



2023

Section: Ophthalmology

Role of Epithelial Mapping in Differentiation Between Early Keratoconus And High Regular Astigmatism Using Anterior Segment Optical Coherence Tomography

Mustafa Muhammed Badawi

Giza Memorial Institute for ophthalmic research, Giza, Egypt, drmustafabadawi@gmail.com

Ahmed Salah Abdel Rehim

Ophthalmology Department , Faculty of Medicine, Al-Azhar University, Cairo , Egypt

Abdel Ghany Ali El Gabbar

Ophthalmology Department , Faculty of Medicine, Al-Azhar University, Cairo , Egypt

Follow this and additional works at: <https://aimj.researchcommons.org/journal>



Part of the [Medical Sciences Commons](#), [Obstetrics and Gynecology Commons](#), and the [Surgery Commons](#)

How to Cite This Article

Badawi, Mustafa Muhammed; Rehim, Ahmed Salah Abdel; and Gabbar, Abdel Ghany Ali El (2023) "Role of Epithelial Mapping in Differentiation Between Early Keratoconus And High Regular Astigmatism Using Anterior Segment Optical Coherence Tomography," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 5, Article 29.

DOI: <https://doi.org/10.58675/2682-339X.1825>

This Original Article is brought to you for free and open access by Al-Azhar International Medical Journal. It has been accepted for inclusion in Al-Azhar International Medical Journal by an authorized editor of Al-Azhar International Medical Journal. For more information, please contact dryasserhelmy@gmail.com.

Role of Epithelial Mapping in Differentiation Between Early Keratoconus and High Regular Astigmatism Using Anterior Segment Optical Coherence Tomography

Mustafa Muhammed Badawi ^{a,*}, Ahmed Salah Abdel Rehim ^b,
Abdel Ghany Ali El Gabbar ^b

^a Giza Memorial Institute for Ophthalmic Research, Giza, Egypt

^b Department of Ophthalmology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Abstract

Background: Epithelial thickness mapping can be used adjunctive tool for sensitivity and specificity improvement in early detection of keratoconus screening using Anterior Segment Optical Coherence Tomography (OCT).

Aim: The aim of this study is to detect the role of epithelial thickness mapping in early detection and differentiation between early keratoconus and high regular astigmatism.

Patients and Methods: A cross-sectional observational study included 25 eyes of early keratoconus cases and 25 eyes of high regular astigmatism controls conducted at Magrabi Eye Hospital –Tanta between October 2021 and August 2022.

Results: The findings revealed that the mean central epithelial thickness was significantly thinner in early keratoconus eyes ($49.84 \pm 1.95 \mu\text{m}$) than that in high regular astigmatism ($53.24 \pm 3.72 \mu\text{m}$) (P value = 0.002). Early keratoconus cases had significantly lower thinnest location ($42.92 \pm 2.53 \mu\text{m}$) compared with high regular astigmatism ($46.00 \pm 5.17 \mu\text{m}$) (P value < 0.001).

Conclusion: Measurement of epithelial thickness provided by anterior segment optical coherence tomography-epithelial-mapping is beneficial for early identification of keratoconus.

Keywords: Anterior segment optical coherence tomography, Astigmatism, Epithelial mapping, Keratoconus

1. Introduction

The epithelium layer of the cornea have a protective function including vital role in preserving high-optical-quality. In Keratoconus the epithelium-thickness becomes altered.¹ Analyzing the corneal epithelial thickness can help in detection of the disease in early stage and to differentiate it from similar conditions especially in cases of progressive myopic astigmatism.² Although the cause is unknown, it is believed to occur due to a combination of genetic, environmental, and hormonal factors. About 7% of those affected have a positive family history.³

Prevalence of Keratoconus were determined high among refractive surgeries more than that of general population.⁴ Preoperative detection of keratoconus in refractive surgeries is important to stop the development of postoperative surgical pathology and make it a symptomatic disease, so the need for diagnostic tools that afford high sensitivity for asymptomatic subclinical keratoconus.

Recently, the Optical Coherence Tomography (OCT) produces highly reliable pachymetry and epithelial maps that can detect keratoconus, ectasia and corneal thinning, it is a noninvasive imaging technique that uses low-coherence light to produce

Accepted 21 November 2022.
Available online 30 December 2023

* Corresponding author.
E-mail address: drmustafabadawi@gmail.com (M.M. Badawi).

