Evaluation of Retinal and Choroidal Parameters in Eyes of Unilateral Pseudoexfoliation Patients

Tek Taraflı Psödoeksfoliasyon Hastalarının Gözlerindeki Koroid ve Retina Parametrelerinin Değerlendirilmesi

Fatih ÇELİK[1], Mete GÜLER[2], Adem SOYDAN[3]

ABSTRACT

Purpose: To compare choroidal thickness (CT), retinal thickness (RT) and retinal nerve fiber layer thickness (RNFL) in eyes of unilateral Pseudoexfoliation (PEX) patients without glaucoma and compare them with healthy controls.

Material and Methods: Sixty eyes of 30 PEX patients without glaucoma and 32 eyes of 32 healthy subjects were included in this study. The CT, RT, RNFL measurements were compared between PEX, PEX unaffected eye and control groups. All optical coherence tomography (OCT) scans and measurements were acquired by Spectralis OCT. CTs were measured with enhanced depth imaging (EDI) mode of Spectralis OCT. The RTs was measured using automatic segmentation values of the Spectralis OCT. Optic disc protocol was used to measure RNFLs.

Results: Compared with controls nasal RT was thinner in PEX (p=0,009) and PEX unaffected eye (p=0,013) groups. Nasal retina in PEX and PEX unaffected eye was similar (p=0,992). Temporal RT was also thinner in PEX (p=0,004) and PEX unaffected eye (p=0,009) than control group. Temporal RT was similar in PEX and PEX unaffected eyes (p=0,975).Global RNFL was thinner in PEX group (p=0,011) than control group. Global RNFL was similar in PEX and PEX unaffected eye groups (p=0,433). Nasal inferior RNFL in PEX group was thinner than control group (p=0,026). Nasal inferior RNFL was similar in PEX and PEX unaffected eye groups (p=0,358).

Conclusion: RT and RNFL may be thinner in eyes with PEX patients without glaucoma and in fellow eyes of PEX patients than age-matched controls.

Key Words: Choroidal thickness, Optical coherence tomography, Pseudoexfoliation, Retinal nerve fiber layer thickness, Retinal thickness.

ÖZ

Amaç: Glokomu olmayan tek taraflı psödoeksfoliasyonlu (PS) hastalar ile sağlıklı kontrollerin gözlerindeki koroid kalınlığı (KK), retina kalınlığı (RK) ve retina sinir tabakası kalınlığını (RSK) karşılaştırmak.

Gereç ve Yöntemler: Glokomu olmayan PS hastasının 30 gözü ile 32 sağlıklı kişinin 32 gözü çalışmaya alındı. KK, RK ve RSK'ları PS'li, PS'li etkilenmeyen göz ve kontrol grupları ile karşılaştırıldı. Tüm optik koherens tomografi (OKT) taramaları ve ölçümleri Spectralis OKT ile alındı. KK'ları Spectralis OKT' nin arttırılmış derinlik görüntüleme (EDI) modu ile yapıldı. RK'ları Spectralis OKT' nin otomatik bölünme değerleri kullanılarak ölçüldü. RSK'ları için optik disk protokolü kullanıldı.

Bulgular: Kontrollerle kıyaslandığında PS (p=0,009) ve PS'lilerin etkilenmeyen gözlerinde (p=0,013) nazal RK kontrollerden daha ince idi. Nazal RK, PS ve PS'lilerin etkilenmeyen gözlerinde benzerdi (p=0,992). Temporal RK da PS (p=0,004) ve PS'lilerin etkilenmeyen gözlerinde (p=0,009) kontrollerden daha ince bulundu. Temporal RK, PS ve PS'lilerin etkilenmeyen gözlerinde benzerdi (p=0,975). Kontrol grubu ile karşılaştırıldığında PS grubunda (p=0,011) genel RSK daha ince idi. Genel RSK, PS ve PS'lilerin etkilenmeyen gözlerinde (p=0,433) benzerdi. PS grubunda nazal inferior RSK, kontrol gurundan daha ince idi (p=0,026). PS ve PS'lilerin etkilenmeyen gözlerinde nazal inferior RSK benzerdi (p=0,358).

