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Corneal Elevation Changes in Normal Population and Keratoconus Patients Using Different Acquisition Diameters with Scheimpflug Imager

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ABSTRACT

Background: Keratoconus is a bilateral, progressive, noninflammatory disease of the cornea which often leads to high myopia and astigmatism with an estimated prevalence of approximately 1 in 2000.

Objective: To detect the changes in corneal elevation values using different acquisition diameters (8, 9 mm) in both normal population and keratoconus patients.

Patients and Methods: This is a cross-sectional clinical trial conducted at the Ophthalmology Department, Menoufia University Hospital, and Tiba eye center, Menoufia, Egypt in the period between January 2019 to December 2020. Two hundred corneas of two hundred subjects were involved and categorized into two groups, a control group with normal cornea100 subjects (group A) and a group with keratoconus100 subjects (group B) both confirmed by clinical examination and pentacam readings.

Results: Receiver operating curve (ROC) analysis was conducted to identify the optimal elevation front parameters levels for prediction of keratoconus. The best cut-off values for front parameters BFS 8mm, BFS 9mm, BFTE 8mm and BFTE 9mm were 6.5, 10.5,2.5,2.5 with (96%,92%,92%,92% sensitivity, and 96%,96%,80%, 72% specificity), respectively. Also, the best cut-off values for back parameters levels for prediction of keratoconus for BFS 8mm, BFS 9mm, BFTE 8mm and BFTE 9mm were 14.0, 25.5, 6.5 and 9.5 mm with (96%, 96%, 80%, 72% sensitivity, and 88%, 96%, 64%, 88% specificity), respectively.

Conclusion: We can conclude that there was a significant increase in elevation back parameters in keratoconus patients compared to control. The best cut-off values for front parameters levels as BFS (8, 9mm) and BFTE (8, 9 mm) was 6.5, 10.5, 2.5, and 2.5 mm, respectively.

Keywords: Corneal elevation, BFS, BFTE, keratoconus, Pentacam**.**

INTRODUCTION

Keratoconus is a bilateral, progressive, non-inflammatory disease of the cornea that often leads to high myopia and astigmatism with an estimated prevalence of approximately 1 in 2000 and an incidence between 50 and 230 per 100,000. It is a multifactorial disease with an unknown exact etiology that impairs the acuity and quality of vision secondary to thinning in and protrusion of the cornea that ultimately affects both eyes [(1)]**.**

Corneal topography is an invaluable screening, diagnostic, and ablation assisting resource. With several million refractive surgery procedures performed annually, corneal topography has gained importance in determining a candidate's suitability for refractive surgery and in monitoring corneal structural changes postoperatively [(2)]**.**

Careful analysis of the preoperative corneal topography is pivotal to avoid postoperative complications, especially corneal ectasia. Iatrogenic keratectasia after refractive surgery is of great interest to refractive surgeons and researchers. Although it is not completely understood, keratectasia is thought to be related to preoperative forme fruste keratoconus or preexisting keratoconus [(3)]**.**

Various parameters in normal eyes, keratoconus suspects as well as established keratoconus have been measured with Scheimpflug imager. Several studies reported that anterior and posterior elevation was the most effective parameters to diagnose early keratoconus. Also, alterations in the corneal thickness, such as a more rapid change from the thinnest point to the periphery, have been reported in early keratoconus even with normal anterior and posterior elevation maps, and evaluating the corneal-thickness (pachymetry) map could help differentiate normal thin corneas from ectaticizing corneas [(4)]**.**

Elevation-based corneal imaging techniques provide valuable information about the anterior and posterior corneal surface elevation properties which were not generated by Placido disk-based topography. Knowledge of these indices is important in the preoperative examination of refractive surgery candidates, the diagnosis of early stages and progression of keratoconus, and keratoconus patients undergoing collagen cross-linking or ring implantation for treatment [(5)]**.**

This study aimed to detect the changes in corneal elevation values using different acquisition diameters

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(8,9 mm) in both normal population and keratoconus patients.

PATIENT AND METHODS

This is a cross-sectional clinical trial including two groups, a control group with normal cornea (group A) and a group with keratoconus (group B) confirmed by clinical examination and Pentacam readings during the period from January 2019 till December 2020.

Ethical considerations:

All study procedures are carried out and approved by the Ethical Committee of Menoufia Faculty of Medicine.

All participants received a detailed explanation about the aim, objectives, and methodology of the study before enrollment with signed informed consent.

