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Comparison of anterior segment parameters between pediatric and adult keratoconus groups

Pediatrik ve erişkin keratokonus gruplarında ön segment parametrelerinin karşılaştırılması

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Abstract

Aim: To determine differences in anterior segment measurements between pediatric and adult keratoconus groups using Scheimpflug imaging system.

Materials and Methods: This retrospective study included 133 patients with keratoconus and 101 healthy controls. Subjects were grouped as pediatric and adult. Differences in anterior chamber depth (ACD), anterior chamber volume (ACV), anterior chamber angle (ACA), pachymetry, corneal volume (CV) and maximum keratometry (Kmax) were sought between the age-based subgroups.

Results: Right eyes of the 133 keratoconus patients (56 pediatrics and 77 adults) and 101 healthy controls (41 pediatrics and 60 adults) were reviewed. Pediatric subgroups had significantly higher ACD and ACV compared to those of the adult subgroups in both groups ($p<0.05$). On the other hand, pediatric and adult keratoconus patients had significantly higher ACD than in the age (subgroup) matched controls ($p< 0.05$). In the pediatric keratoconus subgroup, eyes with stage 3 keratoconus had significantly deeper ACD than in the eyes with stage 2 keratoconus ($p<0.05$). However, in the adult group, only corneal parameters were significantly lower in eyes with stage 3 keratoconus compared to those of the eyes with stage 2 keratoconus ($p<0.05$).

Conclusion: Anterior chamber measurements appear to be altered by aging in both keratoconus and control groups, whereas eyes with keratoconus in all age subgroups appear to have a deeper AC than in the age-matched normals. Moreover, an increase in ACD in pediatric keratoconus might be indicative of progression. However, in the adult keratoconus, corneal parameters appear to decrease with keratoconus progression.

Keywords: Age, anterior segment, keratoconus, pediatrics, scheimpflug.

Öz

Amaç: *Scheimpflug görüntüleme sistemi kullanarak, pediatrik ve erişkin keratokonus grupları arasındaki ön segment ölçümlerindeki farklılıkları belirlemek.*

Gereç ve Yöntem: *Retrospektif özellikteki bu çalışmaya 133 keratokonuslu hasta ve 101 sağlıklı kontrol olgusu dâhil edildi. Olgular pediatrik ve erişkin olmak üzere gruplandı. Ön kamara derinliği (ÖKD), ön kamara hacmi (ÖKH), ön kamara açısı (ÖKA), pakimetri, kornea hacmi (KH) ve maksimum keratometri (Kmaks) değerleri arasındaki farklılıklar bakımından yaş alt grupları karşılaştırıldı.*

Bulgular: *Yüz otuz üç keratokonuslu hastanın (56 pediatrik ve 77 erişkin) ve 101 sağlıklı olgunun (41 pediatrik ve 60 erişkin) sağ gözleri incelendi. Her iki grupta, pediatrik olgular erişkin grup ile karşılaştırıldığında daha yüksek ÖKD ve ÖKV değerlerine sahipti ($p<0.05$). Diğer taraftan, keratokonuslu pediatrik ve erişkin olguların yaş-eşleştirmeli sağlıklı kontrol olgularına kıyasla daha yüksek ÖKD değerine sahip olduğu görüldü ($p<0.05$). Pediatrik grupta, evre 3 keratokonuslu olgular evre 2 keratokonuslu olgulara göre daha yüksek ÖKD değerine sahipti ($p<0.05$). Erişkin grupta ise evre 3 keratokonuslu hastaların evre 2 keratokonuslu hastalara göre daha düşük korneal ölçüm değerlerine sahip olduğu saptandı ($p<0.05$).*

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Sonuç: *Keratokonus ve kontrol gruplarında yaşla beraber ön kamara parametrelerinin değiştiği görülmektedir. Ancak, tüm yaş gruplarında keratokonuslu gözlerin yaş-eşleştirmeli sağlıklı kontrollere göre daha derin ön kamaraya sahip olduğu anlaşılmaktadır. Ayrıca, pediatrik keratokonus olgularında ÖKD değerindeki artma ilerleme açısından işaret edici olabilir. Diğer taraftan, erişkin keratokonus olgularında hastalık ilerlemesi ile sadece korneal parametre değerlerinin azaldığı görüşündeyiz.*