Sonuç: RK ve RSK, glokomu olmayan PS hastaların gözlerinde ve PS'li hastaların etkilenmemiş gözlerinde aynı yaştaki kontrollerden daha ince olabilir.

Anahtar Sözcükler: Koroid kalınlığı, Optik koherens tomografi, Psödoeksfoliasyon, Retina kalınlığı, Retina sinir lifi kalınlığı.

1- Uz. Dr., Elazığ Eğitim ve Araştırma Hastanesi, Göz Hastalıkları Kliniği, Elazığ, Türkiye

2- Doç. Dr., Elazığ Eğitim ve Araştırma Hastanesi, Göz Hastalıkları Kliniği, Elazığ, Türkiye

3- Yrd. Doç. Dr., Gaziosmanpaşa Üniversitesi Tıp Fakültesi, Göz Hastalıkları Anabilim Dalı, Tokat, Türkiye

Geliş Tarihi - Received: 24.03.2017
Kabul Tarihi - Accepted: 25.07.2017
Ret-Vit 2018; 27: 67-72

Yazışma Adresi / Correspondence Adress:
Mete GÜLER
Elazığ Eğitim ve Araştırma Hastanesi, Göz Hastalıkları Kliniği, Elazığ, Türkiye

Phone: +90 533 771 4080
E-mail: meteglr@yahoo.com

INTRODUCTION

Pseudoexfoliation (PEX) syndrome is characterized by the deposition of complex various glycoproteins in the anterior segment of the eye and other systemic tissues.[1] Pseudoexfoliation fibers have been identified in many extra-ocular tissues, such as the heart, lung, gall bladder, kidney, and cerebral meninges.[2] Pseudoexfoliation syndrome (PEXS) is a late onset condition with prevalence that increases markedly with age.[1] Evidence suggests that unilateral PEX is a bilateral but asymmetric disorder and that the percentage of unilateral disease decreases with the corresponding increase in bilateral disease in patients with increasing age. However, the factors affecting the conversion from unilateral to bilateral disease are not known, and the pathogenic mechanism underlying the asymmetrical condition has not been determined.[3]

Anterior segment manifestations of PEX have been well defined, such as iris depigmentation leading to peripupillary transillumination defects, mild trabecular meshwork hyperpigmentation, secondary open-angle glaucoma, and phacodonesis or lens subluxation caused by zonular dehiscence.[4]

Although affecting primarily the anterior ocular segment, PEX material has also been detected in the walls of posterior ciliary arteries, vortex veins, and central retinal vessels passing through the optic nerve sheaths. These have led to the hypotheses that PEXS may be associated with ischemic ophthalmic disorders, and although PEX glaucoma (PEXG) is characteristically a high-pressure disease, pressure-independent risk factors, such as impaired ocular and retrobulbar blood flow may be present.[5] Abnormal choroidal blood supply maybe contribute to the pathogenesis of glaucomatous optic neuropathy.[6] In the light of these findings we aimed to study choroidal thickness (CT), retinal thickness (RT) and retinal nerve fiber layer thickness (RNFL) in eyes of unilateral PEX patients without glaucoma and to compare them with healthy controls**.**

