



# Central Corneal Thickness in Fuchs' Uveitis Syndrome

## Fuchs Uveit Sendromunda Santral Kornea Kalınlığı

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### Summary

**Purpose:** To investigate whether the central corneal thickness (CCT) values of uveitic eyes were different from those of nonuveitic eyes and of control subjects and whether the intraocular pressure (IOP) was associated with the CCT in patients with Fuchs' uveitis syndrome (FUS).

**Material and Method:** Fifty-one unilaterally involved FUS patients and 51 age- and gender-matched control subjects were included in the study. Complete ophthalmologic examinations and pachymetry measurements were performed. CCT and IOP values were compared between involved, uninvolved and control group eyes.

**Results:** The groups were age- and gender-matched. No significant difference was found between the mean CCT values of the involved ( $561.1 \pm 43.7 \mu\text{m}$ ) and uninvolved ( $564.6 \pm 45.7 \mu\text{m}$ ) eyes ( $p = 0.08$ ). When compared with the control group ( $547.7 \pm 36.9 \mu\text{m}$ ), only uninvolved eyes CCT was found to have significant difference ( $p = 0.04$ ). The mean IOP was  $14.4 \pm 7.2 \text{ mmHg}$  and  $14.6 \pm 3.4 \text{ mmHg}$  in involved and uninvolved eyes of FUS patients, respectively. Elevated IOP or glaucoma was present in 13/51 (25.5%) patients in the FUS group. The mean IOP ( $12.9 \pm 2.4 \text{ mmHg}$ ) in the control group did not reveal any significant difference compared to FUS group.

**Discussion:** The chronic low-dose inflammation does not affect corneal thickness as much as an acute inflammation, and the IOP might be associated with CCT in FUS. (Turk J Ophthalmol 2013; 43: 225-8)

**Key Words:** Fuchs, uveitis, central corneal thickness, intraocular pressure

### Özet

**Amaç:** Fuchs üveit sendromlu (FUS) hastaların üveitik gözlerindeki merkezi kornea kalınlık (MKK) değerlerinin non-üveitik ve kontrol grubundan farklı olup olmadığını ve göz içi basıncı (GİB) değerlerinin MKK ile ilişkili olup olmadığını araştırmak.

**Gereç ve Yöntem:** Tek taraflı tutulumu olan 51 FUS hastası ile yaş ve cinsiyet uyumlu 51 kontrol hastası çalışmaya dahil edildi. Tam oftalmolojik muayene ve pakimetri ölçümleri yapıldı. Tutulumu olan, olmayan ve kontrol grup MKK ve GİB değerleri karşılaştırıldı.

**Sonuçlar:** Gruplar yaş ve cinsiyet açısından uyumluydu. Tutulumu olan ( $561,1 \pm 43,7 \mu\text{m}$ ) ve olmayan ( $564,6 \pm 45,7 \mu\text{m}$ ) gözlerde ortalama MKK değerleri açısından fark yoktu ( $p = 0,08$ ). Kontrol grubu ( $547,7 \pm 36,9 \mu\text{m}$ ) ile karşılaştırıldığında yalnız tutulum olmayan göz MKK değeri anlamlı olarak farklıydı ( $p = 0,04$ ). FUS hastalarında ortalama GİB tutulum olan ve olmayan gözlerde sırasıyla  $14,4 \pm 7,2 \text{ mmHg}$  ve  $14,6 \pm 3,4 \text{ mmHg}$  idi. Kontrol grubu ortalama GİB ( $12,9 \pm 2,4 \text{ mmHg}$ ) FUS grubu ile karşılaştırıldığında anlamlı farklılık yoktu.

