Original Article

Assessment of ganglion cell complex, macular thickness, and optic disc parameters in keratoconus patients

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Abstract:

PURPOSE: Keratoconus (KC) is bilateral noninflammatory corneal disorder characterized by progressive corneal thinning, protrusion, and scarring. The purpose of this study was to evaluate ganglion cell complex(GCC), macula thickness(MT) and optic head disc parameters in keratoconus patients.

METHODS: A hospital based prospective clinical case series was performed in Inonu University School of Medicine. 52 eyes of 52 keratoconus patients and 50 eyes of 50 normal patients were enrolled.

RESULTS: There is no statistically significant in MT between groups. GCC in nasal superior, temporal superior and temporal inferior 9 mm from macula were found statistically significant decrease in keratoconus group ($p<0,05$). In optic disc analysis fifth and the eleventh clock-hour quadrants of peripapiller retina nerve fiber layer and cup area ratio were found statistically significant decrease in keratoconic eyes ($p<0,05$).

CONCLUSION: We thought that structural retinal changes seem in keratoconus eyes; keratoconus pathogenesis may affect not only cornea but also retina and optic nerve head.

Keywords:

Keratoconus, Optic coherence tomography, Ganglion cell complex, Macular thickness, Retinal nerve fiber layer

Introduction

Keratoconus (KC) is bilateral noninflammatory corneal disorder characterized by progressive corneal thinning, protrusion, and scarring, has well-described clinical signs. Incidence of KC is approximately 1/2000 in the general population.[1] Histopathology features include breaks in epithelial basement membrane and Bowman's membrane and increased oxidative stress in keratocytes, accumulation of abnormal proteins, and changes in the orientation and distribution of collagen lamellae cause stromal thinning, and anterior stromal scarring.[2-5] KC is able to accompanied with various retinal diseases; choroidal neovascular membrane, central serous chorioretinopathy, macular coloboma, retinitis pigmentosa, and cone–rod dystrophy.[6-9] Therefore, retinal examination is important both for investigating whether the cause of visual loss accompanied by a retinal abnormality and for imaging before corneal transplantation; but it is often difficult to visualize the fundus in patients with KC because of high refractive errors, corneal astigmatism, and corneal scarring. In this context, optical coherence tomography (OCT) helps to differentiate posterior segment pathologies. Already OCT is used in evaluating postkeratoplasty.[10]

The purpose of this study was to investigate optic nerve head (ONH) parameters, retinal nerve fiber layer (RNFL), macular thickness (MT), and ganglion cell complex (GCC) in KC patients. Earlier studies have been shown measurements of the ONH, the RNFL, and MT in KC.[11-14] However, there was no study in literature investigating these parameters altogether in KC patients.

Methods

A hospital-based prospective clinical case series was performed in Inonu University

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School of Medicine. The study was approved by the ethics committee and was performed in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from each individual. All participants underwent a thorough eye exam on the day of imaging including best-corrected visual acuity (BCVA) with the logarithm of the minimum angle of resolution (LogMar) acuity chart, intraocular pressure (IOP) measurement with Goldmann applanation tonometer, dilated fundus examination, corneal topography with Scheimpflug Pentacam (Oculus, Wetzlar, Germany), and spectral-domain OCT (SD-OCT) Scan (Nidek Inc., CA, USA). The KC diagnosis was made as clinically and was also confirmed topographically using a Pentacam.

The macula thickness, GCC, and peripapillary RNFL (pRNFL) were measured with the OCT Retina, which is a high-speed SD-OCT/confocal ophthalmoscope system. Real-time, high-contrast, and wide-view (40° × 30°) confocal scanning laser ophthalmoscope imaging ensures the accuracy of OCT scanning of the pathological target. Mapping a wide area (9 mm × 9 mm) enables the GCC status to be observed, even in peripheral regions.

Glaucoma combo scanning protocol was applied to each participant. This protocol includes six maps; xy macular map [Figure 1], disc ring, x-y disk map, 12 radial macular map, 6 radial disk map [Figure 2], and 12 radial disk map. All of the SD-OCT measurements were obtained by the same clinician (GO). Submitted scans were assessed for signal strength index. Signal strength index >7 was included.