MATERIALS AND METHODS

This prospective, non randomized study was performed at Elazığ Education and Research Hospital. The study was conducted according to the principles of the Declaration of Helsinki rules and was approved by the institutional ethic committee. Informed consent was obtained from each patient. Sixty eyes of 30 PEX patients and 32 eyes of 32 healthy subjects were included in this study. Patients with a history of diabetes mellitus, systemic arterial hypertension, systemic vasculopathies, retinal disease (ie, macular degeneration), ocular surgery, ocular trauma, ocular inflammation, or refractive errors outside -5 to +3 D were excluded. Smoking was also an exclusion criterion. The presence of clinical PEX was determined by slit-lamp examination after mydriasis with the presence of fibrillin deposits on the anterior lens capsule and the pupillary margin. The patients with PEX had no glaucoma history and no clinics. The glaucoma in PEX patients were excluded with complete ophthalmic examination, including a review of medical history, slit-lamp biomicroscopy of anterior and posterior segment, gonioscopy, Goldmann applanation tonometry (GAT), ultrasound pachymetry and visual field testing. GAT measurements were taken in a sitting position and the mean of 3 consecutive readings was calculated. Visual field sensitivity was tested using Humphrey perimetry (Carl Zeiss Meditec, Dublin, CA) with the 30-2 program. The visual field testing was considered reliable if the fixation losses and false-positive and false-negative responses were <20%. To eliminate the learning effect, the second visual field of each eye was included in the statistical analysis. Unilateral PEX patients with normal intraocular pressure, optic nerve and visual fields were evaluated for further analyses. The axial length measurement was obtained with optical biometry (Lenstar LS 900; Haag-Streit AG, Köniz, Switzerland)

All optical coherence tomography (OCT) scans and measurements were acquired by the same experienced operator (FÇ) with Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany, software version 5.3). The operator was blinded to the participants. Measurements were performed between 8:00 a.m to 11:00 a.m. The RT was measured using automatic segmentation values of the Spectralis OCT. The CT was measured by enhanced depth imaging (EDI) mode using the spectral-domain OCT. The CT was measured manually from the outer portion of the hyperreflective line corresponding to the retina pigment epithelium to the inner surface of sclera. Using the manual calipers provided by the SD-OCT software, the experienced operator (FÇ) measured the CT at 100% magnification and fine corrections were performed at 200% magnification. The RT and CT were measured at the central fovea and at 1500 µm nasal and at 1500 µm temporal from the center of the fovea (Figure). The RNFL optic disc protocol was used to measure RNFL. The CT, RT, RNFL measurements were compared between PEX, unaffected PEX eyes and control groups.

Statistical Analyses

Statistical analyses were performed with Statistical Package for the Social Sciences (SPSS ver.17) and P values <0.05 were considered statistically significant. Quantitative variables were expressed as mean values±SD. The one-way analysis of variance test was used to compare results between the groups. Post hoc comparisons were made using the Tukey HSD test.

RESULTS

Of 62 participants, 28 were male and 34 were female with a mean age of 66,69±8,88 years (ranging from 51 to 85 y). The sex (p=0,21), age (p=0,72) and axial length (p=0,32)