Anahtar Sözcükler: *Keratokonus, ön segment, pediatrik, scheimpflug, yaş.*

Introduction

Keratoconus is a non-inflammatory progressive corneal disease characterized by apical protrusion and stromal thinning (1). Environmental and genetic factors play role in the pathogenesis and the disease begins at puberty (1). However, clinical manifestation of keratoconus takes time and diagnosis is generally established in early adulthood. Most of the early cases are detected during the preoperative examinations prior to the refractive surgery over 18 years of age. It is well known that pediatric keratoconus has tendency to progress rapidly and corneal transplantation is generally required in 20% of the patients (1-3). Fortunately, corneal collagen cross-linking (CXL) treatment provides promising visual and topographical improvement in patients with progressive keratoconus (2-5).

Visual deterioration in pediatric age group should be carefully evaluated and a comprehensive ophthalmological examination is needed. Keratoconus should be kept in mind as an important etiology in pediatric patients with myopia and astigmatism. In moderate to advanced keratoconus, typical clinical signs such as stromal thinning, *Fleischer's* ring, *Munson's* sign, *Rizzuti's* phenomenon and scissoring reflex on dilated retinoscopy help for the accurate diagnosis. However, in early keratoconus, new technology anterior segment imaging devices provide valuable anterior segment data for the diagnosis (6-8).

The *Scheimpflug* imaging system has ability of taking high quality slit images of the anterior segment structures from anterior surface of the cornea to the posterior of the lens using a 360^0 rotating camera. This technology provides quantitative data for anterior chamber and lens, corneal curvature, anterior and posterior elevation, corneal pachymetry and corneal volume (6-8).

In the current literature, there are studies comparing *Scheimpflug* parameters between eyes with keratoconus and healthy controls in adult population, whereas there is limited data regarding anterior segment features of eyes with keratoconus in pediatric age group (9,10). In the current study, we performed an age-based comparison (as *pediatrics* and *adults*) in terms of anterior segment measurements obtained from the *Scheimpflug* imaging system (anterior chamber parameters, corneal thicknesses, corneal volume and maximum keratometry [Kmax]) between patients with keratoconus and healthy subjects.

Materials and Methods

This study followed the tenets of the *Declaration of Helsinki* and *Local Ethics Committee* approved the methodology. We retrospectively reviewed the records of 133 right eyes of 133 patients with a confirmed diagnosis of keratoconus (keratoconus group) and 101 right eyes of 101 healthy controls (control group) aged between 10-40 years. Both keratoconus and control groups were divided into two age subgroups as *pediatric* (age< 18 years) and *adult* (age≥ 18 years). In the keratoconus group, age subgroups were matched with each other in terms of gender and keratoconus stage.

Inclusion criteria for the keratoconus group were biomicroscopic examination and corneal topography consistent with keratoconus according to the criteria of *Collaborative Longitudinal Evaluation of Keratoconus Study Group*, (11) inferior–superior (I-S) keratometric asymmetry >1.5, skewing of the steepest radial axes above and below the horizontal meridian, stromal thinning, Fleischer's ring, Munson's sign, Rizzuti's phenomenon and scissoring reflex on dilated retinoscopy.

The control group consisted of age- and gender-matched healthy subjects with normal ophthalmological examination and corneal topography (except regular astigmatism, if any).

Eyes with subclinical or form fruste keratoconus, history of prior corneal surgery, trauma or scarring were excluded from the study.

