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 School of Medicine. 52 eyes of 52 keratoconus patients and 50 eyes of 50 normal patients were enrolled.
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.

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 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 irregularly 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.[10] 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  | 264.1±27.22       | 262.3±22.25   | 0.274|
| Superior 3 mm  | 344.6±47.07       | 341.6±46.71   | 0.318|
| Inferior 3 mm  | 345.7±24.90       | 343.7±15.30   | 0.299|
| Nazal 3 mm     | 348.3±21.57       | 345.9±17.47   | 0.343|
| Temporal 3 mm  | 329.5±30.94       | 331.4±14.48   | 0.425|
| Superior 6 mm  | 304.3±24.56       | 308.9±13.86   | 0.431|
| Inferior 6 mm  | 293.4±23.53       | 294.9±13.14   | 0.955|
| Nazal 6 mm     | 325.6±17.96       | 322.6±14.51   | 0.540|
| Temporal 6 mm  | 276.7±47.49       | 292.8±14.38   | 0.171|

*Statistically significant (p<0.05)

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 | 124.4±9.88  | 124.4±8.93   | 0.973|
| Nasal inferior 4.5 mm | 123.6±7.89  | 122.2±7.56   | 0.791|
| Temporal superior 4.5 mm | 110.0±13.16 | 111.1±17.65  | 0.412|
| Temporal inferior 4.5 mm | 110.6±15.88 | 114.6±9.57   | 0.425|
| Nasal superior 9 mm | 115.9±31.63       | 118.6±12.63   | 0.049*|
| Nasal inferior 9 mm | 129.0±16.84       | 130.2±11.90   | 0.463|
| Temporal superior 9 mm | 70.0±13.19  | 76.2±8.79    | 0.014*|
| Temporal inferior 9 mm | 73.2±13.31 | 79.5±10.39   | 0.026*|

*Statistically 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 | 115.4±26.55 | 124.7±29.80  | 0.89 |
| pRNFL 2nd h quadrant | 83.2±26.18  | 88.2±25.06   | 0.194|
| pRNFL 3rd h quadrant | 53.1±23.40 | 58.0±16.02   | 0.317|
| pRNFL 4th h quadrant | 69.2±20.40  | 78.0±25.43   | 0.99 |
| pRNFL 5th h quadrant | 109.5±31.01 | 125.0±33.77  | 0.044*|
| pRNFL 6th h quadrant | 145.3±31.43 | 147.7±28.36  | 0.758|
| pRNFL 7th h quadrant | 132.4±30.90 | 131.9±26.6   | 0.891|
| pRNFL 8th h quadrant | 78.5±19.56  | 78.5±16.83   | 0.963|
| pRNFL 9th h quadrant | 57.2±22.03  | 62.1±17.35   | 0.174|
| pRNFL 10th h quadrant | 92.3±31.31 | 97.3±22.04   | 0.185|
| pRNFL 11th h quadrant | 128.0±41.72 | 144.5±27.59  | 0.036*|
| pRNFL 12th h quadrant | 142.9±31.93 | 142.8±27.82  | 0.656|

*Statistically 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      | 192.5±103.36      | 152.8±116.20  | 0.946|
| Disc area      | 2.45±1.12         | 2.45±0.55     | 0.309|
| Cup area       | 0.77±0.74         | 0.59±0.27     | 0.029*|

*Statistically significant (p<0.05)