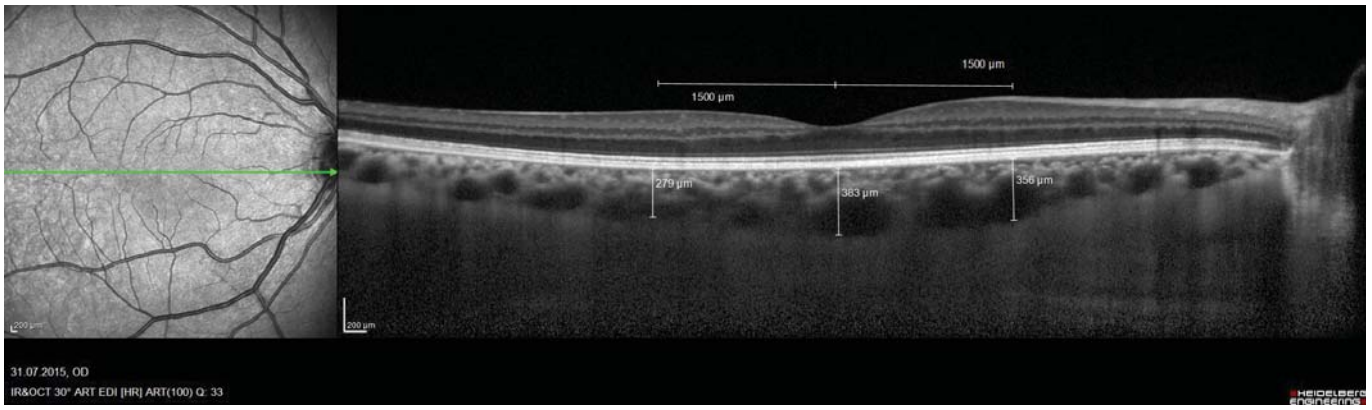

Figure: *Optical coherence tomography scan showing the measurement of choroidal thickness. Lines indicate the choroidal thickness measurement at the central fovea and 1500 µm nasal and 1500 µm temporal from the center of the fovea.*

Table 1. *The demographic characteristics of the patients and axial lengths of eyes.*

GROUP	Axial lenght	Age	Male	Female
PEX uneffected	22.98±0.94	64.55±7.47	12 (19%)	18 (29%)
PEX	22.87±0.76	64.55±7.47	12(19%)	18(29%)
Control	23.26±0.81	67.64±8.03	16(26%)	16(26%)

were similar between PEX and control groups (Table 1). The mean CT, RT, RNFL measurements at each location are shown in Table 2.

There was no significant difference with respect to mean central CT (p=0,081), nasal CT (p=0,423), temporal CT (p=0,256), central RT (p=0,932) between patients with PEX, PEX unaffected eye and controls. Nasal RT (p=0,02), and temporal RT (p=0,01) were significantly different between groups. Compared with controls nasal RT was thinner in PEX (p=0,009) and PEX unaffected eye (p=0,013) groups. Nasal retinal thickness in PEX and PEX unaffected eye was not statistically different (p=0,992). Temporal RT was also statistically thinner in PEX (p=0,004) and PEX unaffected eye (p=0,009) than control group. Temporal RT was not statistically different in PEX and PEX unaffected eyes (p=0,975).

There was no significant difference in terms of temporal superior (p=0,069), temporal (p=0,410), temporal inferior (p=0,319), nasal (p=0,411), nasal superior (p=0,056) RNFL between PEX, PEX unaffected eye and control groups. RNFL at global (p=0,014) and nasal inferior (p=0,035) areas were differrent between three groups. Global RNFL was thinner in PEX group (p=0,011) than control group. Global RNFL was not statistically different in PEX and PEX unaffected eye groups (p=0,433). Nasal inferior RNFL in PEX group was thinner than control group (p=0,026). Nasal inferior RNFL was not statistically different in PEX and PEX unaffected eye groups (p=0,358).

DISCUSSION

Retinal and choroidal parameters in PEX patients have been evaluated in some investigations before. Eltutar et al.[7] evaluated early structural changes of macular ganglion cell complex (GCC), peripapillary nerve fiber layer (NFL), and optic nerve head (ONH) topography in subjects with PEX without glaucoma using 3-D spectral domain optical coherence tomography and compared with healthy controls. In this study PEX group showed a significant thinner superior and total macular NFL and thinner superior and total ganglion cell layer and inner plexiform layer with respect to the normal group. The PEX group also showed a significant thinner superior, inferior, and total GCC with respect to the normal group. According to the peripapillary NFL measurements evaluated by OCT, the PEX group showed a significant thinner inferior, temporal, nasal, and total peripapillary NFL with respect to the normal group.

Riga et al.[8] compared ONH and RNFL measurements obtained with the OCT in normal and in patients with PEX [with or without increased intraocular pressure (IOP)]. They reported that mean RNFL thickness measured by OCT was larger in the normal controls than in the other two groups. They noted that four-quadrant RNFL thickness measurements were significantly different between the normal and the PEX with increased IOP but not with the PEX without increased IOP. Rim area and cup-to-disc ratio was significantly different between the normal and the two groups.

