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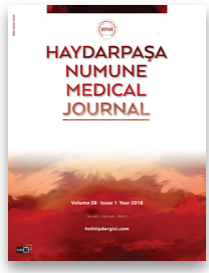

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ORIGINAL ARTICLE

Evaluating Corneal Changes in Patients with Aortic Aneurysm

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Abstract

Introduction: To evaluate corneal changes in patients with aortic aneurysm.

Methods: The study group (Group 1) included 63 eyes of 33 patients diagnosed with aortic aneurysm and the control group (Group 2) included 69 eyes of 35 healthy people who presented at the Ophthalmology Department. Complete ophthalmologic examination was performed and steepest keratometry measurements were taken via rotational Scheimpflug corneal tomography on the following parameters: sagittal curvature map (S steepest), central corneal thickness (CCT), minimum corneal thickness (CT min), corneal volume (CV), mean pachymetric progression index (PPI mean), minimum PPI (PPI min), maximum PPI (PPI max), maximum Ambrosio relational thickness (ART max), posterior corneal elevation (PE) and back difference elevation (BDE).

Results: The groups were similar in terms of age and gender (p=0.082 and p=0.145, respectively). There was no statistically significant difference in visual acuity and intraocular pressure between the groups (p=0.471 and p=0.199 respectively). There was no statistically significant difference in Ks, Kf, Km, CT min, CCT, CV, I-S, S steepest, PE, PPI mean, PPI min, PP max, and ART max values between the groups (p>0.05). BDE value was significantly higher in Group 1 (p=0.04).

Discussion and Conclusion: The patients diagnosed with aortic aneurysm should be evaluated for keratoconus.

Keywords: Aortic aneurysm; corneal tomography; keratoconus; posterior corneal elevation; scheimpflug.

Keratoconus is a primary ectatic corneal disorder. It is a disease caused by the protrusion of the cornea with regional thinning and characterized by bilateral non-symmetrical corneal degeneration. Corneal protrusion affects the quality of vision by causing high myopia and irregular astigmatism. The incidence of keratoconus has been reported as 50.230:100.000 per year and its prevalence as 54.5:100.000 per person [1].

Genetic and environmental factors have been implicated in the etiology, although the cause is not fully understood [1–3]. It is essentially a collagen tissue disorder, and various protease inhibitors and proinflammatory cytokines are thought to be involved in its pathogenesis [2,4–8]. The relation between keratoconus and systemic collagen diseases has been frequently discussed [9–11]. The levels of proinflammatory cytokines and proteinases get increased in this disease and subsequently affect all the body organs including the cardiovascular system [12,13]. At the same time, the increased frequency of both keratoconus and aortic aneurysms in some connective tissue diseases suggests that they may have a common pathology [1,9,12].

Keratoconus is the most frequently observed disorder of the cornea but pellucid marginal degeneration, Terrien's marginal degeneration, and keratoglobus are also enu-

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merated among the ectatic dystrophies of the cornea. It is important to establish a clear distinction between ectatic dystrophies and thinning disorders of the cornea because the treatment and prognosis of these diseases are quite different. The findings are highly variable according to the severity of the disease, in that there may be no symptoms in the early stages of the disease and in advanced cases, corneal findings of keratoconus can be detected via a careful slit lamp examination.

Keratoconus occurs most frequently in its isolated form. However, it can be seen in association with many systemic diseases. Approximately 40 systemic disorders associated with keratoconus have been reported, and in most of them, the extracellular intermediate was effected. In addition, 30 corneal and non-corneal ocular diseases have been detected in keratoconus. The term "isolated keratoconus" may be due to the fact that all investigations of possible concomitant diseases have not been made in the patient [1,2,13].

To understand the relationship between systemic diseases and keratoconus, it may be useful to elucidate the pathophysiological features of the disease. In 2015, the risk factors for the development of keratoconus in the Global Delphi Panel of Keratoconus and Ectatic Diseases were described. These risk factors may be mechanical factors such as Down syndrome, ocular allergy, ethnicity, eye scratching, and atopy; or connective tissue diseases such as Marfan syndrome, Ehler Danlos syndrome and Leber's congenital amaurosis [14].

Collagen and elastin abnormalities are often seen in keratoconus associated with connective tissue disease. This group includes Ehler Danlos syndrome, Osteogenesis imperfect, Marfan syndrome, joint hypermobility, mitral valve prolapse (MVP), GAPO syndrome (growth retardation, alopecia, pseudoanodontia, optic atrophy), and Williams Beuren syndrome. In these diseases, astigmatism (due to deterioration in the extracellular intermediate in the cornea), decreased corneal thickness, and changes in corneal curvature can be seen. In hypermobility syndrome, keratoconus is seen 5 times more frequently [1,2,15,16].