<https://doi.org/10.58675/2682-339X.1825>

2682-339X/© 2023 The author. Published by Al-Azhar University, Faculty of Medicine. This is an open access article under the CC BY-SA 4.0 license (<https://creativecommons.org/licenses/by-sa/4.0/>).

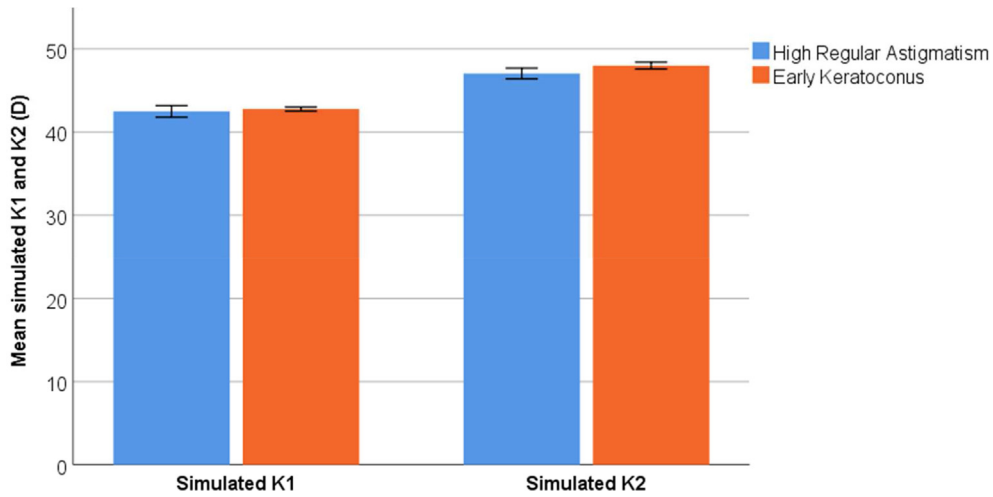


Fig. 1. The mean simulated K1 and K2, in 25 early keratoconus cases and 25 high regular astigmatism controls.

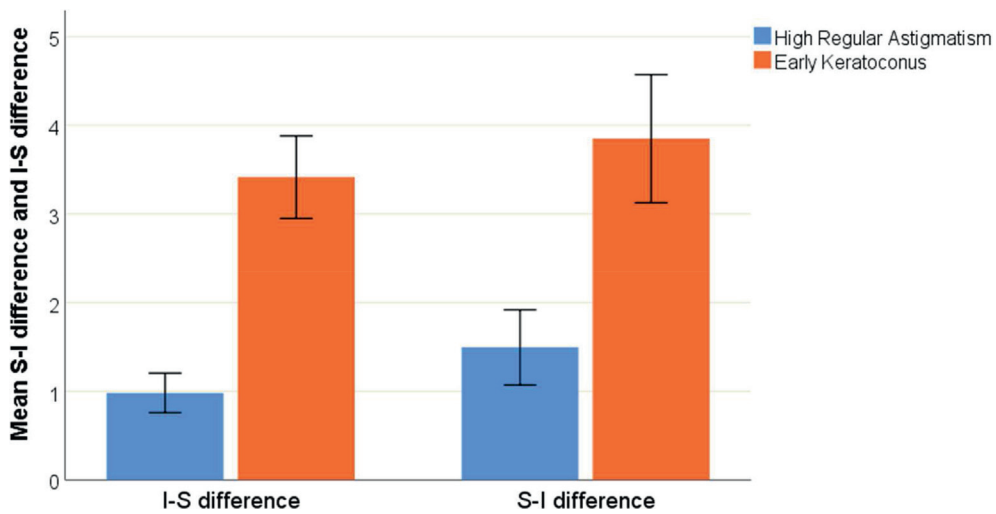


Fig. 2. The mean Superior - Inferior difference (of 11 participants) and Inferior - Superior difference (of 39 participants), in early keratoconus cases and high regular astigmatism controls.