Table 2. *The mean CT, RT, RNFL measurements in groups. PEX:Pseudoexfoliation, CT: Choroidal thickness, RT: Retinal thickness, RNFL: Retinal nerve fiber layer thickness. Statistically different results were denoted with bold and italic font.*

PARAMETER	PEX (1)	PEX Uneffected eye (2)	Control (3)	P value
Subfoveal CT	262,13±109,24 (95-534)	250,46±103,84 (81-430)	300,97±85,97 (143-480)	1-2-3: p=0,081
CT 1500 µm nasal to the fovea	208,00±93,12 (70-360)	213,74±94,21 (50-360)	235,52±83,26 (97-418)	1-2-3 p=0,423
CT 1500 µm temporal to the fovea	231,43±91,51 (83-469)	222,52±88,09 (84-465)	256,36±78,92 (112-410)	1-2-3 p=0,256
Central RT	221,69±20,73 (183-276)	219,65±20,54 (185-270)	221,09±17,37 (194-264)	1-2-3 p=0,932
RT 1500 µm nasal to the fovea	337,35±18,41(303-382)	337,91±17,57 (306-381)	349,69±12,67 (329-383)	***1-2-3 p=0,02*** 1-2 p=0,992 ***1-3 p=0,009*** ***2-3 p=0,013***
RT 1500 µm temporal to the fovea	316,04±17,95 (285-350)	315,04±18,18 (278-350)	328,40±12,82 (300-355)	***1-2-3 p=0,01*** 1-2 p=0,975 ***1-3 p=0,004*** ***2-3 p=0,009***
RNFL global	93,53±11,01 (65-114)	96,80±8,37 (80-110)	100,85±10,82 (74-122)	***1-2-3 p=0,014*** ***1-3 p=0,011*** 1-2 p=0,443
RNFL temp-sup	122,17±21,57 (79-161)	129,00±19,45 (86-167)	134,02±02±21,59 (64-165)	1-2-3 p=0,069
RNFL temporal	67,03±10,38 (46-88)	68,83±11,95 (52-103)	71,15±14,96 (40-97)	1-2-3 p=0,410
RNFL temp-inf	139,53±27,59 (60-177)	138,13±16,00 (110-175)	145,72±22,37 (91-200)	1-2-3 p=0,319
RNFL nasal-sup	103,70±21,78 (60-157)	106,60±23,49 (70-156)	116,40±23,61 (82-187)	1-2-3 p=0,056
RNFL nasal	72,33±14,96 (43-105	76,46±13,64 (57-112)	75,90±11,17 (53-96)	1-2-3 p=0,411
RNFL nasal-inf	102,50±20,63 (59-143)	109,53±20,77 (70-153)	115,10±18,42 (87-165)	***1-2-3 p=0,035*** ***1-3 p=0,026*** 1-2 p=0,358

Vergados et al.[9] evaluated the ONH parameters and RNFL thickness in subjects with bilateral PEX, bilateral PEXG and normal controls. They found that RNFL thickness was significantly lower in the PEX group compared with the normal group, but there was not a statistically significant difference with the PEXG patients.

Rao et al.[10] compared peripapillary RNFL thickness in affected and fellow eyes of patients with unilateral PEXS and with that of bilateral cases. Subjects with elevated IOP or findings suggestive of glaucoma were excluded in this study. It is found that subjects with bilateral PEX have significantly thinner RNFL as compared to unilateral cases. Interestingly they reported that from a total of 32 unilateral PEX cases, 7 subjects demonstrated RNFL thinning in the clinically normal fellow eye. All of these eyes had evidence of pupillary ruff atrophy on slit lamp examination in the absence of evident exfoliation material in the eye.

Ozge et al. compared RNFL thickness and CT measurements in eyes with PEXG, PEXS and healthy control eyes. RNFL thickness in all quadrants and average thickness were significantly lower in PEXG eyes compared to PEXS eyes and healthy control eyes. CT measurements were similar between groups.[11]

Bayhan et al.[12] evaluated the CT in PEXG and age-matched healthy subjects using spectral OCT. Findings of this study indicated that PEXG causes significant thinning in the nasal choroid. There were no significant differences in the subfoveal and temporal CT measurements among the PEXG and controls.

