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Corneal elevation and keratoconus indices in a 40- to 64-year-old population, Shahroud Eye Study

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Abstract

***Purpose*:** To determine the corneal elevation values and keratoconus indices in the 40- to 64-year-old population and their changes with aging.
***Methods*:** The 6311 invitees of this study were selected through random cluster sampling, and 5190 of them participated in the study (response rate = 82.2%). Here, we analyzed results of Pentacam acquisitions in 4148 respondents. Cases of keratoconus and forme fruste keratoconus (FFKC) were determined using topography and clinical data. Studied variables included keratoconus indices, central corneal thickness readings, maximum elevations on the anterior and posterior surfaces, and elevation values at the thinnest point, anterior steepest point, and posterior steepest point in healthy, FFKC, and keratoconus groups.
***Results*:** In all subjects, the mean maximum elevations were 6.80 ± 5.0 μm and 16.60 ± 7.7 μm on the anterior and posterior corneal surfaces, respectively. Maximum elevation values on the anterior and posterior corneal surfaces showed significant correlations in the keratoconus, FFKC, and healthy groups ($P < 0.002$). Maximum anterior elevation correlated with age ($r = 0.11$, $P < 0.001$), but maximum posterior elevation showed no such correlation ($P = 0.476$). Keratoconus indices demonstrated significant changes with age ($P < 0.001$).
***Conclusion*:** Anterior elevation values slightly increase with age, and keratoconus indices change as well. Elevation readings and keratoconus indices in the keratoconus group and FFKC cases are higher than the healthy corneas although their values could be compared with other studies on younger participants.

Keywords: Corneal elevation; keratoconus; Pentacam; cross-sectional study; adult

Introduction

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.[1,2] 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. The Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) employs the Scheimpflug imaging technique and provides information regarding corneal surface irregularity and

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asymmetry in addition to elevation data, and uses them to compute indices for the diagnosis of keratoconus.

In the recent decade, using evidence of natural cross-linking, which occurs with aging[3] and in diabetic patients,[4] collagen cross-linking has become a treatment option to halt disease progression in cases of keratoconus. Stable keratometry and elevation readings from the corneal surfaces are evidence of the efficacy of this treatment method. Studies on keratoconus patients have mainly focused on the 20–40 year age groups, and thus, there is limited information about changes in corneal elevation and irregularity in older ages. Availability of such data in the Shahroud Eye Cohort Study provides more comprehensive knowledge on corneal changes in keratoconic subjects. This report, which is based on a population study, explores these indices in the 40–64 year age group.

Methods

The Shahroud Eye Cohort Study commenced during 2009–2012 using random cluster sampling from the 40- to 64-year-old population of Shahroud city. Detailed methodology of the survey has been published elsewhere.[5] In brief, 300 clusters of 20 persons each were selected, and after determining the households in each cluster, they were invited to participate in the study by approaching them at their door and interviewing household members. Respondents were informed about the objectives and methods of the survey, and they were enrolled after signing written informed consents. The Ethics Committee of Shahroud University of Medical Sciences approved this study.

Examinations included bilateral acquisitions with the Pentacam HR which were done between 9:00 am and 1:00 pm, at least 3 h after participants' wakeup time. In the present report, we used demographic and Pentacam data from the first phase of the survey. Version 1.17r72 of the Pentacam device software and version 6.03r15 of the data management software were used.

From Pentacam data, we recorded readings of the central corneal thickness, mean keratometry, maximum anterior and posterior elevation in the central 6 mm zone (MAE and MPE, respectively), anterior elevation at the thinnest point, posterior elevation at the thinnest point, anterior and posterior elevations at the steepest point of the anterior corneal surface, and anterior and posterior elevations at the steepest point of the posterior corneal surface. Elevation measurements were in reference to a floating sphere that best fit the 8.0 mm zone.

We also extracted Pentacam keratoconus indices including index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, index of height asymmetry, index of height decentration, and minimum sagittal curvature from the topometric display.

To identify cases of keratoconus, we applied Holladay topographic criteria,[6] which are as follows:

1) "Apex of the cone is not centered at the 6-o'clock semimeridian, 2) the cone should appear round on the tangential map, 3) steep keratometry >45.00 diopters, 4) corneal thickness at the apex of the cone is approximately 30 μm thinner than the corresponding distance above the pupil center, and 5) topographic patterns are not symmetric (more than 1.5 diopter superior-inferior power difference in 4 mm central zone)."