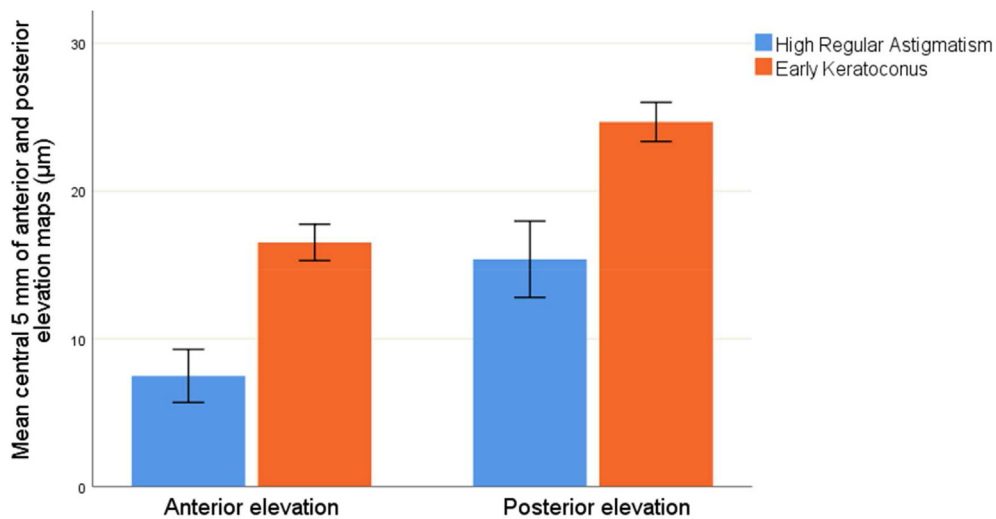


Fig. 3. The mean central 5 mm of anterior and posterior elevation maps in 25 early keratoconus cases and 25 high regular astigmatism controls.

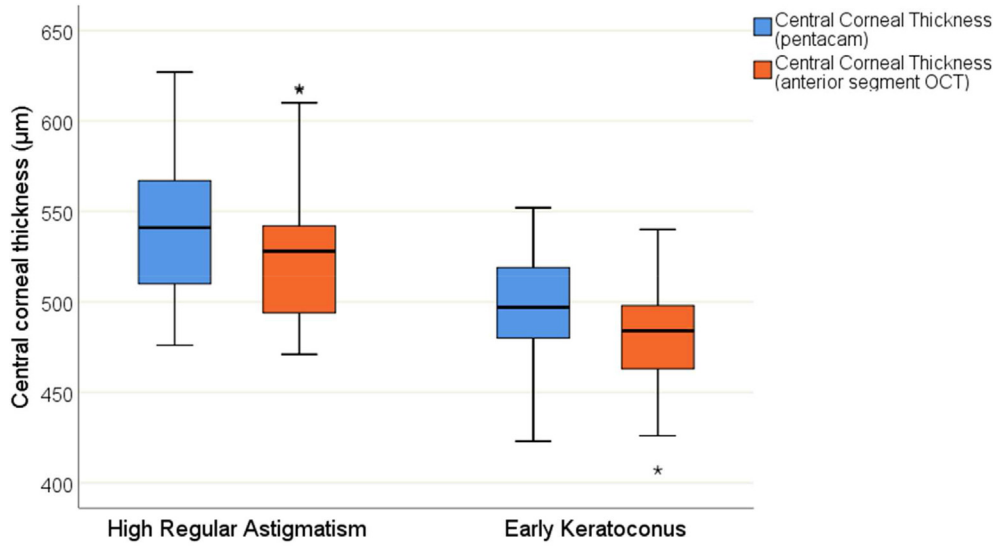


Fig. 4. Central corneal thickness, measured by pentacam and anterior segment OCT in early keratoconus cases and high regular astigmatism controls.

a high-resolution cross-section of tissues.⁵ Epithelial thickness profile maps using Fourier domain OCT provides a significant analysis of the corneal epithelium. These maps have been shown to be useful in detecting subtle epithelial changes, which constitute sign of early keratoconus.⁶ Epithelial thickness profiles may increase the sensitivity and specificity of screening the early keratoconus compared with corneal topography alone and may be useful in clinical practice. As epithelial changes will go before any topographic changes produced on the surface of the cornea, Corneal-epithelial-mapping were developed to detect early keratoconus.⁷

Therefore the aim of this study to evaluate the role of epithelial thickness mapping in early diagnosis of keratoconus differentiate it from the normal high regular astigmatism.

