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Comparison of Choroidal Thickness in Primary Open Angle Glaucoma Patients in the Late Phase After Trabeculectomy and Without Trabeculectomy: Enhanced Depth Imaging Optical Coherence Tomography Study

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ABSTRACT:

Comparison of choroidal thickness in primary open angle glaucoma patients in the late phase after trabeculectomy and without trabeculectomy: enhanced depth imaging optical coherence tomography study

Objective: The aim of this study is to compare choroidal thickness using enhanced depth imaging optical coherence tomography between primary open angle glaucoma patients with or without previous trabeculectomy.

Material and Method: Fourteen eyes of 12 patients with a history of previous trabeculectomy surgery (TRAB) at least 6 months ago and 20 eyes of 12 patients who has a diagnosis of primary open angle glaucoma (POAG) and did not experience trabeculectomy surgery were recruited to this cross-sectional non-randomised study. Patients with a history of uveitis, diabetic retinopathy, age related macular degeneration, refractive errors other than the determined limits, optic neuropathy or other retinal, choroidal or optic nerve diseases were excluded. Following the complete ophthalmologic examination, choroidal thickness was measured between the hyperreflective outer layer of retinal pigment epithelium and inner layer of sclera, at subfoveal region and 1.5 mm temporal and 1.5 nasal to the fovea, respectively, using RTVue-100 5.1 (EDI-OCT) device.

Results: The mean age of the patients in the TRAB group was 59.9±13.4 (range 29-76), while it was 58.4±9.7 (range 29-73) in POAG group. Groups showed homogeneous distribution in terms of age, gender, laterality, IOP, refractive errors, visual acuity, axial length and central corneal thickness (CCT) (p>0.05). The mean subfoveal, temporal and nasal choroidal thickness of TRAB group was higher (388.2±84.1, 372.4±77.1, 374.1±84.1 µm, respectively) compared to the POAG group (383±64, 358.6±62, 357.5±61.5 µm, respectively), but the difference was not statistically significant (p>0.05). There was a moderate negative correlation between IOP and subfoveal and nasal choroidal thickness in patients with POAG (p=0.048, r=-0.458; p=0.042, r=-0.458; respectively)

Conclusion: There was not any statistically significant difference regarding subfoveal and perifoveal choroidal thickness between patients with previous trabeculectomy at least 6 months ago and patients with diagnosis of POAG who had medically regulated IOP rates and did not experienced trabeculectomy. Patients with POAG may experience choroidal thinning in case of high IOP rates.

Keywords: Choroidal thickness, EDI optic coherence tomography, primary open angle glaucoma, trabeculectomy

ÖZET:

Primer açık açılı glokomu olup trabekülektomi sonrası geç dönemde olan olgular ve cerrahi geçirmemiş hastalarda koroid kalınlıklarının karşılaştırılması: Artırılmış derinlik görüntüleme optik koherens tomografi çalışması

Amaç: Bu çalışmanın amacı açık açılı glokomlu hastalardan trabekülektomi cerrahisi uygulanmış olanları (TRAB) ve cerrahi geçirmeyenleri (POAG) koroid kalınlıkları açısından artırılmış derinlik görüntüleme optik koherens tomografi (EDI-OKT) kullanarak karşılaştırmaktır.

Gereç ve Yöntem: Kesitsel, non-randomize klinik olgu serisi olarak planlanan çalışmaya en az 6 ay önce trabekülektomi cerrahisi geçirmiş 12 hastanın 14 gözü ve primer açık açılı glokomlu 12 bireyin 20 gözü dahil edildi. Uveit, diyabetik retinopati, yaşa bağlı makula dejenerasyonu, optik nöropati veya başka bir retina, koroid veya optik sinir hastalığı bulunanlar ile belirlenmiş sınırların dışında bir refraksiyon kusuru olan bireyler çalışmaya dahil edilmedi. Tam bir göz muayenesini takiben koroid kalınlığı RTVue-100 5.1 (EDI-OKT) cihazı ile; retina pigment epitelinin hiperreflektif dış bandı ile skleranın iç yüzeyi arasından, sırasıyla subfoveal alandan ve subfoveal alanın 1.5 mm temporal ile 1.5 mm nazalinden ölçüldü.

