Evaluation of Choroidal and Macular Thickness in Patients with Inactive Thyroid Eye Disease Using Optical Coherence Tomography

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Abstract

Aim: In this study, we aimed to evaluate the choroidal and macular thicknesses according to clinical activity score in thyroid eye disease patients who were inactive period and to compare them with healthy controls.

Methods: For this purpose, 40 eyes of 40 thyroid eye disease patients and 40 healthy controls were included. Subfoveal, temporal, nasal, choroidal thickness measurements and central foveal thickness measurements were performed with spectral-domain optical coherence tomography (SD-OCT). Similar measurements were compared with an equal number of controls.

Results: The mean clinical activity score (CAS) of thyroid eye disease was 1.25 ± 0.47 and the mean Hertel exophthalmometer results were 21.6 ± 2.4 millimeters (mm). The mean central foveal thickness was 285.3 ± 15.2 µm, mean subfoveal choroidal thickness was 285.42 ± 81.3 µm, mean temporal choroidal thickness was 265.6 ± 57.5 µm, and mean nasal choroidal thickness was 232.1 ± 71.7 µm. There is a statistically significant difference between subfoveal and temporal choroidal thickness between both groups p=0.014 and p=0.008, respectively.

Conclusions: In conclusion, the central foveal thickness of patients with thyroid eye disease did not differ from healthy controls, whereas subfoveal and temporal choroidal thickness were higher than controls. There is a need for large-scale and long-term studies on the cause and long-term effects of these differences.

Keywords: *Choroid; Macula, ophthalmopathy, optical coherence tomography, thyroid*

1. Introduction

Thyroid eye disease (TED) is an autoimmune disease characterized orbital adipose tissue proliferation, inflammation of the orbital connective tissue and extraocular muscles enlargement resulting cause an enhancement in orbital tissue volume. TED is observed in roundly 30% of patients with Graves disease and 2% of patients is observed with thyroiditis.[1] Although most patients with TED have mild symptoms, about 3 to 5% patients may develop a more severe form. Clinical signs of TED include dry eye, exposure keratopathy, proptosis, diplopia and decreased visual acuity.[2-4] Some studies on retinal changes in TED patients have recently appeared, including publications on choroidal thickness and its association with macular degeneration.[5-9] TED patients were evaluated according to the Mourits et al. developed Clinical Activity Classification System (CAS) classified as active and inactive in 1989.

A total of seven parameters are queried in this evaluation system. In this scoring system, each parameter is assigned a score, and if the overall score is three or more, the disease is considered to be in the active phase. Criteria; 1) Spontaneous bulbar or retrobulbar pain for the last four weeks, 2) Pain with looking up or down, 3) Redness of the eyelids, 4) Redness of the conjunctiva, 5) Swelling in the caruncle or plica, 6) Swelling of the eyelids and 7) Conjunctival swelling.[10]

In this study, we aimed to estimate the choroidal and macular thickness (according to clinical activity score) in cases with TED who weren't in the active complaint period and to compare them with healthy controls.

2. Materials and methods

This retrospective study included 40 eyes of 40 patients (group 1) admitted to the Endocrinology and Ophthalmology Outpatient Mersin City Hospital between 01 February 2019 and 01 February 2022. Forty healthy controls (group 2) of similar age group were included. Written informed consent was obtained from all participants. This study approved from the Clinical Studies Ethics Committee of Mersin City Hospital (2021 / 799 – 29/12/2021). The

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study was conducted in agreement with the Declaration of Helsinki. Subfoveal, temporal, nasal, choroidal thickness evaluation and central foveal thickness evaluation of the right eyes of all participants were performed, independently, by an educated technician using Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) spectral-domain optical coherence tomography (SD-OCT). Similar measurements were compared with an equal number of controls.

Exclusion criteria: Greater than (- 5.00) diopters myopia (D) or greater than (+ 3.00) diopters (D) hyperopia, anomaly of optic disc, vitreoretinal interface disease, retinal vascular and degenerative diseases, corneal and lens opacity, previous ocular surgery, neurologic diseases, use of cardiovascular drugs, amblyopia, diplopia, uveitis, enlarged extraocular muscles confirmed by orbital magnetic resonance imaging (MRI) and keratitis. A detailed history was taken from all patients and comprehensive ophthalmologic examination with slit lamp biomicroscopy, intraocular pressure measurement and fundus examination was performed.