2. Patients and methods

A cross-sectional observational study included 25 eyes of early keratoconus cases and 25 eyes of normal high regular astigmatism controls conducted at Magrabi Eye Hospital –Tanta between October 2021 and August 2022.

Patients with high regular astigmatism and early keratoconus, Cylinder greater than or equal to -3 , K

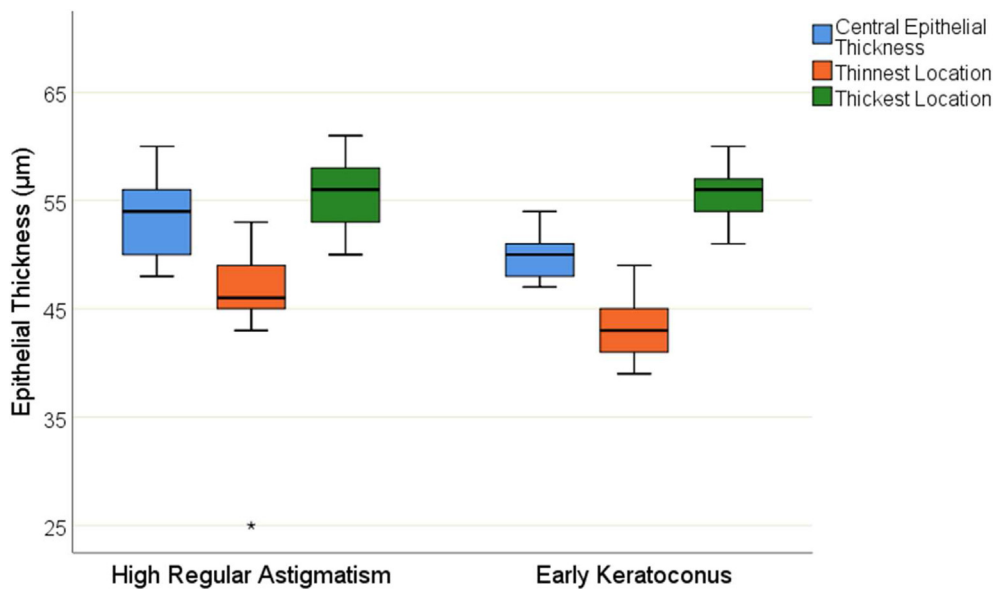


Fig. 5. Central epithelial thickness, Thinnest location and thickest location measured by anterior segment OCT in early keratoconus cases and high regular astigmatism controls.