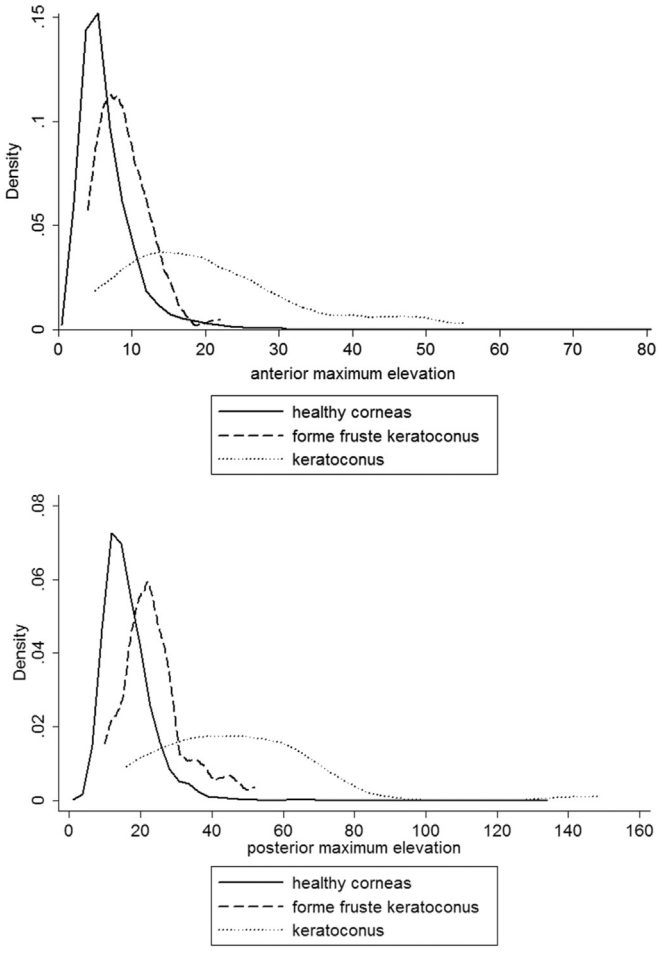

Fig. 1. Distribution of density of anterior and posterior maximum elevation in healthy corneas, forme fruste keratoconus, and keratoconus people.

Cases with all the above criteria in one or both eyes were categorized in the keratoconus group. Individuals who met all criteria except the 2nd and 3rd items were classified as forme frusta keratoconus (FFKC). Cases with any history of ocular surgery and those with evidence of corneal vascularization, corneal irregularities (i.e. PMD), or corneal opacity on clinical examination were excluded from the study. All other participants were grouped as healthy. In all three eye groups, right eye data were used in the analysis unless the diagnosis of keratoconus or FFKC pertained to the left eye only.

Mean central corneal thickness, mean keratometry, and elevation variables were compared among the three groups using multinomial logistic regression tests. The effect of age on the studied variables was assessed in a regression model. Cluster sampling was accounted for in estimating standard errors and averages. Associations between elevation parameters were determined using the Pearson correlation test. Statistical significance was based on a 0.05 level.

Table 1
Means of elevation indices in healthy corneas, forme fruste keratoconus, and keratoconus groups.

Elevation indices (μm)	Study group		
	Healthy	Forme fruste keratoconus	Keratoconus[a]
Maximum anterior elevation at 6 mm zone	6.71 (0.08)	8.86 (0.51)	20.73 (2.03)
Maximum posterior elevation at 6 mm zone	16.31 (0.12)	23.77 (1.36)	47.26 (4.04)
Anterior elevation at thinnest point	0.42 (0.04)	4.64 (0.53)	15.21 (1.60)
Posterior elevation at thinnest point	8.16 (0.11)	15.04 (1.53)	38.78 (3.02)
Anterior elevation at anterior steepest point	−3.61 (0.12)	1.00 (0.99)	9.96 (2.03)
Posterior elevation at anterior steepest point	−6.42 (0.31)	0.40 (2.81)	19.63 (3.90)
Anterior elevation at posterior steepest point	−0.44 (0.06)	2.82 (0.87)	12.94 (1.59)
Posterior elevation at posterior steepest point	−1.44 (0.20)	4.91 (2.04)	28.15 (2.92)

[a] All elevation indices in keratoconus group were significantly higher than forme fruste keratoconus cases (P value < 0.001, for all).