Aortic aneurysm, another connective tissue disease with similar factors in its pathophysiology, is defined as there being 50% segmental dilatation of all layers of the aortic wall, which can be seen in any segment from the aortic arch to the abdominal aorta. In this study, we aimed to investigate corneal changes in patients with an aortic aneurysm, to investigate the findings of keratoconus and to describe the associated corneal changes.

Materials and Methods

Written informed consent was obtained from all patients and volunteers who were included in the study in accordance with the 2008 Declaration of Helsinki at the World Medical Association conference. Ethics Committee approval was obtained from Bülent Ecevit University Clinical Research Ethics Committee.

The patient group (Group 1) consisted of individuals who were diagnosed with aortic aneurysm by transthoracic echocardiographic examination performed at the cardiology outpatient clinic of Bülent Ecevit University Health Care Application and Research Center between February 2016 and January 2017. The control group (Group 2) was selected from healthy volunteers with normal aortic diameters who applied to the ophthalmology outpatient clinic between the same dates.

The inclusion criteria were; patients aged ≥18 years with transparent corneal tissue but without corneal disease, history of eye surgery or trauma, and use of contact lenses with the previous week. The study included 63 eyes of 33 patients in Group 1 and 69 eyes of 35 patients in Group 2.

The best corrected visual acuity examination was performed using the Snellen chart, intraocular pressure was measured with Goldman applanation tonometer, and biomicroscopic anterior segment examination and fundus examination were performed by the same ophthalmologist. The presence of characteristic findings of keratoconus was evaluated. The visual acuities of the Snellen chart were converted to logMAR charts for statistical analysis. All patients were examined using rotated Scheimpflug corneal tomography (Oculus Pentacam, Anterior Segment Tomography version1.20r.78).

Pentacam measurements were taken as indicated in the instruction manual. The participants were asked to lean their foreheads against the visor of the device while sitting on a chair. The patient was instructed to keep both eyes open and to fix the black target in the center of the blue fixation beam that was activated when the instrument was in scan mode.

The device was used in the automatic release mode, which means that eye scanning was started when the x, y and z planes fit the alignment criteria. This method helps to reduce the confusion that may occur in manual scanning due to the practitioner's alignment decision. Measurements were taken within the first 4-8 seconds, after the first blink when the tear film was most stable, to prevent the negative effects of measurements of the tear film layer irregularities. Scanning was performed using 25 single Scheimpflug im-

ages in each eye, and 3 consecutive scans were obtained by the same person. The eye movement of the participant was continuously monitored by a second camera and only those images showing a deviation of less than 0.6 mm and a cornea map of at least 9.0 mm were included in the study. In the examination, only the images that recorded as "OK" on the Specification for The Quality of Examination, which is the only sign indicating that all the necessary parameters of the scan are fulfilled, were included.

Sagittal and tangential curvature maps were evaluated and map patterns were recorded. Corneal dioptric strength of the flat meridian in the central 3.0 mm zone, corneal dioptric strength of the perpendicular meridian in the central 3.0 mm zone, and mean corneal dioptric strength of the 3.0 mm zone were evaluated with the Scheimpflug system as a variable of an anterior and posterior corneal surface. On the sagittal curvature map, the I-S value was obtained manually by subtracting 3 points determined at 30-degree intervals (60 degrees, 90 degrees and 120 degrees) in the corneal central 3.0 mm zone from the 3 points determined at 30-degree intervals at the bottom (240 degrees, 270 degrees and 300 degrees). The Ss value was obtained manually from the sagittal curvature map.

Apical CCT, CT min, and CV values were recorded. Mean PPI value was calculated automatically as the progression values of different rings with reference to the mean curve. PPI min and PPI max values were calculated automatically using the mean value estimated for pachymetric progression index. The value of ART max was determined using the Belin/Ambrosio method, observing enhanced ectasia display images of the Pentacam system, and automatically making calculations based on CT min/PPI max formula. The posterior elevation map was evaluated and posterior corneal elevation (PE) was determined from the corneal apex. The elevation value was measured with reference to the optimum sphere in the fixed optical zone of 9.0 mm. BDE was determined automatically using the Belin/Ambrosio enhanced ectasia imaging technique of the Pentacam system.