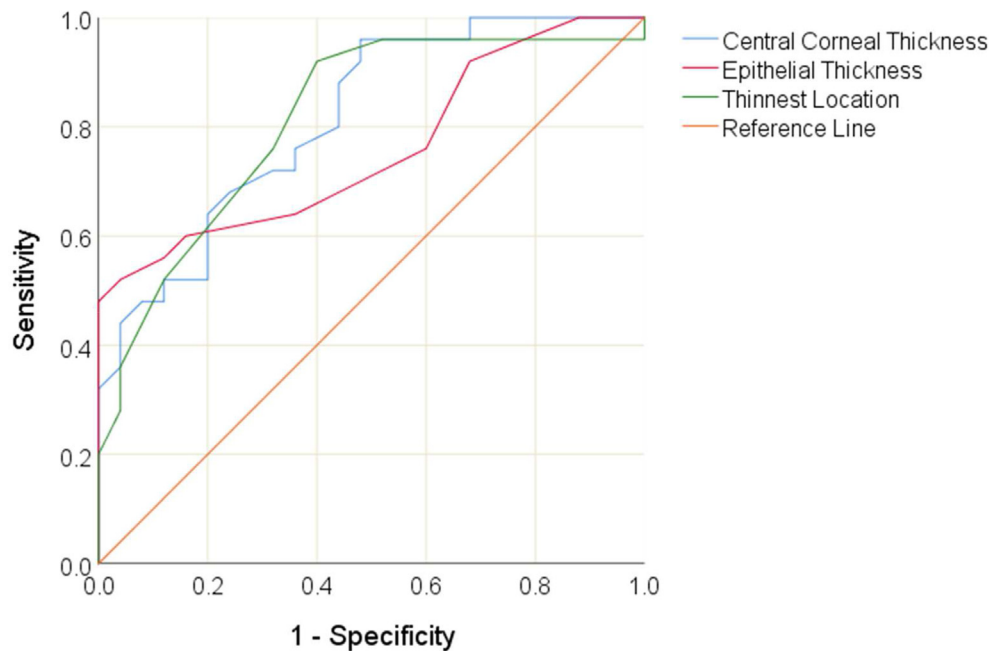


Fig. 6. Receiver Operating Characteristic curve (ROC curve) showing the sensitivity, specificity and total diagnostic accuracy (Area under the curve) of central corneal thickness, epithelial thickness and thinnest location measured by anterior segment OCT in distinguishing early keratoconus cases from high regular astigmatism.

Reading between 45 and 49, and normal fundus were included. While, Patients with corneal opacity, other ocular diseases as uveitis, cataract or

Table 1. Corneal Measurements by Pentacam of 25 early keratoconus cases and 25 high regular astigmatism controls.

Corneal Measurements	High Regular Astigmatism (n = 25)	Early Keratoconus (n = 25)	P value ^b
Simulated K1(D) ^c			
Mean ± SD ^a	42.48 ± 1.68	42.76 ± 0.59	0.662
Range	40.00–44.83	41.90–43.70	
Simulated K2 (D) ^c			
Mean ± SD ^a	47.04 ± 1.55	48.00 ± 0.99	0.013 ^b
Range	45.00–49.90	46.00–49.50	
S–I Difference (n = 11) ^d			
Mean ± SD ^a	1.49 ± 0.62	3.45 ± 0.50	0.036 ^b
Range	0.50–2.30	3.50–4.20	
I–S Difference (n = 39) ^d			
Mean ± SD ^a	0.98 ± 0.43	3.42 ± 1.08	<0.001 ^b
Range	0.40–1.50	1.80–5.20	
Central Corneal Thickness (μm)			
Mean ± SD ^a	546.72 ± 45.53	499.28 ± 32.41	<0.001 ^b
Range	476.00–627.00	423.00–552.00	
Central 5 mm of anterior elevation map (μm)			
Mean ± SD ^a	7.48 ± 4.35	16.52 ± 2.97	<0.001 ^b
Range	2.00–15.00	11.00–20.00	
Central 5 mm of posterior elevation map (μm)			
Mean ± SD ^a	15.38 ± 6.26	24.68 ± 3.21	<0.001 ^b
Range	7.00–28.00	16.00–28.00	

^a SD: Standard deviation.

^b P value is significant if < 0.05.

^c D: Diopter.

^d S - I Difference: Superior - Inferior Difference, I - S Difference: Inferior - Superior Difference.

glaucoma, any pathological abnormality in the fundus, and Frank keratoconus were excluded.

Complete medical history including previous ocular trauma, medications or surgeries. Visual acuity assessment (Best corrected visual acuity) using Snellen's acuity chart and Ophthalmological examination: slit lamp biomicroscopy for assessment of the anterior segment and fundus biomicroscopy for assessment of the retina. Intra ocular pressure measurement by Goldmann applanation tonometry, Pentacam (by OCULUS pentacam, made in Germany) for assessing Simulated K1 and K2,

Table 2. Corneal measurements by anterior segment OCT of keratoconus cases and high regular astigmatism controls.

Corneal Measurements	High Regular Astigmatism (n = 25)	Early Keratoconus (n = 25)	P value ^b
Central corneal thickness (μm)			
Mean ± SD ^a	531.96 ± 44.49	483.52 ± 32.09	<0.001 ^b
Range	471.00–618.00	407.00–540.00	
Central epithelial thickness (μm)			
Mean ± SD ^a	53.24 ± 3.72	49.84 ± 1.95	0.002 ^b
Range	48.00–60.00	47.00–54.00	
Thinnest location (μm)			
Mean ± SD ^a	46.00 ± 5.17	42.92 ± 2.53	<0.001 ^b
Range	25.00–53.00	39.00–49.00	
Thickest location (μm)			
Mean ± SD ^a	55.68 ± 3.38	55.52 ± 2.29	0.807
Range	50.00–61.00	51.00–60.00	

^a SD: Standard deviation.