The level of proptosis was evaluated with Hertel exophthalmometer. All patients were also evaluated using orbital MRI to observe extraocular muscle involvement.

2.1. Statistical Analysis

Statistical analysis of this study data was performed with SPSS 24.0 package program (IBM Corp, Armonk, NY, USA). Categorical variables were epitomized as number, percentage and continuous variables as mean ± standard deviation (minimum – maximum). Normal distribution of continuous variables was checked by Shapiro-Wilk test. Student's t test, was used to compare the means of two independent groups for the variables that conformed to normal distribution. Connection between categorical variables were investigated by Chi-Square analysis. Statistical significance level was taken as $p < 0.05$ for all comparisons.

3. Results

In this study, the mean age of the 40 patients (group 1) was 52.1 ± 14.2 years (37–66 years), while the mean age of the 40 healthy controls (group 2) was 51.2 ± 13.4 years (37–66 years). Group 1 consisted of 17 males (42.5%) and 23 females (57.5%). Group 2 consisted of 21 males (52.5%) and 19 females (47.5%). Both groups were similar in terms of demographics (p=0.166 and p=0.371, respectively) (Table 1).

Table 1

Demographic data of study participants

	Group 1 (n=40)	Group 2 (n=40)	p
Age (years)	52.1 ± 14.2	51.2 ± 13.4	0.166
Male	17 (42.5%)	21 (52.5%)	0.371
Female	23 (57.5%)	19 (47.5%)	

The clinical profile of group 1 showed hyperthyroidism in 25 (62.5%), euthyroidism in 7 (17.5%) and hypothyroidism in 8 (20%) patients. In addition, thyroid function tests revealed a mean thyroid stimulating hormone (TSH) level of 3.3 ± 1.8 (1.5 - 5.1) mIU/L, a mean free thyroxine (T4) level of 1.6 ± 0.6 (1.0 - 2.2) ng/dl, and a mean free triiodothyronine (T3) level of 4.4 ± 1.2 (3.2 - 5.6) ng/dL. (Table 2)

The mean clinical activity score for group 1 was 1.25 ± 0.47 and the mean Hertel ophthalmometry was 21.6 ± 2.4 (19.2 - 24.0) millimeters. Mean intraocular pressure (IOP) was 16.3 ± 3.9 (12.4 – 20.2) mm Hg. The mean of IOP in the group 2 was 15.8 ± 3.1 (12.7 – 18.9) mm Hg. This difference was not statistically significant (p=0.253).

Table 2

Clinical profiles and thyroid function tests of the patients

Group 1 (n = 40)	
Hyperthyroid	25 (%62.5)
Euthyroid	8 (%20)
Hypothyroid	7 (%17.5)
TSH	3.3 ± 1.8 mIU/L
fT4	1.6 ± 0.6 ng/dL
fT3	4.4 ± 1.2 ng/dL

TSH: Thyroid Stimulating Hormone, T4: thyroxine, T3: triiodothyronine

In group 1, mean foveal thickness was 285.3 ± 15.2 (270.1 – 300.5) µm, mean subfoveal choroid thickness was 285.42 ± 81 (204.4 – 366.4) µm, mean temporal choroid thickness was 265.6 ± 57.5 (208.1 – 323.1) µm, mean nasal choroidal thickness was 232.1 ± 71.7 (160.4 – 302.8) µm.

In group 2, the mean foveal thickness was 288 ± 16.1 (272.1 – 304.1) µm, the mean subfoveal choroid thickness was 251.1 ± 57.4 (193.7 – 308.5) µm. The mean temporal choroid thickness was 233.7 ± 51.3 (182.4 – 285.0) µm, and the mean nasal choroid thickness was 221.1 ± 59.9 (172.2 – 281.0) µm. There is a statistically significant difference between subfoveal choroidal thickness and temporal choroidal thickness between both groups (p=0.014 and p=0.008, respectively). (Table 3)