For statistical analysis, the R 3.3.2. package program was used. Descriptive measurements of continuous variables in the study were shown with mean, standard deviation, median, minimum, and maximum values and categorical variables were shown in terms of frequency and percentages. The fitness of continuous variables to normal distribution was examined with the Shapiro-Wilk test. Independent samples t-test was used for the between-group comparisons of the normally distributed variables and Mann-Whitney U test was used for the between-group comparisons of the variables with non-normal distribution. Pearson chi-square and Yates chi-square tests were used for between-group comparisons of categorical variables. In all statistical analyses, results with a p-value less than 0.05 were considered statistically significant.

Results

The mean age of the 68 patients included in the study was 56.75±8.95 years. There was no significant difference in age and gender between the groups (group 1: p=0.082, group 2: p=0.145). There was no significant difference between the groups in terms of visual acuity and intraocular pressure (IOP) (group 1: p=0.471, group 2: p=0.199) (Table 1). No significant difference was found between the two groups in terms of Ks, Kf, Km, CT min, CCT, CV, I-S, and Ks. The PE values determined in Pentacam Scheimpflug imaging (p>0.05) with PPI average, PPI min, PPI max and the ART max values determined using Belin/Ambrosio enhanced ectasia display system on the Pentacam were not statistically significantly different between the two groups (p>0.05). BDE values determined using the Pentacam system Belin/Ambrosio enhanced ectasia images were statistically significantly different between the two groups. BDE was observed in Group 1 more frequently than in Group 2 (p=0.040) (Table 2).

Patients with aortic aneurysm were divided into 2 groups; one having an aortic diameter of <4.5 mm and the other having an aortic diameter of ≥4.5 mm. These measurements and the corneal parameters were recalculated. There was no statistically significant difference between the two groups in the Ks, Kf, K min, S min, CTmin, CV, I-S, Ks and the BDE values determined in Pentacam Scheimpflug imaging (p>0.05). There was no statistically significant difference between the two groups in terms of PPI mean, PPI max,

Table 1. Systemic and ocular demographic characteristics of both groups

	Group 1 (n=33)	Group 2 (n=35)	p
Systemic demographic characteristics			
Age, mean±SD, year	57.8±8.7	55.7±9.0	0.082
Gender			0.145
Male, n (%)	21 (62)	17 (49)	
Female, n (%)	12 (38)	18 (51)	
Ocular demographic characteristics			
GK, Mean±SD, logMAR	0.07±0.18	0.06±0.12	0.471
GİB, Mean±SD, mmHg	13.9±2.9	14.8±3.3	0.199

VA: visual acuity; IOP: intraocular pressure.

Table 2. Imaging parameters of Pentacam Schemplug

	Group 1 (n=33)	Group 2 (n=35)	p
K flat, mean±SD, D	43.61±1.71	44.06±1.42	0.20
K vertical, mean±SD, D	42.91±1.71	43.23±1.33	0.51
K ort, mean±SD, D	43.32±1.74	43.65±1.33	0.41
KK min, mean±SD, µm	543.0±30.70	540.60±35.22	0.59
SKK, mean±SD, µm	551.71±30.10	546.98±35.47	0.41
KH, mean±SD, µm	59.35±3.58	59.61±4.63	0.72
I/S, mean±SD, D	-0.29±0.71	-0.52±0.85	0.33
S d, mean±SD, D	43.88±1.73	44.50±1.51	0.05
AKE, mean±SD	14.30±4.99	14.10±4.86	0.72
PPI mean, mean±SD	0.96±0.12	0.98±0.16	0.39
PPI min, mean±SD	0.67±0.12	0.69±0.17	0.41
PPI max, mean±SD	1.26±0.21	1.28±0.22	0.56
ART max, mean±SD	442.47±81.82	431.46±80.68	0.43
AEF, mean±SD	8.04±4.18	6.94±4.97	0.04

K flat: corneal dioptric power of flat meridian; K vertical: corneal dioptric power of vertical meridian; Kort: mean corneal dioptric power in 3.0 mm zone; I-S: inferior superior dioptric asymmetry value in sagittal curve map; Sd: steepest sagittal value; CCT: central corneal thickness; CT min: minimum corneal thickness; CV: corneal volume; PPI mean: mean pachymetric progression index; PPI min: minimum pachymetric progression index; PPImax: maximum pachymetric progression index; ARTmax: maximum Ambrosio relational thickness; PCE: posterior corneal elevation; BDE: back difference elevation.