^b P value is significant if < 0.05.

Table 3. Sensitivity and Specificity and total diagnostic accuracy (Area Under the Curve) of anterior segment OCT measures in distinguishing early keratoconus cases from high regular astigmatism.

Anterior Segment OCT measure	Cutoff value	Sensitivity	Specificity	AUC ^a	95% CI ^b	P value ^c
Central Corneal Thickness (μm)	496.50	0.72	0.68	0.814	0.700–0.929	<0.001 ^a
Epithelial Thickness (μm)	51.50	0.60	0.84	0.758	0.622–0.893	0.002 ^a
Thinnest Location (μm)	44.50	0.76	0.68	0.814	0.693–0.934	<0.001 ^a

^a AUC: Area Under the Curve.

^b 95% CI: 95% Confidence Interval.

^c P value is significant if < 0.05.

Central corneal thickness, S_I difference or I_S difference, the central 5 mm of the anterior elevation map and the central 5 mm of the posterior elevation map. Then patients matching our inclusion criteria will further subjected to next comparative investigation: OCT (by optovue OCT device, made in USA) for assessing central corneal thickness from pachymetry map and from the epithelial map we measured central epithelial thickness, thickest location, thinnest location and their distribution.

All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 25. Data were statistically described in terms of mean and standard deviation, median, range, number and percentage as appropriate.

3. Results

Pentacam keratometry measures significantly different simulated K2 was 48.00 ± 0.99 D in early keratoconus cases, and 47.04 ± 1.55 D in high regular astigmatism controls (P value = 0.013). However, simulated K1 nonsignificant difference, S–I difference and I–S difference were significantly higher in keratoconus cases (3.45 ± 0.50 and 3.42 ± 1.08 , respectively) compared with controls (1.49 ± 0.62 and 0.98 ± 0.43 , respectively), and showing P values of 0.036 and less than 0.001.

Central corneal thickness was measured by pentacam. The Mean central corneal thickness was significantly thinner in early keratoconus cases (499.28 ± 32.41 μm) than in controls (546.72 ± 45.53 μm), with P value of less than 0.001. Both central 5 mm of the anterior and posterior elevation maps were significantly higher in early keratoconus patients compared with high regular astigmatism (16.52 ± 2.97 and 24.68 ± 3.21 versus 7.48 ± 4.35 and 15.38 ± 6.26 μm , respectively), P values in both comparisons were less than 0.001.

Anterior segment OCT was used to assess corneal and epithelial thickness, early keratoconus cases significantly thinner central corneal thickness (483.52 ± 32.09 μm) compared with high regular astigmatism (531.96 ± 44.49 μm) (P value < 0.001). Similarly, the mean central epithelial thickness was significantly thinner in keratoconus eyes

(49.84 ± 1.95 μm) than that in high regular astigmatism (53.24 ± 3.72 μm) (P value = 0.002). Early keratoconus cases had significantly lower thinnest location (42.92 ± 2.53 μm) compared with high regular astigmatism (46.00 ± 5.17 μm) (P value < 0.001). The mean thickest location was slightly lower in keratoconus cases (55.52 ± 2.29 μm versus 55.68 ± 3.38 μm), but it did not show statistically significant difference (P value = 0.807).

The central corneal thickness had sensitivity of 72%, specificity of 68% and total diagnostic accuracy (Area Under the Curve) of 81.4% at cutoff value of 496.5 μm . Epithelial thickness showed sensitivity of 60%, specificity of 84% and total diagnostic accuracy of 75.8% at cutoff value of 51.50 μm . Thinnest location showed sensitivity, specificity, and total diagnostic accuracy of 76%, 68%, and 81.4%, respectively at cutoff value of 44.50 μm .