Table 3

Central foveal and choroidal thickness of the participants

	Group 1 (n=40)	Group 2 (n=40)	p
Central FT (µm)	285.3 ± 15.2	288 ± 161	0.317
Subfoveal CT (µm)	285.4 ± 81.3	251.1 ± 57.4	0.014
Temporal CT (µm)	265.6 ± 57.5	233.7 ± 51.3	0.008
Nasal CT (µm)	232.1 ± 71.7	221.1 ± 59.9	0.106

FT: Foveal thickness CT: Choroidal thickness

4. Discussion

Thyroid eye disease is an autoimmune disease involving many factors. Inflammatory events occur more frequently during the active phase, whereas fibrosis of the orbital tissue predominates during the inactive phase [8]. Studies have shown that changes in choroidal thickness occur in orbital inflammatory and systemic diseases due to choroidal inflammatory cell infiltration, increased exudate, increased vascular leakage, and altered orbital blood flow.5-7 In TED patients, orbital fibroblasts overexpressing thyroid-

stimulating hormone receptors and insulin-like growth factor-1 receptors play an important role in orbital inflammation, extracellular matrix production, and adipocyte and myofibroblast differentiation. plays. Inflammatory cells normally infiltrate the orbital adipose tissue and extraocular muscles, and under the influence of inflammatory mediator cytokines, cause orbital stromal edema and extraocular muscle hypertrophy. It has been reported that orbital venous drainage is reduced in TED patients and that the reason for orbital venous flow reduction is elevated retroorbital pressure above normal venous pressure. It has been hypothesized that compression exerted by blood flow within the orbital space, restricted by reduced orbital venous outflow, may be associated with increased choroidal thickness.[14-16] We found that the intraocular pressure values in the patient group were higher than those in the control group. In the same study, foveal thickness was thinner in the patient group compared to the control group. In our study, the difference in intraocular pressure between patient and control groups was not significant.[11] In our study, foveal thickness and intraocular pressure were similar between patient and control groups. Elongation of the optic nerve and sclera, with or without muscle involvement, can increase the measured intraocular pressure when the thyroid gland is active or inactive. Macular thickness can be affected by changes in intraocular pressure. Ganglion cell damage in the macula was confirmed in a study by Wu et al. Demonstrated in patients with high intraocular pressure [13]. Macular thickness increases within a month due to the reduction in intraocular pressure after glaucoma filtration surgery. They hypothesized that this was due to the physiological response of the retina to a sudden drop in intraocular pressure. As no differences in intraocular pressure were observed in our study, there are no differences in foveal thickness.

Sen et al. the Graves' disease group was found to have higher intraocular pressure values than the control group (p=0.01).[12] Similarly, Wu et al. found higher intraocular pressure values in the patient group compared to the control group.[13] The reason the results differ from the literature is that the number of patients included in the study was relatively small and patients were inactive. In a study by Ozcan et al., subfoveal choroidal thickness was higher in the patient group than in the control group. Most patients in this patient group were clinically inactive, and it was reported that the increased subfoveal choroidal thickness may be due to the venous occlusion observed in the patient group.[8] In another study, Charshukan et al. They found that subfoveal choroidal thickness increases in active TED patients compared with controls, whereas subfoveal choroidal thickness does not change in non-active TED patients compared with controls.[2] In our study, similar to other literature studies, we found that the inactive TED group had higher subfoveal choroidal thickness than the healthy control group. Increased choroidal thickness in our study has been linked to venous occlusion, periorbital and retroorbital tissue inflammation, vascular macro- and microanatomical alterations due to proptosis, and consequent possible ischemic causes in the pathogenesis of TED. It is hypothesized that it is due to. Limitations of this study include the small number of patients, the lack of automation in the measurements of foveal and choroidal thickness, the lack of subgrouping of patients according to different clinical findings, and the lack of IOP and foveal thickness. and lack of correlation analysis with foveal thickness. It does not evaluate the best visual acuity.

5. Conclusion

In conclusion, foveal thickness in patients with thyroid eye disease did not differ from that in healthy controls, but subfoveal and temporal choroidal thicknesses were thicker than in healthy controls. Large-scale, long-term studies are needed on the causes and long-term effects of these differences.

Statement of ethics

This study approved from the Clinical Studies Ethics Committee of Mersin City Hospital (2021 / 799 – 29/12/2021).

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author Contributions

All authors contributed equally to the article. All authors read and approved the final manuscript.