Bulgular: Çalışmaya dahil edilen hastaların yaş ortalaması TRAB grubunda 59.9±13.4 (yaş aralığı 29-76), POAG grubunda 58.4±9.7 (yaş aralığı 29-73) idi. Yaş, cinsiyet, lateralite, GİB, kırma kusuru, görme keskinliği, aksiyel uzunluk ve SKK açısından gruplar arasında istatistiksel olarak anlamlı fark saptanmadı (p>0.05). Ortalama Koroid kalınlığı TRAB grubunda subfoveal, temporal ve nazalde (sırasıyla 388.2±84.1, 372.4±77.1, 374.1±84.1 µm) POAG grubuna göre (sırasıyla 383±64, 358.6±62, 357.5±61.5 µm) daha yüksek ölçüldü fakat istatistiksel olarak anlamlı değildi (p>0.05). POAG grubunda GİB ile subfoveal ve nazal koroid kalınlıkları arasında orta seviyede negatif korelasyon saptandı. (sırasıyla: p=0.048, r=-0.458; p=0.042, r=-0.458)

Sonuç: Subfoveal ve perifoveal koroid kalınlığı trabekülektomi sonrası geç dönemdeki bireyler ile hiç operasyon geçirmemiş, medikal tedavi ile GİB regüle, primer açık açılı glokom tanılı kişiler karşılaştırıldığında istatistiksel olarak anlamlı farklılık göstermemektedir. POAG hastalarında, GİB yükselmesine koroid incelmesi eşlik edebilir.

Anahtar kelimeler: Koroid kalınlığı, EDI optik koherens tomografi, primer açık açılı glokom, trabekülektomi

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INTRODUCTION

Choroidal blood flow abnormalities are thought to play an important role in the pathogenesis of many sight threatening diseases such as choroidal neovascular membrane, uveal effusion syndrome, central serous chorioretinopathy, Vogt-Koyanagi-Harada disease, angioid streak and polypoidal choroidal vasculopathy (1-9).

Because choroid is a highly vascular tissue, its thickness may vary with intraocular pressure and the perfusion pressure (10). The choroidal thickness has been advocated to be affected by many factors such as age, refractive error, axial length, gender, central corneal thickness, smoking and race (11-16).

In glaucoma, changes in the choroidal structure and the blood flow have been reported, and this may be important in the pathogenesis of glaucomatous optic neuropathy. The histopathological examinations determined choroidal thinning (17-19).

Due to the retinal pigment epithelium and the impedance of pigment in the choroid, it is difficult to view the choroid with conventional examination methods. When the histological sections were considered, the choroidal thickness ranged between 170 and 220 µm, which is much thinner than the measurements obtained using spectral-domain optical coherence tomography (SD-OCT (20-23). This may be due to the shrinkage after the tissue fixation and may cause the thickness to be measured thinner than it is. In the recent years Spaide et al. (21-23) used OCT to obtain more deeper cross-sectional images and with a new method called Enhanced Depth Imaging (EDI) -OCT, the choroidal and deep tissue thicknesses have begun to be able to be measured in vivo (14,21,24). With the advances in OCT, in vivo choroid images were recommended to be used in the follow-up of glaucoma in some studies (25,26).

In this study, we aimed to compare choroidal thickness using enhanced depth imaging optical coherence tomography between primary open angle glaucoma patients with or without previous trabeculectomy, and to reveal any present differences.

MATERIAL AND METHOD

Fourteen eyes of 12 patients with a history of previous trabeculectomy surgery (TRAB) and 20 eyes of 12 patients who has a diagnosis of primary open angle glaucoma (POAG) between August 2012 – June 2015 in our ophthalmology clinic were included in this cross-sectional study. The study was conducted in accordance to the Helsinki Declaration principles and was approved by the ethics committee for local clinical trials.

