± 3.85 mm3 while in the group B the mean corneal volume was 54.15 ± 3.12 mm3, P = 0.089. There is no significant difference between the two groups.

At 3 mm diameter the mean corneal volume was 14.36 ± 1.18 mm3 in the group A and 11.65 ± 0.54 mm3 in the group B. P<0.001. At 5 mm diameter, the mean corneal volume was 26.27 ± 1.88 mm3 in the group A and was 22.94 ± 1.19 mm3 in the group B, P <0.001. The corneal volume at 3 and 5 mm diameter was significantly lower in severe cases.

Table (7): Comparison between the two studied groups according to corneal asphericity

	Group A (n= 10)	Group B (n= 10)	T	P
Corneal asphericity				
Min. – Max.	0.40 – 0.85	0.76 – 1.58	7.383*	<0.001*
Mean ± SD.	0.60 – 0.16	1.22 ± 0.21		

The mean corneal asphericity in group A was 0.60 – 0.16 and was 1.22 ± 0.21 in the group B. P<0.001. It was statistically greater in group B**.**

DISCUSSION

Keratoconus and forme fruste keratoconus should be regarded as contraindications to refractive surgeries specially LASIK because of developing postoperative ectasia [13]. Several topography based screening tools related to the corneal surface have been developed to detect eyes with keratoconus [14].

However, Ambrosio *et al* [10] firstly introduced new corneal tomography findings to determine characteristics which may help to detect keratoconus.

Corneal tomographic indices have been suggested as good descriptors for corneal ectatic conditions, hypothesizing that they could be even better than corneal topography [10].

Corneal tomography provides 3-dimensional reconstruction of the cornea, enabling evaluation of the anterior and posterior corneal surfaces and creation of a pachymetric map [9].

Corneal thickness spatial profile, corneal volume (CV) distribution, percentage increase in thickness, and percentage increase in volume were studied, and it was reported that these parameters could serve as indices to diagnose keratoconus and screen refractive candidates [10].

Among the numerous morphologic parameters that can be measured by modern examination techniques is the CV, it reflects topographical and pachymetric changes and characterizes corneal morphometric changes with single value [11].

It is established that the cornea in keratoconus undergoes thinning with degradation of tissue; however, it is not clear at what stage of the disease this becomes apparent. While it may seem intuitive that the volume in a cylinder of tissue measured within the zone of corneal thinning would be lower (compared to the same diameter in a thicker cornea), the possibility that redistribution of tissue (as opposed to loss of tissue) occurs, cannot be discounted. Since the CV is a numerical value, it may be useful for a statistical analysis of the entire cornea. CV has been proposed as an index to diagnose keratoconus and screen refractive candidates [10].

The present study evaluated corneal volume in subjects with different severities of keratoconus. The volume contained within different diameter discs (3 and 5 diameter) centered on the corneal apex in 20 keratoconic corneas.

10 of them were mild keratoconus (who had steepest Keratometry reading lower than 45 D) compared to 10 severe cases (who had steepest keratometry greater than 52 D) based on pentacam parameters, in an attempt to quantify the loss of corneal tissue in keratoconus.

The mean corneal volume in the mild group at 3mm diameter was 14.36 ± 1.18 and 11.65 ± 0.54 in the sever group. $p < 0.001$.

At 5 mm diameter the mean corneal volume was 26.27 ± 1.8 8 mm in mild group and was 22.94 ± 1.19 mm in sever group. $p < 0.001$.

The CV was statistically significantly lower in the severe keratoconic group in the two diameter analyzed, this could indicate loss of corneal tissue which could be related to increased proteinase activity accompanied by decreased proteinase inhibitors [15].

The pentacam system can evaluate the cornea and anterior segment of the eye from the anterior surface of the cornea to the posterior surface of the lens. Anterior chamber depth (ACD) is a major parameter of the pentacam.

In our study, the mean ACD in the sever group was 3.74 ± 0.26 mm, higher than the mean (3.20 ± 0.43 mm) in the mild group.

ACD was significantly deeper than in mild group and ACD became deeper as the disease progressed.