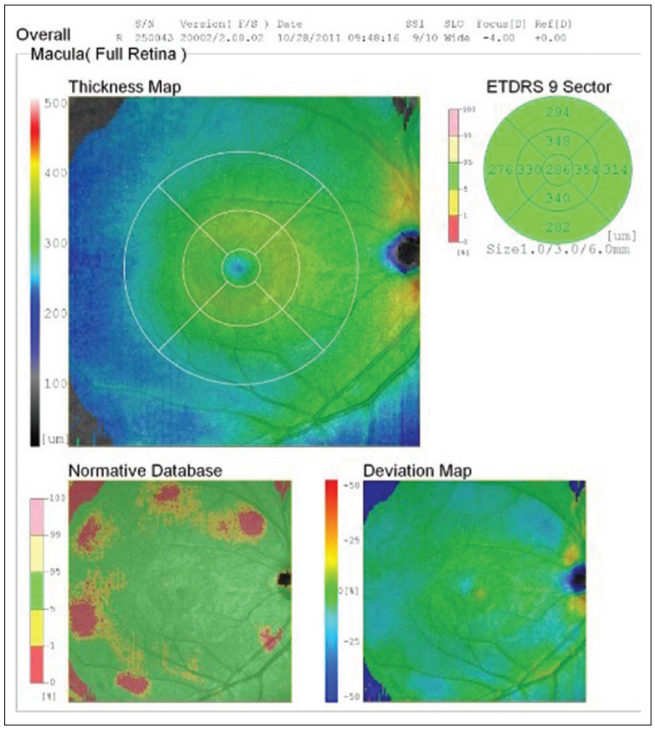

Figure 1: The x-y macula map of the Nidek RS-3000 optical coherence tomography/scanning laser ophthalmoscopesystem. Central in 1 mm, upper, lower, nasal, and temporal in 3 and 6 mm macular thickness are observed in a normal eye's optical coherence tomography scan

SPSS® 17.0 (Statistical Package for Social Science) (SPSS Inc. Chicago, IL, USA) was performed for statistical analysis. A one-way analysis of variance and Pearson Chi-square tests were performed, with age and gender as independent variables. Values showed a normal distribution ($P > 0.05$). RNFL thickness, GCC, ONH analysis, and anterior segment parameter analysis did not show normal distribution between KC and normal groups comparing, Kruskal–Wallis test was used. $P < 0.05$ was considered statistically significant.

Results

Fifty-two eyes of 52 patients (21 female and 31 male) were included in KC group. Fifty eyes of 50 patients (25 female and 25 male) were enrolled in the normal group. The mean age of the patients with KC was 25.5 ± 1.36 years, and the control group was 26.7 ± 1.13 years. No significant difference between sex and the mean age of the groups was observed ($P = 0.329$, $P = 0.10$). Mean BCVA of KC was 0.44 ± 0.46, and the normal group was 0 in LoGMar. The mean IOP was 9.76 ± 2.52 mmHg in the KC group and 13.08 ± 2.01 mmHg in the control group. Mean central corneal thickness (CCT) of KC patients was 475.5 (384–589) µm, and mean CCT of control group was 549 (477–605) µm. The mean axial length (AL) of KC group was 24.50 ± 2.51 mm, and normal group was 23.6 ± 1.6 mm. The demographic values are given in Table 1.

KC group was divided into three groups according to keratometry values. No statistically significant difference was found between these three groups and the control group in terms of age and gender ($P = 0.52$ and $P = 0.77$) [Table 2]. There was no correlation between severity of KC and OCT parameters.

There was no statistically significant difference in MT among the groups ($P > 0.05$). The mean MT among the groups is given in Table 3. The thickness of macular GCC in nasal superior 9 mm, temporal superior 9 mm, and temporal inferior 9 mm from macula measurements in the KC group were statistically decreased from normal group ($P = 0.049$, $P = 0.014$, and $P = 0.026$, respectively). The mean values of macular GCC thickness among the groups are given in Table 4.

In optic disc head analysis, thickness of 5th and 11th h of the pRNFL decreased statistically from the control group ($P = 0.044$ and $P = 0.036$, respectively). The mean value of OHD RNFL thickness among the groups is given in Table 5. Cup area (CA) was larger statistically in KC group compared to the control group ($P = 0.029$). The mean of OHD parameters among the groups is given in Table 6.

There was no statistical difference between AL and OCT thickness parameters.

Discussion

Some region of GCC and pRNFL appears to be thinner and CA larger in KC patients. Uzunel *et al*. found the RNFL, MT, and ganglion cell parameters were lower in KC than normal group.[13] In an another study, Uzunel *et al*. reported that ganglion cell parameters in all KC stages were lower than control group and did not change after fitting contact lens for correcting irregulary astigmatism, but central MT and RNFL measurements statistically increased in KC patients after wearing contact lens.[14] Our findings are in concordance with two prior studies. Furthermore, Moschos *et al*. reported that low visual acuity in KC could be due not only to the corneal abnormality but also to the photoreceptor dysfunction based on multifocal electroretinography results in their study.[15] GCC is consisting of three layers: RNFL, ganglion cell layer, and inner plexiform layer. GCC thickness reduction is known as the most important indicator of neuronal loss.[16] Furthermore, Yen *et al*. hypothesized that amblyopia affects the postnatal maturation of the retina including the postnatal reduction of retinal ganglion cells.[17,18] Poor vision caused by corneal pathology in KC patients may affect GCC maturation and may be caused thinner GCC. These findings may suggest that posterior segment pathologies may effective in KC pathogenesis, not only the anterior segment pathologies.