Inclusion and Exclusion Criteria

The individuals over the age of 18 with no ocular disease other than POAG were included in the study. Patients with intraocular pressure (IOP) at 20 mmHg or lower for at least 1 year and at the last 3 control visits with treatment or surgery, and with reliable 30-2 visual field tests with Swedish Interactive Thresholding Algorithm (Humphrey Visual Field Analyzer [Carl Zeiss Inc., Dublin, CA]) were included. The disease severity was rated as mild (MD>-6 dB), moderate (-12 dB<MD<-6 dB) or severe (MD<-12 dB) glaucoma according to the median deviation (MD) parameter in the visual field (27) and the patients with moderate disease were included in the study.

Patients with spherical refractive error more than 4 diopters, with corneal astigmatism more than 3 diopters, with a known ocular disease (uveitis, optic nerve or retinal diseases, etc.), with an ocular media opacity, with a history of angle closure, with periocular steroid use history during the study or in the last 3 months, use of any systemic or ocular drugs that might affect IOP and the choroidal thickness or patients who cannot adapt to any of the measurement methods were excluded from the study. While presence of any ocular surgery history was an exclusion criteria for POAG group, for the TRAB group, having a trabeculectomy operation 6 months before or previously and having no other ocular surgery history other than this were the inclusion criteria. Patients with a known hypertension diagnosis or suspect were not included in the study.

Eye Examination

Snellen best corrected visual activity test, slit-lamp examination of the anterior segment, IOP mesaurement with Goldmann applanation tonometer (Haag–Streit, Switzerland), axial length measurement (Lenstar LS 900, Haag-Streit ABD, Mason, OH), central corneal thickness measurement (Tomey, Ultrasonic Pachymetry, SP-3000, Germany), gonioscopy, OCT scanning including the measurement of choroidal thickness (RTVue - 100 5.1 Fourier-domain OCT - Optovue Inc., Fremont, California) and the fundus examination were performed to each patient. Priority was given to achieve high signal strength index values during the scanning (>50). OCT measurements with low quality were not included in the study.

Choroidal Thickness Measurement

The high-resolution choroidal images were obtained in RTVue-100 5.1 OCT device with providing the reverse image automatically with the chorioretinal option (EDI-OCT) of vitreoretinal and chorioretinal options and by providing the image to reach to the zero point. In this protocol, the average of 32 B-scan images that were obtained by scanning 1024 A-scans in 1.25 seconds, was taken. Choroidal thickness was measured with vertical lines that were drawn manually using the measuring tool of the device from the retinal pigment epithelium's hyperreflective outer band and the area where the inner surface of the sclera starts, at the subfoveal region and 1.5 mm temporal and 1.5 mm nasal to subfoveal region.

All examinations and the choroidal thickness measurements were done in the morning between 10:00 and 11:00.

Statistics

Statistical analysis were done using SPSS 17.0 version (IBM, A.B.D.) program. The results were given as mean±standard deviation. Normality was assessed using Kolmogorov-Simirnov test. Pearson for normally distributed data, and Spearman correlation for non-normally distributed data were used. ANOVA (Tukey) and Kruskal-Wallis (Mann-Whitney U) tests were performed to illustrate the difference between the groups. $p<0.05$ was considered to be the statistically significance limit.

RESULTS

Of the individuals included in the study, there were 6 female and 8 patients in the TRAB group and there were 12 women and 8 men in the POAG group. The mean age of the patients was 59.9±13.4 (age range: 29-76 years) in the TRAB group, and 58.4±9.7 (age range: 29-73 years) in the POAG group. The intraocular pressures (IOP) were measured as 14.5±3.4 and 16.8±2.3 mmHg. Mean central corneal thickness (CCT) was as 537.7±19 and 542.3±41 µm for TRAB and POAG groups, respectively. The mean axial length was 23.01±1.04 and 23.4±0.5 mm, respectively. No statistically

Table-1: Basic Demographic Data (the values are transmitted as mean±standard deviation)