In the keratoconus group, disease severity was graded according to the *Amsler-Krumeich Classification System* (12) as follows;

Stage 1: Eccentric steepening; myopia, induced astigmatism, or both <5.00 D; mean central K < 48 D

Stage 2: Myopia, induced astigmatism, or both from 5.00 to 8.00 D; mean central K readings < 53.00 D; absence of scarring; corneal thickness >400 microns

Stage 3: Myopia, induced astigmatism, or both from 8.00 to 10.00 D; mean central K readings >53.00 D, absence of scarring; corneal thickness 300 – 400 microns

Stage 4: Refraction not measurable; mean central K readings >55.00 D; central corneal scarring, corneal thickness < 200 microns

All patients underwent detailed ophthalmological examinations included best corrected distance visual acuity (CDVA, including contact lens) measurement with Snellen charts, slit-lamp biomicroscopic examination, applanation tonometry, dilated fundus examination (with +90 D lens) and retinoscopy. Eyes with *stage 4* keratoconus were not included into the study to prevent potential effect of corneal scarring on the *Scheimpflug* measurements.

Scheimpflug imaging

A single experienced technician performed the anterior segment measurements using the *Oculus Pentacam* (Oculus Optikgerate GmbH, Wetzlar, Germany). Images were captured in automatic mode under scotopic conditions with undilated pupils. A single test with the highest quality score (over 95%) was used for the statistical analysis.

Anterior chamber depth (ACD, distance from the corneal endothelium to the anterior lens surface with undilated pupil along the optical axis), anterior chamber volume (ACV, calculated from the corneal endothelium to the anterior lens surface with undilated pupil in a 12 mm diameter around the corneal apex), anterior chamber angle (ACA), pupil-center pachymetry, apical pachymetry, thinnest pachymetry, corneal volume (CV) and Kmax were obtained for each eye.

The differences in *Scheimpflug* measurements between *pediatric* and *adult* subgroups were investigated within the keratoconus and control groups separately. *Pediatric vs. pediatric* and *adult vs. adult* comparisons were also performed regarding the *Scheimpflug* parameters between the keratoconus and control groups. Moreover, in each keratoconus subgroup (*pediatric and adult*), we sought for differences in the *Scheimpflug* measurements based on the *keratoconus stage*.

Statistical analysis

The sample size in this study was calculated using the PASS software version 11.0.1 (NSCC, LLC, Utah, USA). Statistical analysis was performed with the *Statistical Package for Social Sciences* software version 16.0 (SPSS Inc, Chicago, IL, USA). Results were expressed as mean ± standard deviation (SD). The differences in gender and keratoconus stage between the two age subgroups were analyzed using the *Chi Square* test. An *independent samples t test* was used to analyze the differences regarding quantitative variables (*Scheimpflug* system measurements) between the *pediatric* and *adult* subgroups in the keratoconus and control groups.

However, a *Mann-Whitney U* test (nonparametric) or an *independent samples t test* (parametric) was performed to compare two independent subgroups [*Pediatric vs. pediatric and adult vs. adult* comparisons (keratoconus vs. control groups), and comparisons between eyes with *stage 2 and 3* keratoconus] in terms of quantitative variables (*Scheimpflug* parameters).

Pearson correlation coefficients were used to analyze relations between *age* and *Scheimpflug* parameters. A p value less than 0.05 was considered statistically significant at 95 % confidence interval.

Results

This study involved 133 patients with confirmed keratoconus (keratoconus group, 56 pediatrics and 77 adults) and 101 age-and gender-matched healthy controls (control group, 41 pediatrics and 60 adults). Table-1 presents age, gender distribution and *Scheimpflug* measurements between the keratoconus and control groups. The keratoconus group consisted of only eyes with *stage 2* (n=61) and *stage 3* (n=72) keratoconus.

In the keratoconus group, age-based analysis showed that the *pediatric* subgroup had significantly higher ACD and ACV values when compared to those of the *adult* subgroup (Table-2, $p<0.001$, $p=0.011$, respectively). Similarly, in the control group, ACD and ACV values were significantly higher in the *pediatric* subgroup than in the *adults* (Table-2, $p=0.002$, $p<0.001$, respectively). Table-2 shows comparisons for the *Scheimpflug* parameters within the keratoconus and control groups based on the age subgroups.

Furthermore, *pediatric* patients with keratoconus had higher ACD than in the healthy *pediatrics* (3.60±0.33 vs. 3.43±0.36 mm, respectively, $p=0.020$). Similarly, *adult* patients with keratoconus had higher ACD (3.39±0.30 vs. 3.22±0.28 mm, respectively, $p=0.001$), and lower ACA (37.9±6.2 vs. 40.1±5.2 degrees, respectively, $p=0.031$) values than in the healthy *adults*.