We enrolled subjects age between 15 and 40 years, phakic patients with clear lenses, maximum keratometry of less than 60 D in Keratoconic eyes based on Pentacam readings, stop wearing contact lenses for at least for 3 weeks.

Pseudophakia or cataract, corneal scarring in either eye, previous corneal or intraocular surgery, ocular surface or tear problems, the coexistence of ocular pathology other than keratoconus were excluded from the study.

All the patients underwent: History taking included detailed ophthalmic history clinical examination e.g., visual acuity (unaided corrected), refraction, IOP, anterior segment (cornea, anterior segment, and lens), and fundus examination.

Investigations included Scheimpflug imaging (WaveLight® Oculyzer™, AG, Germany) measurements of K-readings, thinnest location, anterior chamber depth, elevation front included maximum readings using different diameters (8,9 mm), elevation back maximum readings using different diameters (8,9 mm).

After the subject's data (name, sex, and date of birth) were entered, the program changed to imaging mode. Then the subject was asked to place his/her chin on the chin rest and the forehead against the headrest. The subject was asked to open both eyes and look at the fixation target. The examiner aligned the joystick until the rotating Scheimpflug camera automatically captured 25 single images within 2 seconds for each eye.

The control group was selected from among the candidates of refractive surgery who did not have a history of ocular surgery and their corneal topography with Pentacam was normal. Keratoconus group diagnosis had been confirmed by thorough clinical examination and corneal topography.

Statistical Analysis

Results were tabulated and statistically analyzed using standard computer program using MICROSOFT EXCEL 2019 and SPSS V.25 program for Microsoft Windows 10. Chi-Squared (χ^2), Mann-whinny test, Student t-test test, and ROC curve were used. P-value is considered statistically significant when it is less than 0.05.

RESULTS

In the current study, there was no significant difference regarding age, gender, and affected side between the studied groups regarding their demographic data **(Table 1)**.

Table (1): Demographic data of studied groups.

Parameter			Control (n=100)	Keratoconic patients (n=100)	P-value
Age*		Mean ± SD	27.4 ± 6.81	27.6 ± 7.75	0.935
Gender	**Male**	Count	20	36	0.075
		%	20.0	36.0	
	Female	Count	80	64	
		%	80.0	64.0	
Affected side	**OS**	Count	44	44	1.00
		%	44.0	44.0	
	OD	Count	56	56	
		%	56.0	56.0	

Chi-Square test, independent T-test*.

There was a significant difference of sphere, cylinder, and spherical equivalent in keratoconus patients compared to control and the comparison of elevation front parameters between different studied groups. There was a significant increase in elevation front parameters in keratoconus patients compared to control **(Table 2).**

Table (2): Comparison of refraction parameters and maximal elevation front points among studied groups

Parameter		Control (n=100)	Keratoconus patients (n=100)	P-value
Sphere	Median	-1.5	-3.25	<0.001
	Min. – Max.	-3.0 to -0.5	-21.5 to -1.00	
Cylinder	Median	-1.0	-3.12	<0.001
	Min. – Max.	-3.0-1.5	-7.25-1.0	
Spherical equivalent	Median	-2.5	- 4.5	<0.001
	Min. – Max.	-3.5 to -1.25	-24.5 to -1.5	
BFS 8mm	Median	4.0	20.0	<0.001
	Min. – Max.	1.0-10.0	6.0-66.0	
BFS 9mm	Median	5.0	28.0	<0.001
	Min. – Max.	2.0-12.0	9.0-85.0	
BFTE 8mm	Median	2.0	5.0	<0.001
	Min. – Max.	1.0-4.0	2.0-18.0	
BFTE 9mm	Median	2.0	7.0	<0.001
	Min. – Max.	1.0-5.0	2.0-18.0	

Mann-Whitney tests. **P** between 2 groups **significant (P-value < 0.05)

The comparison of Pentacam parameters between different studied groups. There is a significant elevation of front parameters as K1 (46.7 vs. 42.7), K2 (49.6vs. 44.2), Km (47.9vs. 43.5) in keratoconus patients compared to control. On the other hand, back parameters as K1 (-6.9 vs. -6.00), K2 (-7.9 vs. -6.3), and Km (-7.3 vs. -6.2) are significantly different in keratoconus patients compared to control, **(Table 3).**