Zengin et al.[13] evaluated the CT using spectral-domain OCT in patients with PEXS and compared them with healthy controls. Although PEX patients had lower mean CT than controls their results did not reach any statistical significance.

Yuksel et al.[14] compared RNFL thickness between eyes with PEX and contralateral fellow eyes without PEX and control eyes. They found that the RNFL thickness was lower in eyes with PEX than contralateral eyes and the control group.

Demircan et al.[15] investigated RNFL and CT in patients

with PEXS and PEXG compared with healthy volunteers. They analysed RNFL and macular thickness with standard OCT protocol while CT with EDI. The RNFL thickness was found higher in the PEXS and control groups compared to the PEXG group. The CT was significantly higher in the control group compared to the PEXG and PEXS groups. In their study, the finding that the lowest macular thickness in all quadrants was detected in the PEXG group was interpreted as an effect of PEXG on the retina. It is found that there was no significant difference in macular thickness between healthy controls and the PEXS group except for the outer temporal segment. In this segment, macular thickness was higher in the control group. They suggested that PEXS and PEXG have variable effects on the macula.

Dursun et al.[16] compared the macular and peripapillary CT in eyes with PEXS and PEXG with the normal eyes of healthy controls. They found that the mean values of CT in the macular and peripapillary areas (except the superior quadrant) in the patients with PEXS and PEXG were lower compared with controls. In this study the mean values of the macular and peripapillary CT in the PEXG group were lower compared with PEXS group; however this difference was not significant.[16]

Eroglu et al.[17] compared four groups of patients in their study. Group 1 consisted of affected eyes of patients with unilateral PEXS; group 2 consisted of clinically unaffected eyes of patients with unilateral PEXS; group 3 consisted of patients with bilateral PEXS; and group 4 control group. They determined significant differences in the mean subfoveal CT between groups 1 and 2, groups 1 and 4, groups 2 and 3, and groups 3 and 4. The differences in mean subfoveal CT between groups 1 and 3 and groups 2 and 4 were not statistically significant. They concluded that clinically affected eyes of patients with PEXS have significantly thinner choroids compared with the clinically unaffected eyes of patients with unilateral PEXS and eyes of healthy controls.[17]

Pseudoexfoliation subjects may be at greater risk of RNFL thinning. PEXS causes histological, physiological and mechanical changes in the ocular structures which may lead to axonal damage long before the IOP rise.[7,18] Several studies point to an association of PEX and vascular pathology. Pseudoexfoliation material has been identified by electron microscopy in the walls of the posterior ciliary arteries, vortex veins, and the central retinal vessels passing through the meninges.[19-21] Vascular change with alteration of ocular blood flow or the PEX material may be the main casual factors in NFL damage.[2]

In this study we aimed to evaluate the early effects of the PEX on CT, RT, RNFL parameters before glaucomatous changes occur. There are scanty information about this issue in the literature. There are many different results have been reported in terms of CT, RT, RNFL in PEXS and PEXG patients. Generally patients with clinically PEX affected eyes tend to have thinner choroids, RTs and RNFLs than both the fellow eye and the eyes of healthy individuals. Our study have some limitations. The results could have been even stronger if there were a group of PEXG.

This study suggests that eyes of PEX patients without glaucoma and fellow eyes of PEX patients may be associated with a thinner RT and RNFL compared with those of age-matched control subjects. Further studies are needed to clarify the relationship between the decrease in RT and RNFL thickness and the development of glaucomatous damage in eyes with PEX.