As expected, all keratoconus subgroups had significantly higher Kmax, and lower corneal pachymetry and corneal volume compared to those of the healthy age-based subgroups ($p<0.001$).

In the keratoconus group, there were no statistically significant differences in terms of gender, keratoconus severity (based on the *Amsler-Krumeich Classification System*), corneal thicknesses, corneal volume and Kmax between the *pediatric* and *adult* subgroups ($p>0.05$).

Table-1. Age, Gender Distribution and *Scheimpflug* Measurements Between The Keratoconus and Control Groups.

Variables	Keratoconus group *(n= 133)*	Control group *(n= 101)*	p
Age *(years)*	23.4±7.6	23.7±7.6	0.841[a]
Gender *(M/F)*	72/61	53/48	0.895[b]
ACV (mm^3)	218.3±36.6	213.3±39	0.649[a]
ACD (mm)	3.4±0.33	3.3±0.34	***< 0.001*** [a]
ACA (degrees)	38.9±6.7	41.1±6.5	***0.015***[a]
Pupil center pachymetry (microns)	480.6±43.2	566.3±29.3	***< 0.001***[a]
Apical pachymetry (microns)	475.5±44.8	566.6±29.0	***< 0.001***[a]
Thinnest pachymetry (microns)	465.7±45.2	563.2±29.1	***< 0.001***[a]
CV (mm^3)	57.3±4.1	61.7±3.1	***< 0.001***[a]
Kmax (D)	54.3±5.0	44.8±1.4	***< 0.001***[a]

ACA: Anterior chamber angle; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; Kmax: Maximum keratometry
Values were presented as mean ± SD (standard deviation); p< 0.05, bold and italic values indicate statistical significance
[a]Independent samples t test
[b]Chi Square test

Table-2. Comparison of the *Scheimpflug* Measurements Based on Age Subgroups Within the Keratoconus and Control Groups.

	Keratoconus group			Control group		
Variables	**Pediatric subgroup (n=56)**	**Adult subgroup (n=77)**	**p[a]**	**Pediatric subgroup (n=41)**	**Adult subgroup (n=60)**	**p[a]**
ACV (mm^3)	**227.7±37.6**	**211.9±34.3**	***0.011***	**232.9±40.9**	**204.5±33.4**	***<0.001***
ACD (mm)	**3.60±0.33**	**3.39±0.30**	***<0.001***	**3.43±0.36**	**3.22±0.29**	***0.002***
ACA, degrees	40.3±7.2	37.9±6.2	0.052	42.5±7.8	40.1±5.2	0.095
Pupil center pachymetry (microns)	485.3±49.8	477.2±36.8	0.284	563.6±34.9	567.2±24.9	0.537
Apical pachymetry (microns)	479.5±50.7	472.6±40.1	0.383	564.1±34.5	568.3±24.7	0.502
Thinnest pachymetry (microns)	471.5±52.0	461.5±39.3	0.210	560.7±34.6	564.9±24.9	0.507
CV (mm^3)	58.1±4.7	56.8±3.4	0.098	61.8±3.3	61.6±2.9	0.854
Kmax (D)	54.4±5.3	54.2±4.6	0.892	44.7±1.3	44.8±1.4	0.707

ACA: Anterior chamber angle; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; Kmax: Maximum keratometry
Values were presented as mean ± SD (standard deviation); p< 0.05, bold and italic values indicate statistical significance
[a]Independent samples t test

The *Scheimpflug* measurements were also compared according to the *keratoconus stage* within the each age-based subgroup (*pediatric* and *adult*). In the *pediatric* subgroup, ACD was significantly higher in eyes with *stage 3* keratoconus (n=30) than in the eyes with *stage 2* keratoconus (n=26) (p=0.045). In the *adult* subgroup, AC parameters did not change between the eyes with *stage 2* (n=35) *and stage 3* (n=42) keratoconus, whereas eyes with *stage 3* keratoconus had lower corneal thicknesses (p<0.001) and CV (p=0.006) than in the eyes with *stage 2* keratoconus. Figure 1, Figure 2 and Figure 3 present the comparisons of the *Scheimpflug* AC parameters based on the keratoconus stage in each age subgroup.