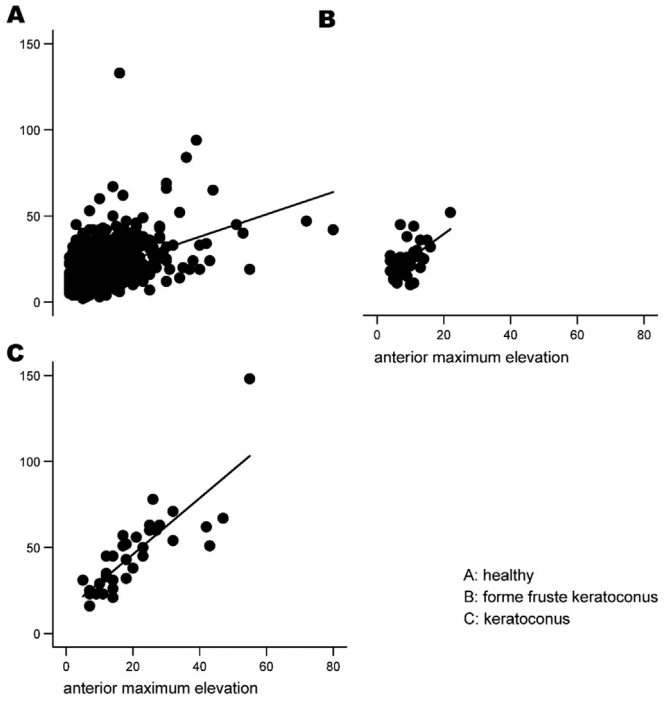

Fig. 2. Correlation between anterior maximum elevation and posterior maximum elevation.

Table 2
Related findings of different studies on cornea variance indices.

	Mean age	Koller[13]	Greenstein[7]	Current study
		32.3	NA[b]	50.50
Normal group	ISV	NA	NA	15.48
	IVA	NA	NA	0.12
	KI	NA	NA	1.01
	CKI	NA	NA	0.99
	IHA	NA	NA	3.92
	IHD	NA	NA	0.007
	RMin	NA	NA	7.47
control group[a]	ISV	54	NA	27.02
	IVA	0.65	NA	0.29
	KI	1.14	NA	1.07
	CKI	1.01	NA	1.00
	IHA	19.3	NA	8.33
	IHD	0.05	NA	0.022
	RMin	6.94	NA	7.26
Keratoconus group	ISV	98	122.2	57.55
	IVA	1.10	1.29	0.61
	KI	1.27	1.37	1.13
	CKI	1.08	1.05	1.02
	IHA	31.4	35.2	15.13
	IHD	0.09	0.12	0.055
	RMin	6.14	5.71	6.55

ISV: Index of Surface Variance, IVA: Index of Vertical Asymmetry, KI: Keratoconus Index, CKI: Central Keratoconus Index, IHA: Index of Height Asymmetry, IHD: Index of Height Decentration, Rmin: minimum sagittal curvature.

[a] We showed results of Forme Fruste Keratoconus cases in this group, and Koller used data of fellow eyes of patients as the control group.

[b] Unavailable data for this variable in regarded study.

Results

Overall, 6311 people were invited, and with a response rate of 82.2%, 5190 of them participated in the study. After applying exclusion criteria, we used Pentacam data from 4177 individuals who were 1764 men (42.2%) and 2413 women (57.8%), and their mean (SD) age was 50.5 (6.11) years. Of these, 35 were diagnosed with keratoconus, 47 met the criteria for FFKC, and 4095 people were in the healthy group. The mean age of keratoconus cases (47.6 years ± 4.7) was lower than that in normal subjects (50.9 years ± 6.2) (P < 0.001). Gender distribution was same among all subgroups.

Mean (SD) MAE and MPE were 6.85 (4.99) μm (95% confidence interval (CI), 6.69−7.02) and 16.64 (7.95) μm (95% CI, 16.38−16.90), respectively. The distributions of these variables in the keratoconus, FFKC, and healthy groups are demonstrated in Fig. 1.