REFERENCES / KAYNAKLAR

1. Sangal N, Chen TC. Cataract surgery in pseudoexfoliation syndrome. Semin Ophthalmol 2014;29:403-8.
2. Wang W, He M, Zhou M et al. Ocular pseudoexfoliation syndrome and vascular disease: a systematic review and meta-analysis. PLoS One 2014;9:e92767
3. Zheng X. New findings for an old disease: morphological studies on pseudoexfoliation syndrome-related keratopathy and binocular asymmetry. Cornea 2013;32:S84-90.
4. Elhawy E, Kamthan G, Dong CQ et al. Pseudoexfoliation syndrome, a systemic disorder with ocular manifestations. Hum Genomics 2012;6:22.
5. Bayhan HA, Bayhan SA, Can İ. Evaluation of the Macular Choroidal Thickness Using Spectral Optical Coherence Tomography in Pseudoexfoliation Glaucoma. J Glaucoma 2016;25:184-7.
6. Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. Prog Retin Eye Res 2012;31:377-406.
7. Eltutar K, Acar F, Kayaarası Öztürker Z et al. Structural Changes in Pseudoexfoliation Syndrome Evaluated with Spectral Domain Optical Coherence Tomography. Curr Eye Res 2016:41-513-20.
8. Riga F, Georgalas I, Tsikripis P et al. Comparison study of OCT, HRT and VF findings among normal controls and patients with pseudoexfoliation, with or without increased IOP. Clin Ophthalmol 2014;8:2441-7.
9. Vergados A, Papaconstantinou D, Diagourtas A et al. Correlation between optic nerve head parameters, RNFL, and CCT in patients with bilateral pseudoexfoliation using HRT-III. Semin Ophthalmol 2015;30:44-52.
10. Rao A. Clinical and Optical Coherence Tomography Features in Unilateral versus Bilateral Pseudoexfoliation Syndrome. J Ophthalmic Vis Res 2012;7:197-202.
11. Ozge G, Koylu MT, Mumcuoglu T et al.Evaluation of retinal nerve fiber layer thickness and choroidal thickness in pseudoexfoliative glaucoma and pseudoexfoliative syndrome. Postgrad Med. 2016 May;128(4):444-8. doi: 10.1080/00325481.2016.1170579.
12. Bayhan HA, Bayhan SA, Can İ. Evaluation of the Macular Choroidal Thickness Using Spectral Optical Coherence Tomography in Pseudoexfoliation Glaucoma. Clin Experiment Ophthalmol. 2015;43:139-44
13. Zengin MO, Cinar E, Karahan E et al. Choroidal thickness changes in patients with pseudoexfoliation syndrome. Int Ophthalmol. 2015;35:513-7.

14. Yüksel N, Altintaş O, Celik M et al. Analysis of retinal nerve fiber layer thickness in patients with pseudoexfoliation syndrome using optical coherence tomography. Ophthalmologica 2007;221:299-304.

15. Demircan S, Yılmaz U, Küçük E et al. The Effect of Pseudoexfoliation Syndrome on the Retinal Nerve Fiber Layer and Choroid Thickness. Semin Ophthalmol 2016 Apr 14:0. DOI:10.3109/08820538.2015.1090611

16. Dursun A, Ozec AV, Dogan O et al. Evaluation of Choroidal Thickness in Patients with Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma. J Ophthalmol. 2016;2016:3545180. doi: 10.1155/2016/3545180.

17. Eroglu FC, Asena L, Simsek C et al.Evaluation of choroidal thickness using enhanced depth imaging by spectral-domain optical coherence tomography in patients with pseudoexfoliation syndrome. Eye (Lond). 2015 Jun;29(6):791-6. doi: 10.1038/eye.2015.34.

18. Ritch R, Schlötzer-Schrehardt U, Konstas AG. Why is glaucoma associated with exfoliation syndrome? Prog Retin Eye Res 2003;22:253-75.

19. Mitchell P, Wang JJ, Smith W. Association of pseudoexfoliation syndrome with increased vascular risk. Am J Ophthalmol 1997;124:685–7.

20. Shrum KR, Hattenhauer MG, Hodge D. Cardiovascular and cerebrovascular mortality ass ociated with ocular pseudoexfoliation. Am J Ophthalmol 2000;129:83-6.

21. Schumacher S, Schlotzer-Schrehardt U, Martus P et al. Pseudoexfoliation syndrome and aneurysms of the abdominal aorta. Lancet 2001;357:359-60.