**Tartışma:** Kronik düşük dereceli enflamasyon kornea kalınlığını akut enflamasyon kadar etkilememektedir ve FUS' da GİB ile MKK arasında ilişki olabilir. (Turk J Ophthalmol 2013; 43: 225-8)

**Anahtar Kelimeler:** Fuchs, üveit, merkezi kornea kalınlığı, göz içi basıncı

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## Introduction

Since first described by Ernst Fuchs<sup>1</sup> in 1906, the uveitic entity called Fuchs' uveitis syndrome (FUS) has dragged the attention of ophthalmologists. It is a chronic, low-grade, mainly anterior uveitis with varied degree of vitreous opacities, characteristic diffusely spread small to medium sized keratic precipitates (KPs), diffuse iris atrophy with or without obvious heterochromia and lack of posterior synechiae. Due to its silent course without acute exacerbations, patients mostly present with floaters or complications like cataract and glaucoma.<sup>2,3</sup>

The corneal thickness is a major parameter for corneal integrity and depends on endothelial barrier and pump functions. The effect of intraocular inflammation on corneal thickness was studied both *in vitro*<sup>4,5</sup> and *in vivo*.<sup>6,7</sup> MacDonald et al.<sup>5</sup> showed that anterior segment inflammation affects both endothelial barrier and pump functions leading to increased corneal thickness. Pillai et al.<sup>7</sup> studied the corneal endothelium in acute uveitis and have found a significant difference in cell size and density of the endothelium in the vicinity of KP. Similarly, studies that were conducted to compare CCT values in acute and remission phase of Behçet's disease patients have found a significant difference in corneal thickness.<sup>8,9</sup>

The aim of this study was to investigate whether the CCT values of uveitic eyes were different from those of nonuveitic eyes and of age- and gender-matched normal individuals, and also, whether the intraocular pressure (IOP) was associated with the CCT in patients with FUS.

## Materials and Methods

The study included 51 unilaterally involved patients diagnosed as FUS who were being followed at our Uvea and Behçet's Disease department and 51 age- and gender-matched control subjects who had undergone a daily outpatient examination. Subjects having bilateral uveitic involvement, corneal diseases, and history of contact lens wear or ocular surgery were excluded. All subjects were informed about the study and their consents were taken. The study adhered to the tenets of Declaration of Helsinki guidelines. The clinical diagnosis of FUS was made or confirmed by the same clinician. Clinical findings taken into consideration for the diagnosis of FUS were low-grade chronic anterior inflammation, diffuse iris atrophy with or without heterochromia, typical diffusely spread KPs, vitreous opacities, presence of posterior subcapsular cataract, lack of posterior synechiae and cystoid macular edema, resistance to steroid therapy, absence of acute exacerbations, and posterior inflammation. When several of these findings were present, the diagnosis was made as FUS, and no diagnostic examination was performed in most of the patients. All patients underwent detailed ophthalmic examination including best-corrected visual acuity on a Snellen chart, tonometry, slit-lamp biomicroscopy, and dilated fundus examination. The examinations and the measurements were performed between 9 and 11 a.m. by the same doctor to avoid diurnal and interobserver variations.

Intraocular pressure was measured by non-contact tonometer (Reichert AT-555; Reichert Ophthalmic Instruments, NY, USA) without any topical anesthetic, and the average of 4 readings was recorded. CCT was measured by ultrasound pachymeter (Tomey Bio-pachymeter AL-1000; Tomey Corporation, Nagoya, Japan) under topical anesthesia and again the average of 4 consecutive readings was recorded. Patients in whom the IOP was >21 mmHg without any glaucomatous cupping and visual field defects were considered as elevated IOP. Patients with IOP readings greater than 21 mmHg with glaucomatous cupping and visual field defects were diagnosed as having glaucoma. The statistical analysis was performed by SPSS 15.0, and  $p < 0.05$  was accepted as statistically significant.