Table (3): Comparison of pentacam parameters among studied groups

Parameter			Control (n=100)	Keratoconus patients (n=100)	P-value
Front	**K1**	Median	42.7	46.7	<0.001
		Min. – Max.	38.9-45.4	42.0 - 58.2	
	K2	Median	44.2	49.6	<0.001
		Min. – Max.	41.0-46.5	45.5 - 63.3	
	KM	Median	43.5	47.9	<0.001
		Min. – Max.	40.7-45.9	44.1- 59.0	
Back	**K1**	Median	-6.00	-6.9	<0.001
		Min. – Max.	-6.5 to -5.5	-9.0 to -6.1	
	K2	Median	-6.3	-7.9	<0.001
		Min. – Max.	-7.0 to -5.9	-10.6 to -6.7	
	KM	Median	-6.2	-7.3	<0.001
		Min. – Max.	-6.7 to -1.6	-9.7 to -6.4	

Mann-Whitney tests. P between 2 groups. **significant (P< 0.05)

ROC analysis was conducted to identify the optimal **elevation front parameters** levels for prediction of keratoconus. BFS 8mm best cut-off values were 6.5 (96.0% sensitivity, 96.0% specificity). The area under the curve (AUC) was 0.987 (p<0.001). BFS 9mm best cut-off values were 10.5(92.0% sensitivity, 96.0% specificity). The area under the curve (AUC) was 0.994 (p<0.001). BFTE 8mm best cut-off values were 2.5(92.0% sensitivity, 80.0% specificity). The area under the curve (AUC) was 0.955 (p<0.001). BFTE 9mm best cut-off values were 2.5(92.0% sensitivity, 72.0% specificity).

The area under the curve (AUC) was 0.954 (p<0.001). Also, ROC analysis was conducted to identify the optimal **elevation back parameters** levels for prediction of keratoconus. BFS 8mm best cut-off values were 14.0(96.0% sensitivity, 88.0% specificity). The area under the curve (AUC) was 0.988 (p<0.001). BFS 9mm best cut-off values were 25.5(96.0% sensitivity, 96.0% specificity). The area under the curve (AUC) was 0.995 (p<0.001).

BFTE 8mm best cut-off values were 6.5(80.0% sensitivity, 64.0% specificity). The area under the curve (AUC) was 0.932 (p<0.001). BFTE 9mm best cut-off values were 9.5(72.0% sensitivity,

88.0% specificity). The area under the curve (AUC) was 0.840 ($p<0.001$), **(Table 4, Figs 1 & 2).**

Table (4): Performance characteristics of elevation back and front parameters for prediction of keratoconus

		AUC	SE	*p-value*	Cut off	Sensitivity (%)	Specificity (%)
Back parameters	**BFS 8mm**	0.988	0.007	<0.001	14.0	96.0	88.0
	BFS 9mm	0.995	0.004	<0.001	25.5	96.0	96.0
	BFTE 8mm	0.932	0.043	<0.001	6.5	80.0	64.0
	BFTE 9mm	0.840	0.043	<0.001	9.5	72.0	88.0
Front parameters	**BFS 8mm**	0.987	0.008	<0.001	6.5	96.0	96.0
	BFS 9mm	0.994	0.005	<0.001	10.5	92.0	96.0
	BFTE 8mm	0.955	0.018	<0.001	2.5	92.0	80.0
	BFTE 9mm	0.954	0.019	<0.001	2.5	92.0	72.0

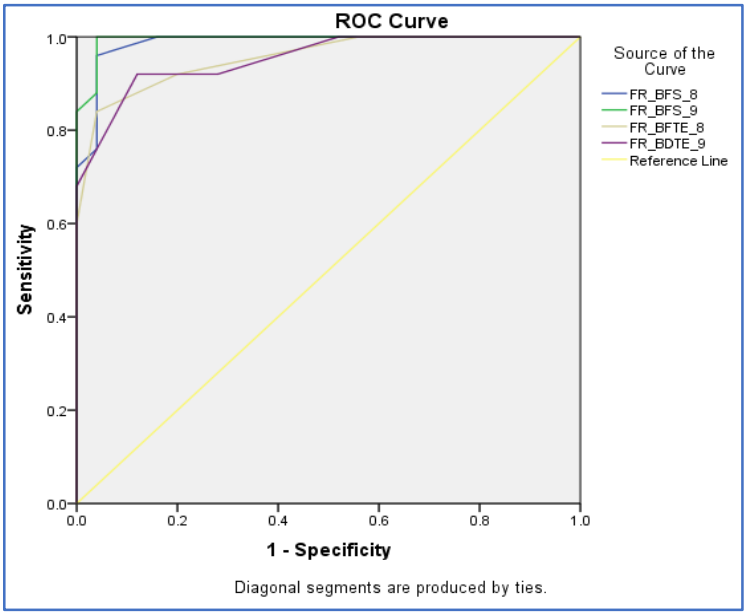

Fig. (1): Performance characteristics of elevation front parameters for prediction of keratoconus.