Accurate measurement of the ACD is important in the implantation of phakic intraocular lenses (pIOLs), and there are reports of pIOL implantation for the management of keratoconus [20]. Thus, the progressive increase in ACD may be an advantage in keratoconic patients in terms of implantation of pIOLs.

Our results are broadly in agreement with previous work from **Emre *et al.*** [12] they reported that the ACD was significantly deeper in seveer keratoconus. The mean ACD in mild cases was 3.2 ±0.3mm and 3.7 ±0.4 mm in severe cases. This study also showed a progressive decrease in corneal volume (CV) with the progression of the disease. The mean CV in the severe keratoconus group was 2.30 mm^3 smaller than that in the mild group.

There were statistically significant differences in corneal volume between the mild and severe groups. In 2006, **Ambrosio *et al.*** [10] reported that the CV measurement in eyes with mild to moderate keratoconus were significantly lower than those in a group of normal eyes. According to the authors, keratoconic corneas had

a mean volume 0.94 mm3 less than the mean volume in the normal eyes.

In our study, the mean corneal asphericity was statistically greater in the severe group, this indicates that the severe keratoconic corneas had a significant prolate shape in concordance with the steepening occurs.

Similarly, **David *et al.*** [17] worked on 71 eyes of 51 patients divided in to 4 groups keratoconus stage 1, keratoconus stage 2, subclinical and control groups. They evaluated corneal volume, corneal asphericity and pachymetry in these groups. They found that eyes with keratoconus stage 2 had significantly lower corneal volume.

In their study, the central and minimum pachymetry values were statistically significantly lower in the stage 2 keratoconus and stage 1 than in subclinical and control groups ($p < 0.03$).The corneal asphericity was greater in clinical keratoconus than control and subclinical groups, $P<0.01$.

According to the results of our study, the corneal keratometry readings were statistically significantly greater in severe group. Similarly, **Mihältz *et al*.**[19] compared the keratometric, and pachymetric parameters of normal with keratoconic corneas measured by pentacam, they reported that corneal keratometry readings were statistically significantly greater in keratoconic group ($P < 0.001$) and they found the central and minimum pachymetry values were statistically significantly lower in keratoconic group; $P < 0.001$.

In our study, the mean corneal thickness at the apex in severe group was statistically significantly lower than that of mild group.

We found that the thinnest corneal thickness (TCT) measurements progressively decreased with the progression of the disease. The mean TCT in mild group was 487.1 ± 46.20 and in the severe group was 390.1 ± 21.27. These results were in agreement with the results of **Emre *et al.*** [12], the mean TCT in mild group was 484.8±51.6 and in severe group was 374.3±97.4. Progressive corneal thinning is a well-known indicator of the progression of keratoconus.

Similarly, **Ambrósio *et al.*** [16], measured central corneal thickness (CCT), thinnest point (TP) in normal and keratoconic eyes using the Pentacam HR. they found that single-point values, CCT and TP, were statistically significantly lower in keratoconic corneas $P<.001$.

Implantation of Intacs is an alternative surgical modality for patients with clear corneas who are not satisfied with contact lenses or spectacles. Surgeons have tried to implant the ring segments to 70% depth of the cornea with in a 7.0 mm optical zone. Even with procedures performed by the most experienced surgeons, there are reports of ring-segment extrusion [18].

Previously, corneal thickness was the only major parameter to consider before implantation of ring segments. However, it is believed that if surgeons focus on the CV, the risk of extrusion may be reduced [12].

CONCLUSION

Based on the data in our study, we think the effect of keratoconus is not limited to corneal thickness. Rather, it affects all anterior segment parameters of the eye and results in significant alternations with the progression of the disease.

There is a clear reduction of corneal volume in early keratoconus, and such reduction increases significantly with the severity of the disease.

Measurement of corneal volume could prove to be a useful tool to monitor the progression of the disease and in other applications, such as assessing the effect of treatments including corneal collagen crosslinking and Implantation of INTACS.

RECOMMENDATIONS

Further studies on a larger scale of patients are needed to confirm the results obtained by this work.

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