ART max, and BDE values determined by Belin/Ambrosio advanced eCTasia images of the Pentacam system (p>0.05). A statistically significant difference was observed between the two groups in the PPI min values determined by Belin/Ambrosio advanced ectasia images of the Pentacam system. PPI min value was higher in the group with an aortic diameter of ≥4.5 mm compared to the group of <4.5 mm (p=0.04). PPI min values were 0.63 and 0.70 respectively.

The number of hypertensive patients in both groups was higher than the number of non-hypertensive patients. Most of the hypertensive patients (80.6%) had an aortic diameter of <4.5 mm, while the aortic diameter was ≥4.5 mm in 62.5% of hypertensive patients. Non-diabetic patients were more numerous in both groups than diabetic patients; 71% of non-diabetic patients had an aortic diameter of <4.5 mm and 81.3% of non-diabetic patients had a diameter of ≥4.5 mm.

Discussion

Proinflammatory cytokines and proteinases found to be increased in keratoconus disease may also affect all the organs including the cardiovascular system [12,13]. Similar biochemical and biomechanical factors that are effective in collagen metabolism may cause concomitant abnormalities in the structure of collagen. Structural changes in the cornea can be observed in various connective tissue diseases where collagen and elastin abnormalities occur [2]. The association between keratoconus and cardiac diseases was first examined by Beardsley and Foulks in 1982, who observed a relationship between MVP and keratoconus [9]. The prevalence of MVP in patients with advanced keratoconus was found to be 22.6-58% [10].

During embryogenesis, both the corneal stroma and collagen forming the mitral valves occur at the sixth and seventh weeks of fetal life. Therefore, any disorder affecting the fetus in these weeks may affect both structures [11,15]. In 2012 and 2013, Dudokova et al. found a decrease in lysyl oxidase (LOX) enzyme in keratoconus patients [8,13]. The LOX enzyme is effective in cross-linking extracellular intermediates. It is found in corneal epithelium, stroma, and endothelial layers. Lack of this enzyme may lead to inadequate collagen cross-linking and may be involved in the development of keratoconus.

Similar changes in the extracellular intermediate, especially collagen metabolism disorders involved in the impairment of the LOX enzyme in the mitral valves, may explain the relationship between keratoconus and MVP. In a patient with congenital keratoglobus presented by Ozer et al. [12], concomitant cardiovascular problems such as coarctation, patent foramen ovale, and MVP were identified.

As in keratoconus, changes in some enzymes and proinflammatory cytokines that are effective in collagen metabolism are observed in aortic aneurysm. The development of similar biochemical changes and the increase in the incidence of connective tissue diseases in both diseases suggests the presence of similar pathogenesis.

Our study is the first to evaluate the relationship between aortic aneurysm and keratoconus. In a study by Woodward et al., the relationship between keratoconus, systemic disease, and socio-demographic factors was evaluated. In this large-scale study, 2653 patients were investigated in terms of gender, ethnicity, race, education level, economic gain, DM, asthma, allergic rhinitis, MVP, collagen vascular diseases, aortic aneurysm, Down syndrome, sleep apnea syndrome, and depression. Aortic aneurysms were diagnosed in 186 patients and keratoconus was present in only 90. As a result, no significant relationship was found between the occurrence of aortic aneurysm and keratoconus [17].

While imaging techniques used to define corneal ectasia were initially limited to Placido disc-based video-keratography, Scheimpflug imaging techniques are often used today. New parameters such as K flat, K vertical, cylindri-

cal value, CCT, CT min, front face, and rear face have been added to initially used ones with the development of technology. When we compared the normal cornea to the keratoconal cornea, the values of K flat, K vertical, cylindrical value, I-S, and CCT-CC min (the difference between the central cornea and the finest corneal thickness) were higher, whereas the CCT and CT min values were lower [18]. With Scheimpflug imaging, it is possible to determine early corneal abnormalities in subclinical diseases. The elevation maps that evaluate the cornea as a whole allow us to access the posterior cornea and anterior segment information. With the help of these maps, it has become easier to define normal eyes and forme fruste keratoconus (FFK) eyes, which show a lighter involvement [14].