Table 1 presents a summary of MAE, MPE, anterior and posterior elevation readings at the thinnest point, anterior and posterior elevations at the steepest point of the anterior corneal surface, and anterior and posterior elevations at the steepest point of the posterior corneal surface in the 3 groups. All elevation indices were significantly higher in the keratoconus group compared to FFKC and healthy groups (P < 0.001). In this regard, posterior elevation at the thinnest point, MPE, and posterior elevation at the steepest point of the posterior corneal surface showed the largest differences between keratoconus cases and the FFKC and healthy groups. MAE and MPE significantly correlated with each other in all three keratoconus (r = 0.86; P < 0.001), FFKC

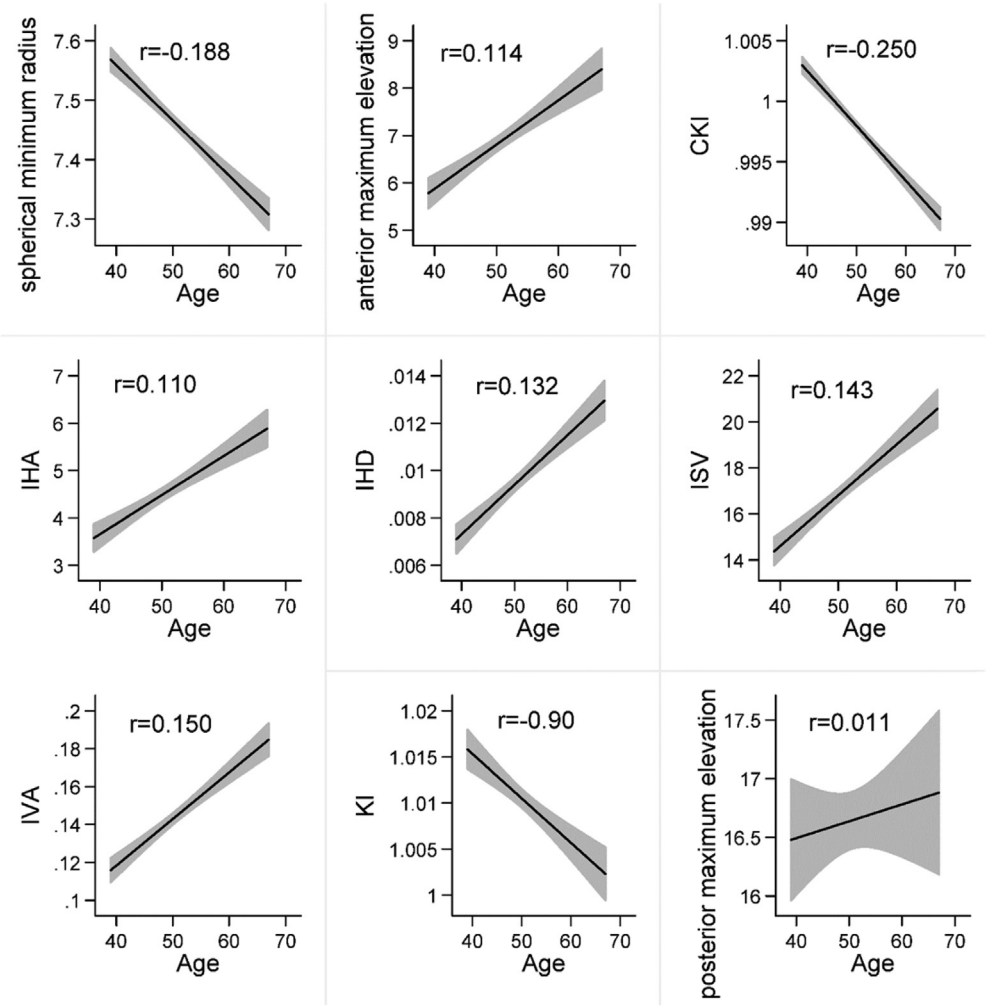

Fig. 3. Correlation of age with MAE, MPE, and keratoconus indices.

(r = 0.56; P < 0.001), and healthy (r = 0.43; P < 0.001) groups (Fig. 2).

Mean keratometry in the keratoconus and FFKC groups was 45.65D (95% CI, 44.40–46.89) and 43.90D (95% CI, 43.45–44.37), respectively, and 43.71D (95% CI, 43.66–43.77) in the healthy group.

Mean central corneal thickness was 471 μm (95% CI, 461–480) in the keratoconus group, 516 μm (95% CI, 507–526) in the FFKC group, and 529 μm (95% CI, 527–530) in the healthy group.