	TRAB		POAG		p
Gender	F 6	M 8	F 12	M 8	0.507
Laterality	Right 7	Left 7	Right 11	Left 9	0.506
Age	59.90±13.40		58.40±9.70		0.717
IOP (mmHg)	14.50±3.40		16.80±2.30		0.055
SE (D)	-0.85±2.00		-0.25±1.20		0.703
BCVA (Snellen)	0.56±0.30		0.69±0.30		0.261
AL (mm)	23.01±1.04		23.40±0.50		0.396
CCT (µm)	537.70±19.00		542.30±41.00		0.904

TRAB: The TRAB patient group, POAG: primary open angle glaucoma group, F: female, M: male, IOP: intraocular pressure, SE: spherical equivalent, BCVA: best corrected visual acuity, AL: axial length, CCT: central corneal thickness

significant difference was detected between the groups in terms of age, gender, laterality, IOP, refractive error, visual acuity, axial length, CCT and the anti-glaucomatous treatment (p>0.05). Demographic and clinical data are given in Table-1, 2 and 3. The bleb was not functional in the TRAB group. The mean choroidal thickness was measured thicker at subfoveally, temporally and nasally

Table-2: The demographic and clinical data of the TRAB group

Patient	Group	Gender	Age	Eye	Treatment	The number of molecules used
1	TRAB	M	63	OS	-	0
2	TRAB	M	48	OD	Dorzolamide, timolol, latanoprost	3
3	TRAB	M	48	OS	Dorzolamide, timolol, latanoprost	3
4	TRAB	M	54	OS	-	0
5	TRAB	F	29	OS	Travoprost	1
6	TRAB	F	72	OD	-	0
7	TRAB	F	76	OD	Brinzolamide, timolol, travoprost	3
8	TRAB	F	76	OS	Brinzolamide, timolol, travoprost	3
9	TRAB	F	59	OS	-	0
10	TRAB	M	71	OD	-	0
11	TRAB	M	59	OD	-	0
12	TRAB	F	55	OS	Dorzolamide, timolol, bimatoprost	3
13	TRAB	M	54	OD	-	0
14	TRAB	M	74	OD	-	0

TRAB: TRAB group, M: Male, F: Female, OD: Oculus Dextra, OS: Oculus Sinistra

Table-3: The demographic and clinical data of the POAG group

Patient	Group	Gender	Age	Eye	Treatment	The number of molecules used
1	POAG	M	63	OD	Dorzolamide, timolol, brimonidine	3
2	POAG	M	54	OD	Bimatoprost	1
3	POAG	M	54	OD	Latanoprost	1
4	POAG	M	54	OS	Latanoprost	1
5	POAG	M	73	OD	Dorzolamide, timolol, latanoprost	3
6	POAG	M	73	OS	Dorzolamide, timolol, latanoprost	3
7	POAG	M	62	OD	Dorzolamide, timolol	2
8	POAG	M	62	OS	Dorzolamide, timolol	2
9	POAG	F	29	OD	Brimonidine, timolol	2
10	POAG	F	51	OD	Travoprost	1
11	POAG	F	51	OS	Travoprost	1
12	POAG	F	72	OS	Brimonidin, timolol, bimatoprost	3
13	POAG	F	58	OD	Brinzolamide, timolol	2
14	POAG	F	58	OS	Brinzolamide, timolol	2
15	POAG	F	65	OD	Dorzolamide, timolol	2
16	POAG	F	65	OS	Dorzolamide, timolol	2
17	POAG	F	56	OD	Dorzolamide, timolol	2
18	POAG	F	56	OS	Dorzolamide, timolol	2
19	POAG	F	56	OD	Brimonidine	1
20	POAG	F	56	OS	Brimonidine	1

POAG: Primary Open Angle Glaucoma, M: Male, F: Female, OD: Oculus Dextra, OS: Oculus Sinistra

(388.2±84.1, 372.4±77.1, 374.1±84.1 µm, respectively) in the TRAB group than to the POAG group (383±64, 358.6±62, 357.5±61.5 µm, respectively), but there was statistically no significant difference in any measurement site (p>0.05).