4. Discussion

Identifying patients at risk for subclinical keratoconus and distinguishing them from normal individuals have been elusive goals for refractive surgeons. Although many studies focused on the role of scheimpflug imaging in the diagnosis of keratoconus, role of epithelial mapping in the early diagnosis of keratoconus is still under investigation Silverman and colleagues⁸

Therefore; in this cross-sectional observational study included 25 eyes of early keratoconus cases and 25 eyes of normal high regular astigmatism controls conducted at Magrabi Eye Hospital –Tanta between October 2021 and August 2022.

According to previous study Yang and Yuli,⁹ in Cross-sectional observational study, a spectral-domain OCT was used to acquire corneal and epithelial thickness maps in normal, manifest keratoconic, subclinical keratoconic, and forme fruste keratoconic (FFK) eyes. The study comprised 54 eyes from 29 normal participants, 91 manifest keratoconic eyes from 65 patients, 12 subclinical keratoconic eyes from 11 patients, and 19 FFK eyes from 19 patients. They got the following results, OCT correctly classified all normal eyes (100% specificity) and had good sensitivities for detecting manifest

keratoconus (97.8%), subclinical keratoconus (100.0%), and FFK (73.7%) and they concluded that this study provides evidence that OCT corneal and epithelial thickness map parameters and patterns provide diagnostic information, in addition to topography, for characterizing corneal ectatic conditions. Therefore, these maps can be used in conjunction with topography to potentially improve diagnostic accuracy for keratoconus.

In addition, Temstet and Cyril¹⁰ investigated the difference in the central corneal thickness and the central epithelial thickness between normal individuals and patient's showing early, moderate, and severe keratoconus. Their study involved 145 eyes divided into four groups: normal, early keratoconus, moderate keratoconus, severe keratoconus. In early keratoconus group, the mean thickness of central epithelial thickness was 52.8 ± 3.3 and the mean thickness of central corneal thickness was 500.8 ± 34.2 . In control group, the mean thickness of central epithelial thickness was 53.0 ± 3.1 and the mean thickness of central corneal thickness was 542.00 ± 31.4 . Their results agreed with those of our study and they concluded that early keratoconus eyes have thinner central epithelial thickness and thinner central corneal thickness than normal eyes.

Another similar observational study conducted by Marco and Claudia¹¹ including 184 eyes, showed that keratoconus group have thinner central epithelial thickness than normal group, thus agreeing with the results of our study.

Furthermore, another study by Li and colleagues¹ further analysed the epithelial thickness in the rest of the corneal quadrants in addition to the central part using Fourier domain OCT and correlated it with keratoconic indices of the Scheimpflug camera. They found out that keratoconic eyes had significantly lower inferior ($P = 0.03$), minimum corneal epithelial thickness ($P < 0.0001$) and greater S-I ($P = 0.013$). Their results agreed with our study in determining that central epithelial thickness measured by anterior segment OCT has an important role in early diagnosis of keratoconus (early keratoconus eyes have thinner central epithelial thickness than normal eyes). They also agreed with our study in determining that keratoconus eyes have steeper *k* readings than normal eyes.

Moreover, Yan and David¹² in a cross-sectional observational study including 37 keratoconic eyes from 21 patients and 36 eyes from 18 normal patients concluded that keratoconic corneas were thinner than normal cornea. Their results were similar to those of our study. However our study correlated both central epithelial thickness and central corneal thickness concluding that

keratoconic eyes have thinner central epithelial thickness than normal eyes.

Currently, Uçakhan and Omur¹³ in comparative study including 44 eyes with mild to moderate keratoconus and 63 normal eyes with myopic astigmatism, concluded that posterior corneal elevation measured by scheimpflug imaging was higher in the keratoconus group, thus agreeing with the results of our study.

Finally, the results of the comparative study conducted by Haque and colleagues¹⁴ in which 20 individuals with keratoconus and 20 controls (without keratoconus) were enrolled, agreed with ours. However, in their study they used time domain OCT whereas in our study, spectral-domain OCT instruments.

Similarly, Gordon-Shaag and colleagues⁵ the corneal epithelium is the first cellular protective layer of the human cornea. Analysis of this layer and determining its thickness as well as its distribution plays an important role in refractive surgery, as it may help in the screening of normal individuals for early keratoconus especially if showing suspicious criteria in Scheimpflug imaging, thus helping to differentiate early keratoconus from mimicking conditions such as corneal astigmatism.