Table 2 contains a summary of Pentacam keratoconus indices in our 3 groups. Keratoconus indices were higher in cases of keratoconus compared to FFKC and healthy groups (P < 0.001). Also, cases of FFKC showed higher values than the healthy group (P < 0.001).

We found significant correlations between age and MAE and keratoconus indices (P < 0.001). MPE did not correlate with age (P = 0.476) (Fig. 3). In the healthy group, age significantly correlated with mean keratometry (r = 0.06, P < 0.001) and central corneal thickness (r = −0.04, P = 0.004). However, we found no age-related changes in mean keratometry or central corneal thickness in the keratoconus and FFKC groups.

Discussion

Presented findings regarding anterior and posterior corneal elevation values and keratoconus indices in the 40- to 64-year-old age group provide a suitable reference for comparison with other studies. Separating results in keratoconus, FFKC, and healthy groups provide for even more detailed comparisons. One of the interesting findings of this study was the age-related changes in MAE and keratoconus indices (Fig. 3). Thus, some of the considerable differences seen in our results compared to previous studies (Tables 2 and 3) may be explained by the impact of participants' age, although measurement methods should be considered as well.

Comparisons among our three groups showed that elevation indices were considerably different in the keratoconus group (Table 1). Comparing keratoconus with FFKC groups, differences in posterior indices were more evident than anterior corneal indices. This was also seen as a stronger correlation between MAE and MPE in keratoconus cases, compared to the FFKC. In cases of confirmed keratoconus, changes are typically seen in both the anterior and posterior corneal surfaces, while in FFKC, severities differ, and this is

Table 3
Related findings of different studies on elevation indices.

	Device[a]	Diameter (mm)	Normal			Keratoconus suspect[b]			Keratoconus		
			Age	MAE	MPE	Age	MAE	MPE	Age	MAE	MPE
De Sanctis[8]	Pentacam	5	43.00 ± 14.00		19.80 ± 6.37	35.00 ± 14.00		39.90 ± 15.00	40.00 ± 15.00		100.70 ± 49.20
Quisling[9]	Pentacam	–							46.00 (–)		34.86 (–)
Current study	Pentacam	6	50.29 ± 6.05	6.71 ± 4.73	16.31 ± 7.09	49.28 ± 6.10	8.86 ± 3.62	23.77 ± 9.04	47.97 ± 4.73	20.73 ± 12.13	47.26 ± 24.18

MAE: Maximum Anterior Elevation; MPE: Maximum Posterior Elevation.
[a] Measurements are done based on BFS floating mode at 9 mm, but the current study was done at 8 mm.
[b] Current study data in this column belong to the Forme Fruste Keratoconus group.

reflected in the elevation values of the anterior and posterior corneal surfaces. Also, from a clinical point of view, noting differences in the posterior elevation at the thinnest point and posterior elevation at the steepest point of the anterior corneal surface is interesting. As we improve our understanding about the impact of cone location (central vs. peripheral) on treatment results with options such as ring implantation,[10] more similar research can help determine the best indicator of cone location.

In our study, MAE and MPE in the keratoconus, FFKC, and healthy groups were significantly different; however, as displayed in Table 3, readings, especially in the keratoconus group, were much lower than those reported by De Sanctis et al.[8] In both studies, the Pentacam, though with different BFS fit values, was used for corneal imaging. In this regard, the study by Quisling et al[9] was more comparable to our study. Although they included only 29 cases with a confirmed diagnosis of keratoconus in their research, their results were closer to ours (Table 3). As evident in Table 3, our results with the anterior elevation values differ with other studies as well. The overall conclusion from these studies seems to be a decrease in corneal elevation in cases of keratoconus with aging after the age of 30.

As demonstrated in Fig. 3, keratoconus indices and anterior elevation values showed a slight change with aging. Other studies have suggested that aging is associated with an increase in corneal irregularity index.[11] In this regard, ISV readings were higher in cases of keratoconus than in the FFKC and healthy groups. A comparison of studies in Table 2 shows an interesting point. If we take corneal surface irregularities as an indicator of keratoconus severity,[12] considering the age range of the studied population, these findings could be indicative of reduced keratoconus severity at older ages. However, ethnic varieties and diagnostic criteria of different studies should not be neglected. Another noteworthy point is how indices in our FFKC compare to the control group in the study by Koller et al[13] which included fellow eyes of keratoconus patients treated with collagen cross-linking. The trend and pattern of keratoconic changes can be an interesting subject for future studies.