## Results

The mean age was  $35.7 \pm 11.9$  years in FUS patients and  $36.3 \pm 5.0$  years in control subjects. The male to female ratio was 26/25 in FUS group and 25/26 in control group. The two groups were age- and gender-matched (independent-sample t-test,  $p = 0.75$  and Mann-Whitney U-test,  $p = 0.84$  respectively). In the FUS group, the inflammation was on the right eye in 62.7% of the patients. Mean values of involved and uninvolved eyes of FUS group and control group IOP and CCT values are shown in Table 1. The mean CCT values of the involved and uninvolved eye in the FUS group were  $561.1 \pm 43.7$   $\mu\text{m}$  and  $564.6 \pm 45.7$   $\mu\text{m}$ , respectively. There was no statistically significant difference between the CCTs of involved and uninvolved eyes (paired-sample t-test,  $p = 0.08$ ). The mean right and left eye CCT values of the control group were  $547.7 \pm 36.9$   $\mu\text{m}$  and  $549.6 \pm 37.2$   $\mu\text{m}$ , respectively. Since there was a strong correlation between right and left eye values, the right eye CCT values of the control group were used for statistical analysis (Pearson's correlation test,  $r = 0.97$   $p = 0.00$ ). Although the CCT values of both the involved and uninvolved eyes of FUS group were found to be higher than those of the control group, this difference was statistically significant only for the uninvolved eyes (independent-sample t-test,  $p = 0.09$  and  $p = 0.04$ , respectively).

Since there was a significant correlation between right and left eye IOP values of the control subjects and FUS group, the right eye IOP values were used for statistical purposes (Pearson's correlation test,  $r = 0.731$   $p = 0.00$  and  $r = 0.421$  and  $p = 0.00$ , respectively). There was no statistically significant difference between the mean IOP values of FUS group ( $14.4 \pm 7.2$  mmHg) and the control group ( $12.9 \pm 2.4$  mmHg) (independent sample t-test,  $p = 0.15$ ). Elevated IOP or glaucoma was present in 13/51 (25.5%) patients in FUS group but in none of the control group.

In the FUS group, the mean IOP was  $14.4 \pm 7.2$  mmHg and  $14.6 \pm 3.4$  mmHg in involved and uninvolved eyes, respectively. Although statistically insignificant, the mean IOP in the uninvolved eyes was slightly higher than that of the involved eyes (paired-sample t-test,  $p = 0.89$ ). Number of patients having higher IOP readings in the uninvolved eye was 28 (55%).

The mean CCT of 13 FUS patients with elevated IOP or glaucoma was  $556.2 \pm 52.9$   $\mu\text{m}$ , while it was  $562.8 \pm 40.7$   $\mu\text{m}$  in

patients with normal IOP. This difference was not statistically significant (Mann-Whitney U-test,  $p=0.56$ ).

## Discussion

Fuchs' uveitis syndrome is a unique condition characterized by chronic, low-grade and mostly asymptomatic ocular inflammation leading to complications like cataract, glaucoma, or severe vitreous opacities. Although the diagnosis of FUS is entirely clinical, it is often misdiagnosed mostly because of the vitreous involvement which is not commonly recognized as an association with FUS.<sup>3,10-12</sup>

The etiology of this particular entity is still unclear. Infectious etiologies like Herpes simplex virus,<sup>13</sup> toxoplasma-toxocara-histoplasma<sup>3</sup> and rubella,<sup>14</sup> hereditary associations<sup>15,16</sup> and neurogenic dysfunction theories<sup>17,18</sup> are being argued to clarify the underlying pathology.

The effect of intraocular inflammation on corneal endothelium has been studied both in experimental<sup>4,5</sup> and in clinical studies.<sup>6,8,9</sup> In an experimental model, MacDonald et al.<sup>5</sup> injected serum bovine albumin intravitreally and created an ocular inflammation. They showed that ongoing inflammation causes a breakdown in apical junctions of corneal endothelium leading to compromised barrier function. They also detected a breakdown in endothelial pump sites. These two conditions have resulted in an increment of the corneal thickness. Different studies have also demonstrated polymegathism and polymorphism of endothelial cells in specular microscopic examinations.<sup>6,7,19,20</sup> The endothelial changes that occur in the active inflammatory phase are believed to be temporary and return to normal after the inflammation subsides.