Our study investigated the role of epithelial corneal thickness in the early diagnosis of keratoconus especially in young individuals using Fourier domain OCT and correlated it with other indices detected in Scheimpflug imaging. Anterior segment OCT is a user friendly, noncontact instrument, which could provide a screening tool for the early diagnosis of keratoconus especially in the suspicious group of young individuals suffering from high corneal astigmatism. This could further help in the early detection of keratoconus thus providing early measures to halt progression of keratoconus in line with previous findings Grajciar and colleagues.⁶

5. Conclusion

From the data supported by the study, we found that measurement of epithelial thickness provided by anterior segment optical coherence tomography-epithelial-mapping is useful for early diagnosis of keratoconus and have important role to differentiate it from normal high regular astigmatism. We recommend further studies on larger sample size to emphasize our conclusion [Figs. 1–6](#), [Tables 1–3](#).

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

There are no conflicts of interest.

References

- Li Y, Tan O, Brass R, Weiss JL, Huang D. Corneal epithelial thickness mapping by fourier-domain optical coherence tomography in normal and keratoconic eyes. *Ophthalmology*. 2012;119:2425–2433.
- Reinstein DZ, Gobbe M, Archer TJ, et al. Epithelial, stromal, and total corneal thickness in keratoconus: three-dimensional display with Artemis very-high frequency digital ultrasound. *J Refract Surg*. 2010;26:259–271.
- Crawford Alexandra Z, Zhang Jie, Gokul Akilesh B, Optom (Hons), McGhee Charles NJ, Ormonde Sue E. The enigma of environmental factors in keratoconus. *Asia-Pac J Ophthalmol*. November–December 2020;9(6):549–556. <https://doi.org/10.1097/APO.0000000000000334>.
- Saro Adham Sa, Radwan Gamal Ab, Mohammed Usama Ab, Abozaid Mortada Ab. Screening for keratoconus in a refractive surgery population of Upper Egypt. *Delta J Ophthalmol*. Jan–Mar 2018;19(1):19–23. https://doi.org/10.4103/DJO.DJO_39_17.
- Gordon-Shaag Ariela, Millodot Michel, Shneur Einat. *The epidemiology and etiology of keratoconus Epidemiology*. 2012: 7–15, 70.
- Grajciar B, Pircher M, Hitzenberger CK, Findl O, Fercher AF. High sensitive measurement of the human axial eye length in vivo with Fourier domain low coherence interferometry. *Opt Express*. 2008;16:2405–2414.
- Haque S, Jones L, Simpson T. Thickness mapping of the cornea and epithelium using optical coherence tomography. *Optom Vis Sci*. 2008;85:963–976.
- Silverman Ronald H, Urs Raksha, RoyChoudhury Arindam, Archer Timothy J, Gobbe Marine, Reinstein Dan Z. Epithelial remodeling as basis for machine-based identification of keratoconus. *Investig Ophthalmol Vis Sci*. 2014;55: 1580–1587.
- Yang F, Yuli H. Keratoconus detection using OCT corneal and epithelial thickness map parameters and patterns. *J Cataract Refract Surg*. 2021;47:759–766.
- Temstet H, Cyril M. Corneal epithelial thickness mapping using Fourier-domain optical coherence tomography for detection of form fruste keratoconus. *J Cataract Refract Surg*. 2015;41:812–820.
- Lombardo Marco. Claudia Cali Role of corneal epithelial thickness mapping in the evaluation of keratoconus. *Contact Lens Anterior Eye*. 2019;42:662–665.
- Li Yan. David Keratoconus diagnosis with optical coherence tomography pachymetry mapping. *Ophthalmology*. 2008; 115(12):2159–2166.
- Uçakhan Ömür Ö. Evaluation of Scheimpflug imaging parameters in subclinical keratoconus, keratoconus, and normal eyes. *J Cataract Refract Surg*. 2011;37:1116–1124.
- Haque Sameena, Simpson Trefford, Jones Lyndon. Corneal and epithelial thickness in keratoconus: a comparison of ultrasonic pachymetry, Orbscan II, and optical coherence tomography. *J Refract Surg*. 2006;22:486–493.