A mean keratometry of 45.6 ± 3.6D in the keratoconus group was well-matched with the mild classification based on recent method by McMahon, et al[14] However, mean keratometry was not able to discriminate normal and FFKC cases. As argued by Saad and Gatinel,[15] elevation indices or the corneal thickness indices may be better criteria for identifying cases of FFKC.

According to studies on the corneal thickness of keratoconus patients (Table 4), the central corneal thickness appears to be lower in younger age groups such as those in studies by Reinstein[20] and Uckakhan.[21] The corneal thickness readings observed in our keratoconus patients were highest compared to all other reports, except the 33 patients in the 19–61.

year age range studied by de Sanctis.[16] However, it must be noted that the patients in the study by Pinero et al[17] had grade 2 keratoconus. Since the same device was used in all studies,

Table 4
Related findings of different studies on central corneal thickness.

Study	Device	Normal cornea		Keratoconus suspect		Manifest keratoconus	
		Age	Mean CCT	Age	Mean CCT	Age	Mean CCT
Reinstein D.Z[16]	Artemis VHF	–	–	–	–	29.3 ± 6.1	450[a] ± 44
Ucakhan O.O[17]	Pentacam	26.6 ± 9.9	557.6 ± 6	–	–	26.2 ± 9.0	456.3 ± 9
Ertan A.[18]	Pentacam	–	–	–	–	28.0 ± 9.0	464.0 ± 54
De Sanctis U.[18]	Pentacam	–	–	–	–	37.0 ± 6.0	478.9 ± 35
Grewal D.S[19]	Pentacam	32.6 ± 4.4	525.8 ± 41	–	–	30.6 ± 3.1	446.4 ± 58
Pinero D.P[19,b]	Pentacam	32.3 ± 6.6	549.9 ± 28	30.0 ± 9.1	514.3 ± 44	39.0 ± 11.7	457.61 ± 39
Current study	Pentacam	50.3 ± 6.0	530.3 ± 32	48.6 ± 5.6	518.3 ± 35	49.0 ± 6.0	472.60 ± 28

[a] Corneal thickness at the thinnest location is reported and the used device is Artemis very high-frequency digital ultrasound scanning.
[b] Grade II of keratoconus patients from this study are mentioned in this table.

except the one by Reinstein,[20] the next question is whether the corneal thickness increases with aging in cases of keratoconus.

In this study, we aimed at assessing anterior and posterior elevation readings and keratoconus indices in a database of a population older than 40 years of age. Results may vary in different populations as an effect of race and geographic location. To the best of our knowledge, this is the first population-based study of these indices; thus, more similar studies may be warranted in other populations so that corneal topographic data can be interpreted better. When comparing results of different studies the topographer used for measurements, definitions of KCN and FFKCN, and confounding factors such as acquisition time, use of contact lenses, and measurement errors should be considered. These limitations applied to our comparison with other studies too, but we tried to take them into account when drawing conclusions. Also, the numbers of keratoconus and FFKC cases were not proportionate to healthy cases, and more accurate estimates of these indices would need studies with more patients. A more important area of study would be the indices in FFKC cases to get a better understanding of the development of keratoconus and the determinants of its progression.

Corneal variance indices and anterior corneal surface elevation readings slightly increase in the over 40-year age range. Since the most important aspect of the Shahroud Eye Cohort Study is perhaps the age distribution, a comparison of results with other studies, which are not population-based either, points to a decreased severity of disease in keratoconus and FFKC groups. Since few studies have investigated corneal changes in older age groups of such patients, long-term studies of older samples are necessary to have a better assessment of treatment options and factors that impact keratoconus progression.

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Contributions to authors in each of these areas

Design and conduct of the study (HH, AB, MK, MHE, MS, AF); collection and management of the data (HH, MK, MHE, AB, SM, MS, AF); analysis and interpretation of the data (HH, MK, AB, MHE, MS, AF); and preparation, review, and approval of the manuscript (HH, MK, AB, SM, MHE, MS, AF).

Statement about conformity with author information

The Ethics Committee of Shahroud University of Medical Sciences approved the study, which was conducted in accord with the tenets of the Helsinki Declaration.

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