The appearance of the ONH can indicate ocular pathologic features; pRNLF measurements are used in the diagnosis and monitoring of various ocular and neurologic diseases. It was well-established pRNFL thickness used for the detection of early glaucoma and pRNFL thinning associated with neurodegenerative changes such as axonal loss and brain atrophy in multiple sclerosis (MS).[16,18] In our study, there was no difference AL between KC and normal group and also there was no correlation between AL and RNFL thickness. On the other hand, AL is correlated negatively with pRNFL in myopic eyes. Previous studies showed that AL influences RNFL thickness, of which the longer eyes have thinner.[19] Withal we found thinned pRNFL in our study may be associated with myopia seemed in KC, as well as retinal degeneration and caused neural loss such as glaucoma or MS. The progressive degeneration of retinal ganglion cells results in neuroretinal rim thinning and cupping, an appearance of cup/disc ratio increases, and CA parameter refers to cup/disc ratio. In our study, CA was larger in the KC group in our study;

Table 1: Demographic values of the keratoconus and normal groups

	Keratoconus group	Control group	*P*
Age (years)	25.5±1.36	26.7±1.13	>0.05
Gender (%)			
Female	21 (40.4)	25 (50.0)	>0.05
Male	31 (59.6)	25 (50.0)	>0.05
IOP (mmHg)	9.76±2.52	13.08±2.01	<0.001
CCT (µm)	475.5 (384-589)	549 (477-605)	<0.001
BCVA (LogMAR)	0.44±0.46	0	<0.001
AL (mm)	24.50±2.51	23.6±1.6	>0.05

IOP=Intraocular pressure; CCT=Central corneal thickness; BCVA=Best-corrected visual acuity; AL=Axial length; LogMAR=Logarithm of the minimum angle of resolution

Table 2: Demographic characteristics of the groups of keratoconus patients according to keratometry values

	Subject number	Mean of years	Sex
Group 1: Keratometry <47D	18	23.27±7.59	Women 44.4%, men 55.6%
Group 2: Keratometry 47-52D	18	27.27±12.85	Women 38.9%, men 61.1%
Group 3: Keratometry >52D	16	26.00±8.30	Women 37.5%, men 62.5%
Group 4: Control group	50	26.7±1.13	Women 50%, men 50%

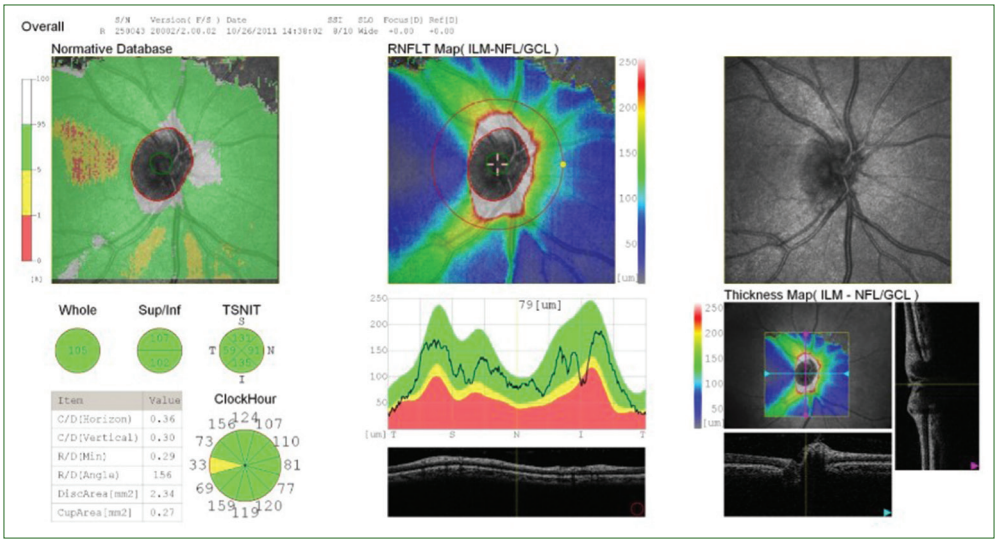

Figure 2: Twelve radial disc maps of the Nidek RS-3000 optical coherence tomography/scanning laser ophthalmoscope system. Hourly quadrant of retinal nerve fiber layer thickness and optic disc parameters are observed in a normal eye's optical coherence tomography scan

Table 3: Comparison of the mean macular thickness between keratoconus and normal groups