In the keratoconus group, correlation analysis revealed a significant negative relation between age and AC parameters (ACD, p<0.001 r=-0.349; ACV, p=0.001 r=-0.295). In the control group, ACD and ACV were negatively correlated with age (p= 0.001, r=-0.317; p<0.001, r=-0.346, respectively). However, in both groups, age was not significantly correlated with corneal thicknesses, CV and Kmax (p>0.05).

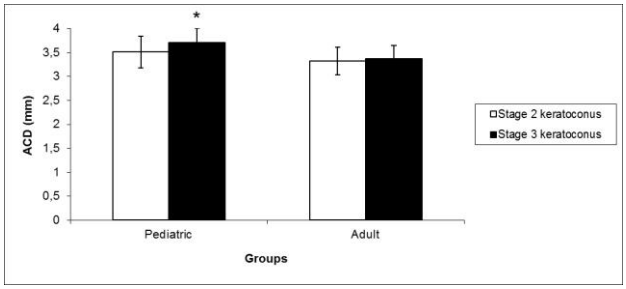

Figure-1. Comparison of anterior chamber depth (ACD) between eyes with *stage 2* and *stage 3* keratoconus in the *pediatric* and *adult* keratoconus subgroups (**statistically significant difference, p<0.05*).

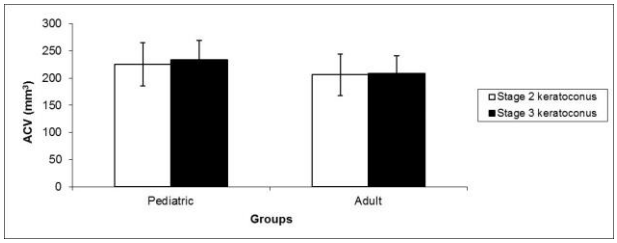

Figure-2. Comparison of anterior chamber volume (ACV) between eyes with *stage 2* and *stage 3* keratoconus in the *pediatric* and *adult* keratoconus subgroups (p>0.05).

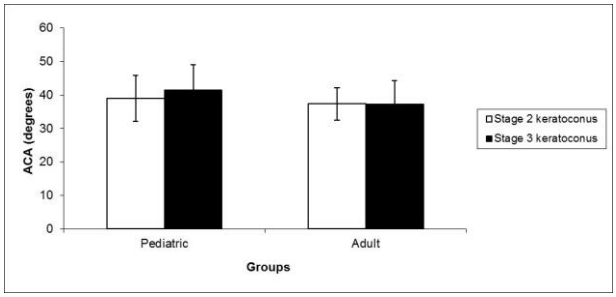

Figure-3. Comparison of anterior chamber angle (ACA) between eyes with *stage 2* and *stage 3* keratoconus in the *pediatric* and *adult* keratoconus subgroups (p>0.05).

Discussion

Keratoconus is a bilateral and asymmetric corneal disease. Although underlying mechanisms begin at puberty, the disease generally manifests at early adulthood and typical findings make the diagnosis easy (1-3). However, a complete anterior segment imaging is crucial for establishing the diagnosis. A relatively new anterior segment imaging device, the *Scheimpflug* system, provides reliable and reproducible quantitative data for anterior segment structures (13-16).

In the current literature, several researchers evaluated anterior chamber parameters of eyes with keratoconus using the *Scheimpflug* system and it was suggested that keratoconic eyes had a higher ACD compared to that of the healthy eyes (17-19). A further analysis by Emre et al. (9) showed statistically significant differences in ACA and CV measurements between the mild and severe keratoconus groups and ACV was higher in the severe keratoconus group than in the control group. In terms of corneal parameters, previous studies reported reduced corneal volume and corneal thickness in eyes with keratoconus compared to those of the healthy controls (17-19).