REFERENCES

1. Krachmer JH, Feder RS, Belin MW. Keratoconus and related non inflammatory corneal thinning disorders. Surv Ophthalmol. 1984;28:293-322.
2. Rabinowitz YS. Keratoconus. Surv Ophthalmol. 1998;42: 297–319.
3. Lichter H, Loya N, Sagie A, Cohen N, Muzachier L, Yassur Y, Weinberger D. Keratoconus and mitral valve prolapse. Am J Ophthalmol. 2000;129:667–8.
4. Lema I, Sobrino T, Durán JA, Brea D, Diez-Fejoo E. Subclinical keratoconus and inflammatory molecules from tears. Br J Ophthalmol. 2009;93:820-4.
5. Jun AS, Cope L, Speck C, Feng X, Lee S, Meng H, Hamad A, Chakravarti S. Subnormal cytokine profile in the tear fluid of keratoconus patients. PLoS One. 2011;27:6.
6. Oh JY, Yu HG. Keratoconus associated with choroidal neovascularization: a case report. J Med Case Rep. 2010;19:4:58.
7. Endi CM, Del Priore LV, Bertelli E, Ober MD, Yannuzzi LA. Central serous chorioretinopathy in patients with keratoconus. Retina. 2008;28:94-96.
8. Freedman J, Gombos GM. Bilateral macular coloboma, keratoconus, and retinitis pigmentosa. Ann Ophthalmol. 1971; 3:664-665.
9. Fogla R, Iyer GK. Keratoconus associated with cone-rod dystrophy: a case report. Cornea. 2002;21:331-332.
10. Koytak A, Kubalaglu A, Sari ES, Atakan M, Cufa S, Ozerturk Y. Changes in central macular thickness after uncomplicated corneal transplantation for keratoconus: penetrating keratoplasty versus deep
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11. Çankaya AB, Beyazyildiz E, İleri D, Yılmazbaş P. Optic disc and retinal nerve fiber layer parameters of eyes with keratoconus. Ophthalmic Surg Lasers Imaging. 2012;43:401-7.
12. Sahebjada S, Amirul Islam FM, Wickremasinghe S, Daniell M, Baird PN. Assessment of Macular Parameter Changes in Patients with Keratoconus Using Optical Coherence Tomography. J Ophthalmol. 2015;2015:245953.
13. Uzunel UD, Küsbeci T, Yüksel B. Does the Stage of Keratoconus Affect Optical Coherence Tomography Measurements? Semin Ophthalmol. 2016; 1:1-6.
14. Uzunel UD, Kusbeci T, Yuce B, Yüksel B. Effects of rigid contact lenses on optical coherence tomographic parameters in eyes with keratoconus. Clin Exp Optom. 2015;98:319-22.
15. Moschos MM, Chatziralli IP, Koutsandrea C, Siasou G, Droutsas D. Assessment of the macula in keratoconus: an optical coherence tomography and multifocal electroretinography study. Ophthalmologica. 2013;229:203-7.
16. Saidha S, Sotirchos ES, Oh J, Syc SB, Seigo MA, Shiee N, et al. Relationships between retinal axonal and neuronal measures and global central nervous system pathology in multiple sclerosis. JAMA Neurol. 2013;70:34-43.
17. Yen MY, Cheng CY, Wang AG. Retinal nerve fiber layer thickness in unilateral amblyopia. Invest Ophthalmol Vis Sci. 2004; 45:2224-30.
18. Bsteh G, Hegen H, Teucher B, Amprosi M, Berek K, Ladstätter F, et al. Peripapillary retinal nerve fibre layer as measured by optical coherence tomography is a prognostic biomarker not only for physical but also for cognitive disability progression in multiple sclerosis. Mult Scler. 2019;25:196-203.
19. Savini G, Barboni P, Parisi V, Carbonelli M. The influence of axial length on retinal nerve fibre layer thickness and optic disc size measurements by spectral-domain OCT. Br J Ophthalmol. 2012;96:57-61.
20. Samarawickrama C, Pai A, Huynh SC, Burlutsky G, Wong TY, Mitchell P. Influence of OCT signal strength on macular, optic nerve head, and retinal nerve fiber layer parameters. Invest Ophthalmol Vis Sci. 2010;51:4471-5.
21. Hwang YH, Lee SM, Kim YY, Lee JY, Yoo C. Astigmatism and optical coherence tomography measurements. Graefes Arch Clin Exp Ophthalmol. 2012;250:247-54.