In addition, the CTSP (corneal thickness spatial profile), PTI (percentage thickness increase), CVD (corneal volume distribution) were evaluated. CTSP values were significantly lower in eyes with keratoconus, and HRV and PTI were significantly higher as per a study done by Ambrosio et al. [18] Scheimpflug corneal tomography and anterior segment parameters are also important in the diagnosis of keratoconus. CTSP values were found to be significantly higher and had a higher diagnostic value for keratoconus [20]. A study by Mas-Aixala et al. [21], in which the anterior segment and topographic parameters were used together, showed that corneal changes were present in the central and peripheral regions of keratoconus eyes.

The success of Scheimpflug corneal tomography in diagnosis was not equally high for each parameter. Presence of PE is helpful in the diagnosis of subclinical keratoconus but its sensitivity and specificity are limited [14,22–25]. In a study conducted by Schlegel et al. [23] In 2008, PE and CC values were significantly different in eyes with suspected keratoconus compared to normal eyes. Muftioglu et al. in his study in 2013, found that the K value, PPI, PE, BDE values were found to be significantly higher in patients with keratoconus and FFK. Therefore, the diagnosis of BDE was suggested to be more important than PE [24].

Müftüoğlu et al. conducted a study in 2015 to investigate the relationship between new multimetric D index and keratoconus disease. In this study, multimetric D index values were found to have higher diagnostic specificity in keratoconus and subclinical keratoconus than other single parameters. However, its sensitivity was limited to the diagnosis of subclinical keratoconus [25].

In our study, none of the patients had any clinical findings of keratoconus. Only BDE was found to be significantly elevated in aortic aneurysm (8.04 µm) patients. A BDE value higher than 20 µm is a confirmed indicator of corneal ectasia and a value between 10 µm and 20 µm indicates a suspicion for keratoconus. Although the difference between the control group and the aortic aneurysm group is significant, this value is below the 10-20 µm range that indicates a suspicion for keratoconus. Nevertheless, it can be thought that ectatic changes in the cornea may be a very early finding. BDE value was also high in the patient group but the difference was not statistically significant. Corneal parameters were evaluated in diabetic and non-diabetic subgroups of patients with aortic aneurysms and BDE values were statistically higher in the diabetic group. This result contradicts the knowledge that diabetic disease is protective for keratoconus. However, a multivariate analysis is needed to arrive at the conclusion that these systemic diseases are common among these patient groups.

Our study had a few limitations, the primary one being that there was a limited sample size. Studies with a greater number of patients are needed. In addition, the median age of patients included in our study was 56.7 years, and systemic hypertension was found to be higher in patients with aortic aneurysm. This may raise controversies about whether aortic changes are associated with hypertension or connective tissue disorders. In order to eliminate the degenerative effects of systemic hypertension and atherosclerosis on the aorta, further studies may be done on a younger age group. The study may be extended by investigating other parameters that may be significant in the diagnosis of subclinical keratoconus.

Conclusion

In light of our findings, we conclude that it is appropriate to evaluate corneal ectasia in patients with aortic aneurysm. An aortic aneurysm is a vascular disease. Although atherosclerosis is its most common cause, collagen disorder is also considered among its etiologic factors. The main etiology in corneal ectasia, especially keratoconus, is a collagen structure disorder, which indicates that there may be common factors in the etiology of both diseases.