References

1.Hiromatsu Y, Eguchi H, Tani J, et al. Graves' ophthalmopathy: epidemiology and natural history. Intern Med. 2014;53(5):353-60. https://doi.org/10.2169/internalmedicine.53.1518
2.Çalışkan S, Acar M, Gürdal C. Choroidal Thickness in Patients with Graves' Ophthalmopathy. Curr Eye Res. 2017 Mar;42(3):484-90. https://doi.org/10.1080/02713683.2016.1198488
3.Imamura Y, Fujiwara T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. Retina. 2009 Nov-Dec;29(10):1469-73. https://doi.org/10.1097/IAE.0b013e3181be0a83
4.Switzer DW Jr, Mendonça LS, Saito M, Zweifel SA, Spaide RF. Segregation of ophthalmoscopic characteristics according to choroidal thickness in patients with early age-related macular degeneration. Retina. 2012 Jul;32(7):1265-71. https://doi.org/10.1097/IAE.0b013e31824453ac
5.Fong AH, Li KK, Wong D. Choroidal evaluation using enhanced depth imaging spectral-domain optical coherence tomography in Vogt-Koyanagi-Harada disease. Retina. 2011 Mar;31(3):502-9. https://doi.org/10.1097/IAE.0b013e3182083beb
6.da Silva FT, Sakata VM, Nakashima A, et al, Enhanced depth imaging optical coherence tomography in long-standing Vogt-Koyanagi-Harada disease. Br J Ophthalmol. 2013 Jan;97(1):70-4. https://doi.org/10.1136/bjophthalmol-2012-302089
7.Coskun E, Gurler B, Pehlivan Y, et al. Enhanced depth imaging optical coherence tomography findings in Behçet disease. Ocul Immunol Inflamm. 2013 Dec;21(6):440-5. https://doi.org/10.3109/09273948.2013.817591
8.Özkan B, Koçer ÇA, Altintaş Ö, et al. Medscape. Choroidal changes observed with enhanced depth imaging optical coherence tomography in patients with mild Graves orbitopathy. Eye (Lond). 2016 Jul;30(7):917-24. https://doi.org/10.1038/eye.2016.93
9.Ulas F, Dogan Ü, Dikbas O, et al. Investigation of the choroidal thickness in patients with hypothyroidism. Indian J Ophthalmol. 2015 Mar;63(3):244-9. https://doi.org/10.4103/0301-4738.156976
10.Mourits MP, Koornneef L, Wiersinga WM, et al. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: a novel approach. Br J Ophthalmol. 1989 Aug;73(8):639-44. https://doi.org/10.1136/bjo.73.8.639
11.Sayın O, Yeter V, Arıtürk N. Optic Disc, Macula, and Retinal Nerve Fiber Layer Measurements Obtained by OCT in Thyroid-Associated Ophthalmopathy. J Ophthalmol. 2016;2016:9452687. https://doi.org/10.1155/2016/9452687
12.Sen E, Berker D, Elgin U, et al. Comparison of optic disc topography in the cases with graves disease and healthy controls. J Glaucoma. 2012 Dec;21(9):586-9. https://doi.org/10.1097/IJG.0b013e31822e8c4f

13.Wu Y, Tu Y, Wu C, et al. Reduced macular inner retinal thickness and microvascular density in the early stage of patients with dysthyroid optic neuropathy. Eye Vis (Lond). 2020 Mar 10;7:16.
https://doi.org/10.1186/s40662-020-00180-9
14.Nakase Y, Osanai T, Yoshikawa K, Inoue Y. Color Doppler imaging of orbital venous flow in dysthyroid optic neuropathy. Jpn J Ophthalmol. 1994;38(1):80-6.
15.Otto AJ, Koornneef L, Mourits MP, et al. Retrobulbar pressures measured during surgical decompression of the orbit. Br J Ophthalmol. 1996 Dec;80(12):1042-5.
https://doi.org/10.1136/bjo.80.12.1042
16.Somer D, Ozkan SB, Ozdemir H, et al. Colour Doppler imaging of superior ophthalmic vein in thyroid-associated eye disease. Jpn J Ophthalmol. 2002 May-Jun;46(3):341-5.
https://doi.org/10.1016/s0021-5155(02)00485-9