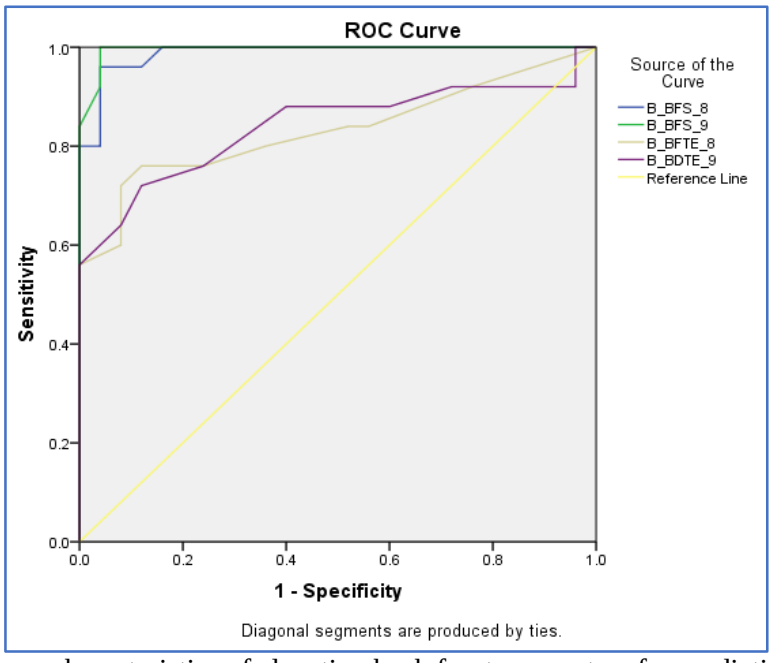

Fig. (2): Performance characteristics of elevation back front parameters for prediction of keratoconus.

DISCUSSION

The last decade has seen a dramatic change in the diagnosis and early identification of keratoconus and other ecstatic disorders. imaging techniques have played a large part in this change. This new information offered by anterior segment tomography not only allows for earlier identification of disease but has altered our perception of what constitutes keratoconus. Tomographic imaging offers significant advantages over traditional Placido-based curvature analysis (topography) [6].

Elevation-based imaging allows for the measurement of both the anterior and posterior corneal surfaces. The accurate measurement of both the anterior and posterior corneal surfaces and the anterior lens allows for the creation of a three-dimensional reconstruction of the anterior segment which gives much more diagnostic information than was previously available. Posterior measurements are often the first indicators of future ecstatic disease, despite completely normal anterior curvature. Examination of the posterior corneal surface can often reveal pathology that would otherwise be missed if one was relying on anterior analysis alone. The ability of elevation- based topography to analyze both anterior and posterior corneal surfaces allows identifying eyes at risk. **Martin [7],** Also, **Uçakhan and Yeşiltaş [8]** investigated several Pentacam parameters in subclinical keratoconus, keratoconus, and normal eyes. They found that the Scheimpflug system could differentiate between ectatic and normal eyes. Scheimpflug devices provide elevation maps of both the anterior and the posterior corneal surface. Posterior elevation analysis is considered to provide valuable adjuvant diagnostic data in discriminating cases of subclinical KC from normal ones; therefore, it is commonly used in clinical settings. To provide accurate elevation maps, a series of reference bodies have been developed to simulate the human corneal surface.

Pentacam allows for measuring local elevation points by fitting the corneal shape to a best-fit sphere (BFS) reference surface with variable diameters or to a best-fit toric ellipsoid surface (BFTE), which simulates more the corneal shape than the BFS. For instance, some prefer using BFS based on the analysis of 8mm zone around the corneal apex, especially for refractive surgery screening others keep the device default at 9mm zone, although there are some concerns about it; that is, it is more difficult to get reliable scans without wide palpebral fissure [9].

On the contrary, BFTE has been recommended for use by other studies, as they concluded that toric ellipsoid reference surface is the most sensitive reference body to compare KC to normal corneas**. Roshdy *et al.* [10].** reported that posterior elevation from both 8mm BFS and BFTE had the highest AUROC (0.983 and 0.986, respectively).