Although above-mentioned studies investigated differences in anterior chamber measurements, CV and pachymetry in adult keratoconus, current literature has limited data comparing anterior segment parameters between the *pediatric* and *adult* patients with keratoconus. In the present study, we sought for differences in ACD, ACV, ACA, corneal pachymetry, CV and Kmax obtained from the *Scheimpflug* imaging system between *pediatrics* and *adults* within/between the keratoconus and control groups. Statistical analysis revealed that, in both keratoconus and control groups, *pediatric* subjects (<18 years of age) had a deeper AC and larger ACV when compared to those of the *adults* (≥ 18 years of age). This result might be associated with the role of aging on AC shallowing as stated by previous studies (10,20).

It was suggested that age, gender, refractive error, body type and cataract formation are related with ACD measurement (10,20). A study by Edmonds et al. (10) showed that ACD was decreased by an average of 0.012 mm/year in a normal eye and by 0.014 mm in eyes with keratoconus. Similarly, in the current study, correlation analysis revealed a negative relation between age and AC measurements in the keratoconus and control groups. Moreover, the results of our study demonstrated a similar decrease in ACD and ACV values between the *pediatric and adult* groups in patients with keratoconus and healthy subjects. Hence, it can be suggested that shallowing of AC in the *pediatric* keratoconus subgroup over time was due to physiological process as in normal population. On the other hand, we did not have lens thickness measurements (which could be a valuable parameter) for all subjects so this parameter was not included into the statistical comparisons. This point can be considered as a limitation of the present study. Although both keratoconus patients and healthy subjects seem to show similar trend in AC measurements with aging, our study showed that *pediatrics and adults* with keratoconus had deeper AC than in the age-matched corresponding healthy subgroups.

In our study, corneal thicknesses, CV and Kmax showed no significant differences between the *pediatric and adult* keratoconus subgroups. In the current study, age subgroups were *matched* with each other in terms of gender and keratoconus severity. Therefore, we were able to perform a reliable analysis to evaluate the effect

of age on differences in anterior segment parameters between the keratoconus subgroups, whereas this condition might have led similar Kmax values between the subgroups.

In the current literature, there are few number of studies comparing *Scheimpflug* parameters between *pediatric* and *adult* patients with keratoconus, whereas Emre et al. (9) evaluated the *Scheimpflug* anterior segment parameters with a severity-based comparison in keratoconus patients, and their study group included patients with an age between 12 to 63 years. In our study, we performed a similar comparison in terms of *Scheimpflug* parameters between the eyes with *stage 2* and *stage 3* keratoconus in the *pediatric* and *adult* keratoconus subgroups separately (our study group consisted of only eyes with *stage 2 and 3* keratoconus). In the *pediatric* subgroup, ACD was significantly higher in eyes with more severe keratoconus, whereas there were no significant differences in AC parameters between the *stage 2* and *stage 3* keratoconus in the *adult* subgroup. When corneal parameters were evaluated, in the *pediatric* subgroup, there were no differences in terms of corneal thicknesses and volume between the *stage 2* and *stage 3* keratoconus, whereas in the *adult* subgroup, eyes with *stage 3* keratoconus had lower corneal thicknesses than in the eyes with *stage 2* keratoconus. Moreover, Kmax was significantly higher in *stage 3* keratoconus than in the *stage 2* keratoconus in all age subgroups as expected. In summary, in *pediatric* keratoconus, ACD seems to increase with disease severity, whereas in *adult* patients with keratoconus, corneal parameters appear to worsen with progression. A similar report from Sahebjada et al. (19) demonstrated reduced corneal thicknesses (pupil center, apical and thinnest location) in the severe keratoconus group than in the mild keratoconus group.

Conclusion

In conclusion, shallowing in AC over time appears to affect both patients with keratoconus and normals; however, it can be suggested that patients with keratoconus in *all age subgroups* have deeper AC than in the healthy controls. Furthermore, an increase in ACD value might be indicative of progression in *pediatric* patients with keratoconus. Although corneal parameters seem not to differ between age-based keratoconus subgroups, in *adult* patients with keratoconus corneal thicknesses and volume can be monitored to detect disease progression. However, long-term prospective clinical trials are needed to demonstrate the changes in anterior segment measurements from a pediatric age to the adulthood.

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