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References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42:297–319. [CrossRef]
2. Sugar J, Macsai MS. What causes keratoconus? Cornea 2012;31:716–9. [CrossRef]
3. Rabinowitz YS. The genetics of keratoconus. Ophthalmol Clin North Am 2003;16:607–20. [CrossRef]
4. Pescosolido N, Barbato A, Pascarella A, Giannotti R, Genzano M, Nebbioso M. Role of Protease-Inhibitors in Ocular Diseases. Molecules 2014;19:20557–69. [CrossRef]
5. Sawaguchi S, Twining SS, Yue BY, Chang SH, Zhou X, Loushin G, et al. Alpha 2-macroglobulin levels in normal human and keratoconus corneas. Invest Ophthalmol Vis Sci 1994;35:4008–14.
6. Mootha VV, Kanoff JM, Shankardas J, Dimitrijevich S. Marked reduction of alcohol dehydrogenase in keratoconus corneal fibroblasts. Mol Vis 2009;15:706–12.
7. Kenney MC, Chwa M, Atilano SR, Tran A, Carballo M, Saghizadeh M, et al. Increased levels of catalase and cathepsin V/L2 but decreased TIMP-1 in keratoconus corneas: evidence that oxidative stress plays a role in this disorder. Invest Ophthalmol Vis Sci 2005;46:823–32. [CrossRef]
8. Dudakova L, Liskova P, Trojek T, Palos M, Kalasova S, Jirsova K. Changes in lysyl oxidase (LOX) distribution and its decreased activity in keratoconus corneas. Exp Eye Res 2012;104:74–81.
9. Beardsley TL, Foulks GN. An association of keratoconus and mitral valve prolapse. Ophthalmology 1982;89:35–7. [CrossRef]
10. Lichter H, Loya N, Sagie A, Cohen N, Muzmacher L, Yassur Y, et al. Keratoconus and mitral valve prolapse. Am J Ophthalmol 2000;129:667–8. [CrossRef]
11. Kalkan Akcay E, Akcay M, Uysal BS, Kosekahya P, Aslan AN, Caglayan M, et al. Impaired corneal biomechanical properties and the prevalence of keratoconus in mitral valve prolapse. J Ophthalmol 2014;2014:402193. [CrossRef]
12. Ozer PA, Yalniz-Akkaya Z. Congenital keratoglobus with multiple cardiac anomalies: a case presentation and literature review. Semin Ophthalmol 2015;30:305–12. [CrossRef]
13. Dudakova L, Jirsova K. The impairment of lysyl oxidase in keratoconus and in keratoconus-associated disorders. J Neural Transm (Vienna) 2013;120:977–82. [CrossRef]
14. Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr, Guell JL, et al. Global consensus on keratoconus and ectatic diseases. Cornea 2015;34:359–69. [CrossRef]
15. Pinsard L, Touboul D, Vu Y, Lacombe D, Leger F, Colin J. Keratoconus associated with Williams-Beuren syndrome: first case reports. Ophthalmic Genet 2010;31:252–6. [CrossRef]
16. Greenfield G, Stein R, Romano A, Goodman RM. Blue sclerae and keratoconus: key features of a distinct heritable disorder of connective tissue. Clin Genet 1973;4:8–16. [CrossRef]
17. Woodward MA, Blachley TS, Stein JD. The Association Between Sociodemographic Factors, Common Systemic Diseases, and Keratoconus: An Analysis of a Nationwide Heath Care Claims Database. Ophthalmology 2016;123:457–65. [CrossRef]
18. Ambrósio R Jr, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: tomographic indices to detect keratoconus. J Cataract Refract Surg 2006;32:1851–9. [CrossRef]
19. Miháltz K, Kovács I, Takács A, Nagy ZZ. Evaluation of keratometric, pachymetric, and elevation parameters of keratoconic corneas with pentacam. Cornea 2009;28:976–80. [CrossRef]
20. Toprak I, Yaylalı V, Yildirim C. A combination of topographic and pachymetric parameters in keratoconus diagnosis. Cont Lens Anterior Eye 2015;38:357–62. [CrossRef]
21. Mas-Aixala E, Gispets J, Lupón N, Cardona G. The variability of corneal and anterior segment parameters in keratoconus. Cont Lens Anterior Eye 2016;39:466–70. [CrossRef]
22. Bae GH, Kim JR, Kim CH, Lim DH, Chung ES, Chung TY. Corneal topographic and tomographic analysis of fellow eyes in unilateral keratoconus patients using Pentacam. Am J Ophthalmol 2014;157:103–109.e1. [CrossRef]
23. Schlegel Z, Hoang-Xuan T, Gatinel D. Comparison of and correlation between anterior and posterior corneal elevation maps in normal eyes and keratoconus-suspect eyes. J Cataract Refract Surg 2008;34:789–95. [CrossRef]
24. Muftuoglu O, Ayar O, Ozulken K, Ozyol E, Akıncı A. Posterior corneal elevation and back difference corneal elevation in diagnosing forme fruste keratoconus in the fellow eyes of unilateral keratoconus patients. J Cataract Refract Surg 2013;39:1348–57. [CrossRef]
25. Muftuoglu O, Ayar O, Hurmeric V, Orucoglu F, Kılıc I. Comparison of multimetric D index with keratometric, pachymetric, and posterior elevation parameters in diagnosing subclinical keratoconus in fellow eyes of asymmetric keratoconus patients. J Cataract Refract Surg 2015;41:557–65. [CrossRef]
26. Belin MW, Khachikian SS. Keratoconus / ectasia detection with the Oculus Pentacam: Belin/Ambrosio enhanced ectasia display. In: New Advances and Technology With Pentacam. Wetzlar, Germany, Oculus Optikgerate GmbH; 3–7. Available at: http://www.oculus.de/en/downloads/dyn/oculus/presse/158/oculus_low_res.pdf. Accessed March 26, 2013.