In our study, there was no significant difference in age and gender between the 2 included groups (p=0,935and$p$=0,075). There is a significant reduction of Corneal volume (Mean ± SD normal group(A)58.59 ± 3.7 keratoconus group(B)55.14 ± 3.52) and thinnest location (normal group(A)525.0, keratoconus group(B) 443.0) in keratoconus patients compared to control. on the other hand, Maximal Keratometry (K max) (K max normal group (A) 44.5, K max keratoconus group(B) 55.2) and Anterior Chamber Depth (ACD)(group(A) 3.2, group(B) 3.32) are significantly elevated in keratoconus patients compared to control (p<0.001).

Comparing Pentacam k-reading (k1, k2, km) between different studied groups showed that there is a significant elevation of front parameters in keratoconus patients compared to control. On the other hand, back parameters are significantly decreased in keratoconus patients compared to control (p<0.001). With the appearance of many KC indices and suggestion of various best-fit reference surfaces, the goal of our study was to evaluate the accuracy (including both sensitivity and specificity) of such indices with the use of different reference surfaces, at different diameters between the included groups BFS 8mm (96% sensitivity, 88% specificity). BFS 9mm (96% sensitivity, 96% specificity). BFTE 8mm (80% sensitivity, 64% specificity). BFTE 9mm (72% sensitivity, 88% specificity).

Another study by **Hashemi *et al.* [11]** stated that keratoconus should be suspected in eyes with an anterior elevation greater than 15μm and posterior elevation greater than 20 μm. In this study, we found that elevation data (anterior and posterior) were statically different between the two studied groups**.** Elevation front values (BFS 8mm best cut-off values were 6.5, BFS 9mm best cut-off values were 10.5, BFTE 8mm best cut-off values were 2.5, BFTE 9mm best cut-off values were 2.5) showed significantly higher numbers in keratoconus patients compared to control(p<0.001). Another study by **Hwang *et al.* [12]** stated that mean values of maximum posterior elevation and irregularities were higher in keratoconus than control eyes. In our study, the comparison of elevation back parameters using best fit sphere and best fit toric ellipsoid as reference surfaces and using different radii of curvature 8mm and 9mm between the two studied groups showed significantly higher numbers in keratoconus patients compared to control (p<0.001). The Receiver Operating Characteristic (ROC) curves were used to compare the mean measurements and to evaluate the sensitivity and specificity of the parameters.

In this study anterior elevation from 8mm and 9mm using BFS had higher accuracy with AUROC was 0.987 and 0.994 respectively with best cut off values was 6.5 (which had a sensitivity and specificity

of 96%) and 10.5 (with sensitivity 92% and specificity 96%) respectively than that using BFTE from 8mm and 9mm with AUROC was 0.955 and 0.954 with the best cut off values was 2.5 for both (with sensitivity 92% for both and specificity 80 % and 72%). Concerning the posterior elevation from 8mm and 9mm using BFS had higher accuracy with AUROC was 0.988 and 0.995 respectively with the best cut off values was 14.0 and 25.5 respectively (which had sensitivity 96% for both and specificity 88% and 96%) than that using BFTE from 8mm and 9mm with AUROC was 0.932 and 0.840 with cut off values was 6.5(with sensitivity 80 % and specificity 64%) and 9.5(with sensitivity 72% and specificity 88%)**.** The sensitivity and specificity of the analyzed topographic parameters were higher in keratoconus corneas (Group B) than in normal corneas (Group A). Anterior and Posterior elevations from different reference best-fit surfaces did not differ greatly in their accuracy with various. diameters(8mm,9mm). The AUROC analyses showed high overall predictive accuracy of anterior elevation and posterior elevation for KC (AUROC 0.99 for 9mm BFS with sensitivity and specificity 96%). Contrary to our study **Itoi *et al.*** [(13)] reported that posterior elevation from both 8mm BFS and BFTE had the highest AUROC (0.983 and 0.986, resp).

CONCLUSION

We can conclude that there was a significant increase of elevation back parameters in keratoconus patients compared to control. The best cut-off values for front parameters levels as BFS (8, 9mm) and BFTE (8, 9 mm) was 6.5, 10.5, 2.5, and 2.5 mm, respectively. Also, the best cut-off values for back parameters levels for BFS (8, 9mm), BFTE (8, 9mm) was 14.0, 25.5, 6.5, and 9.5 mm, respectively. Also, anterior elevation values slightly increase with keratoconus indices change. Elevation readings and keratoconus indices in the keratoconus group are higher than the healthy corneas.

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