In the examination, a moderate negative correlation between the subfoveal and nasal choroidal thicknesses and IOP in the POAG group (p=0.048, r=-0.458; p=0.042, r=-0.458, respectively). The correlation of temporal choroidal thickness with IOP was just above the significance limit (p=0.055, r=-0.436). When the same parameters were evaluated in the TRAB group, no similar correlation was found, however in the TRAB group, a strong negative correlation was present between the age and the axial length (p=0.009, r=-0.670).

DISCUSSION

Choroidal blood flow constitutes a large portion of the ocular blood flow, such as 90% (28). The number of publications indicating that the changes in this region may be important in the pathogenesis of glaucoma in increasing (17,25,26). In our study with the aim to present the changes that occur in the choroidal thickness with trabeculectomy in POAG patients, there was statistically no significant difference between the TRAB and POAG groups in terms of choroidal thickness.

In a study of Saeedi et al.'s (26) that they published in 2014 which was designed with a similar idea, the choroidal thicknesses of 20 patients who were planned to have trabeculectomy, were measured at preoperative and postoperative 1st week, 1st month, 3rd month and 6th month and in each patient, and increase in the choroidal thickness with the decrease of IOP were shown. Each 1 mmHg of decrease caused an increase in the choroidal thickness. In other words, each 1 mmHg decrease presented 1.7% of increase. However, they found that each 1 mmHg decrease showed association with 6.8 µm shortening in the axial length (26). When our results are evaluated, in the POAG group, there was a moderate negative correlation between the IOP and subfoveal and nasal choroid thicknesses. In the same patient group, the correlation of temporal choroid thickness with IOP was immediately over the significance level. In addition, although there was no significant difference found, as Saeedi et al.'s stated, in the TRAB Group with lower IOP the choroid was measured thicker, and the mean axial length shorter. The insignificant results may result from Saeedi et al. measuring the choroidal thicknesses at postoperative 1st week, 1st, 3rd and 6th months; and us, obtaining our results from the patients at least 6 months after the operation. We believe that when the sudden IOP fall or rise, inflammation and the so early changes are taken into account, the early postoperative period choroidal thickness assessments may possibly be obtained different from what it is. In our study, the small number of patients included in the groups is the limitation of our study and not to get significant results may be connected to this situation.

In Spaide et al.'s study which was published in 2008, in the first OCT measurements in 17 eyes, the mean subfoveal choroidal thickness was found as 318 µm in the right eye and 335 µm in the left eye (23). In the following studies, the mean subfoveal choroidal thickness was detected as 287 µm by Margolis and Spaide (21), 354 µm by Ikuna et al. (29), 342 µm by Li et al. (30) and 268.8±49.2 µm by Tuncer et al. (31). We also showed that the mean subfoveal choroidal thickness as 388.2±84.1 µm in the TRAB group, and as 383±64 µm in the POAG group; and this result was similar with Spaide, Ikuna and Li's studies, whereas it was different from the previous studies of Margolis and Spaide and Tuncer et al.'s. This difference, is thought to be related to the mean age, gender, refractive errors, axial lengths or the devices used of the individuals included in the study (21,23,29-31).

The IOP of the patients included in our study who were assessed in the late period after trabeculectomy, which were measured after a long period following 6 monhts after the operation were within normal limits. In 4 patients, these values were provided with the support of topical antiglaucomatous drugs, while in the other patients, it was achieved with only the bleb function. In the patients with high measured IOP values, the presence of thin choroid was shown in the previous studies (32). In the early period in patients who underwent trabeculectomy, the

prominent functional drainage and the presence of related low IOP values may be related to the choroidal blood flow increase and accordingly, thicker choroidal measurements.

As a result, the subfoveal and perifoveal choroidal thicknesses showed no statistically significant difference between the patients who underwent trabeculectomy 6 months or before, and the patients with POAG diagnosis who had no operation, and with regulated IOP with medical treatment. Further comprehensive, prospective studies with greater number of patients included should be performed.

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