Ozdamar et al.<sup>8</sup> and Evereklioglu et al.<sup>9</sup> studied CCT in Behçet's disease patients. Both studies have found that the CCT values of patients with active inflammation are greater than inactive Behçet's disease and control group. The mean CCT value of the active Behçet's disease patients was found to be approximately 30-40  $\mu\text{m}$  thicker. They also emphasized that this CCT increase was temporary and returned to normal values as the active inflammation subsided.

Differently from Behçet's disease, inflammation is always low-grade and chronic in FUS. One of the characteristic clinical features of this typical inflammatory pattern is the presence of diffusely spread, fine, stellate or medium-sized round non-pigmented KPs.<sup>2,3,12</sup> As we mentioned before, KPs are blamed for changing the endothelium metabolism.<sup>7</sup> To see if the corneal endothelium is affected by the chronic inflammation due to FUS, we evaluated CCT values of patients with this specific uveitic entity. As it is directly influenced by the endothelial function, CCT is an ideal parameter to evaluate the endothelial changes.<sup>22,23</sup> To the best of our knowledge, this study is the first and only study to evaluate CCT in FUS. Since we excluded bilateral involvement, we had chance to compare the involved and uninvolved eyes in same patient which neutralizes the subjects variations. In our study, the mean CCT of the involved eye was  $561.1 \pm 43.7 \mu\text{m}$  and in the uninvolved eye was

$564.6 \pm 45.7 \mu\text{m}$ . Whereas the mean CCT value of the control group was  $547.7 \pm 36.9 \mu\text{m}$ . The CCT values of patients with FUS both in involved and uninvolved eyes were higher than those of the control subjects. This difference was significant only for the uninvolved eyes. These results may be considered as evidence showing that the chronic inflammation in FUS does not disturb the endothelial functions as much as in acute inflammatory conditions and that the cornea is thicker than the normal population probably due to hereditary factors.

Elevated IOP or glaucoma is considered to be the most serious problem of FUS.<sup>2</sup> Its incidence is reported to vary between 6.3% and 59% in a review by Jones.<sup>21</sup> Elevated IOP has been reported in 12.7% of patients in Tugal-Tutkun et al.'s<sup>12</sup> study and in 24% in Norrsell and Sjödel's<sup>2</sup> study in accordance with our result which is 25.5%. The thickness of the cornea is closely related to IOP measurements with thicker cornea leading to higher IOP readings. Ocular Hypertension Treatment Study (OHTS) had revealed that CCT is also an independent risk factor for glaucoma conversion of ocular hypertension.<sup>24</sup> In the meta-analysis of 80 studies, Doughty and Zaman<sup>25</sup> reported that 20  $\mu\text{m}$  change in CCT corresponded to 1 mmHg change in IOP. Although statistical significance appeared only for the uninvolved eyes of FUS patients, the mean CCT of FUS patients in both involved and uninvolved eyes were approximately 20  $\mu\text{m}$  thicker than the control group, which may result in approximately 1 mmHg higher IOP readings. The mean IOP of involved ( $14.4 \pm 7.2 \text{ mmHg}$ ) and uninvolved eyes ( $14.6 \pm 3.4 \text{ mmHg}$ ) were approximately 1.5 mmHg higher when compared to the mean IOP of the control group ( $12.9 \pm 2.4 \text{ mmHg}$ ). The higher IOP readings in FUS patients might be attributable to their thicker corneas. Although elevated IOP is an important problem in FUS and is observed in 25.5% of our patients, interestingly, the mean IOP was lower in most of the involved eyes (55%) when compared with the uninvolved eyes. Bouchenaki and Herbot<sup>10</sup> had reported similar finding regarding the IOP difference between healthy and affected eyes of their FUS patients. The mean IOP was lower in 50% of affected eyes in their series.

As a conclusion, although an acute ocular inflammation affects endothelial functions and thus the corneal thickness as reported in previous studies,<sup>4-6,8,9</sup> a chronic inflammation does not affect the corneal endothelial functions and corneal thickness as much as the acute ocular inflammatory conditions. However, higher CCT readings in FUS patients may result in high IOP measurements.

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