	Keratoconus group	Control group	*P*
Macula center	264.11±27.22	262.34±22.25	0.274
Superior 3 mm	344.63±47.07	341.64±46.71	0.318
Inferior 3 mm	345.71±24.90	343.70±15.30	0.299
Nazal 3 mm	348.38±21.70	345.94±17.47	0.343
Temporal 3 mm	329.57±30.94	331.44±14.48	0.425
Superior 6 mm	304.32±24.56	308.94±13.86	0.431
Inferior 6 mm	293.44±23.53	294.94±13.14	0.955
Nazal 6 mm	325.69±17.96	322.64±14.51	0.540
Temporal 6 mm	276.71±47.49	292.82±14.38	0.171

Table 4: Comparison of the mean thickness of macular ganglion cell complex between keratoconus and normal groups

	Keratoconus group	Control group	*P*
Nasal superior 4.5 mm	124.48±9.88	124.44±8.93	0.973
Nasal inferior 4.5 mm	123.63±7.89	122.24±17.56	0.791
Temporal supeior 4.5 mm	109.01±13.16	111.12±17.65	0.412
Temporal inferior 4.5 mm	110.67±15.88	114.64±9.57	0.425
Nasal superior 9 mm	115.92±31.63	118.60±12.36	0.049*
Nasal inferior 9 mm	129.05±16.84	130.24±11.90	0.463
Temporal supeior 9 mm	70.01±13.19	76.22±8.79	0.014*
Temporal inferior 9 mm	73.28±13.31	79.56±10. 39	0.026*

*Statiscically significant (P<0.05)

Table 5: Comparison of the mean thickness values of optic disc head retina nerve fiber layer between keratoconus and normal groups

	Keratoconus group	Control group	*P*
pRNFL 1st h quadrant	115.40±26.55	124.72±29.80.	0.89
pRNFL 2nd h quadrant	83.23±26.18	88.28±25.06	0.194
pRNFL 3rd h quadrant	53.11±23.40	58.04±16.02	0.317
pRNFL 4th h quadrant	69.23±20.40	78.06±25.43	0.99
pRNFL 5th h quadrant	109.53±31.01	125.04±33.77	0.044*
pRNFL 6th h quadrant	145.30±31.43	147.70±28.36	0.758
pRNFL 7th h quadrant	132.48±30.90	131.96±26.66	0.891
pRNFL 8th h quadrant	78.51±19.56	78.56±18.63	0.963
pRNFL 9th h quadrant	57.23±22.03	62.16±17.35	0.174
pRNFL 10th h quadrant	92.38±31.31	97.34±22.04	0.185
pRNFL 11th h quadrant	128.00±41.72	144.56±27.59	0.036*
pRNFL 12th h quadrant	142.96±31.93	142.84±27.82	0.656

*Statiscically significant (P<0.05). RNFL=Retina nerve fiber layer

Table 6: Comparison of optic disc head parameters between keratoconus and normal groups

	Keratoconus group	Control group	*P*
c/d H	0.54±0.14	0.51±0.12	0.142
c/d V	0.50±0.14	0.45±0.11	0.75
r/d min	0.15±0.07	0.33±1.06	0.89
r/d angle	192.58±103.36	152.80±116.20	0.946
Disc area	2.45±1.12	2.45±0.53	0.309
Cup area	0.77±0.74	0.59±0.27	0.029*

*Statiscically significant (P<0.05). c/d H=Horizontal cup/disc ratio; c/d V=Vertikal cup/disc ratio; r/d min=Rim/disc minimum value; r/d angle=Rim/disc angle

in concordance with Çankaya *et al*. found a wider optic disc area, CA in eyes with KC than normal eyes.[11] There was no difference MT between KC and control group; the literature establishing the same finding as our study.[15]

This study needs to be viewed in light of the following limitations. Probably, the biggest limitation is that high refractive errors in KC patients may affect OCT measurement quality. In our all participants, the signal strength of the OCT measurements was >7. The signal strength ranged from 6 to 10, values which have been referred to as moderate to excellent.[20] However, it may be a better study to repeat the OCT measurements after using contact lenses in KC patients. Recently, Uzunel *et al*. measured RNFL, MT, and ganglion cell in KC required the correction of irregular astigmatism before and after fitting rigid gas-permeable contact lenses. This study demonstrates that RNFL and central thickness and mean signal strength are affected by irregular astigmatism; ganglion cell analysis is not affected.[14] Although Hwang *et al*. measured MT in healthy participants before and after fitting a soft contact lens-induced astigmatism. No changes in MT could be found although RNFL thickness measurements were affected.[21] In light of these two studies, OCT measurements are taken after the correction of refractive error.

In conclusion, some regions of GCC and pRNFL appear to be thinner and CA larger in KC patients. These findings may contribute to vision decrease in KC patient may be associated with posterior segment pathologies, not only cornea. But also histopathologic studies are needed to confirm these findings.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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