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ORIGINAL ARTICLE

# Measurement of Sub-foveal Choroidal Thickness in Hyperthyroid Patients with Thyroid-associated Ophthalmopathy Using Spectral Domain OCT

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**Abstract**

*Introduction*: **Thyroid-associated ophthalmopathy (TAO), also identified as Graves' ophthalmopathy or dysthyroid opthhalmopathy, is the most frequent extra-ocular manifestation of thyroid dysfunction.**

*Aim*: **Purpose of this research was to measure the central choroidal thickness in hyperthyroid cases with active and inactive TAO with Optical Coherence Tomography (OCT) and compare it to the control group.**

*Patients and methods*: **The research was a cross-sectionally in Al-Azhar University hospitals and National Institute of Diabetes and Endocrinology. Patients recruited for the study classified into two groups: (A): 15 eyes of hyperthyroid cases with TAO. (B): 15 eyes of healthy participants as control group.**

*Results*: **There was a significant rise of CT in the case group (331 $\pm$ 86.23) in comparison to control group (268.57 $\pm$ 56.58) (*P*.$\leq$0.05). No significant difference of vision, IOP and CMT amongst 2 groups (*P*.>0.05).**

*Conclusion*: **The outcomes of this research indicate that there is a significant affection of sub-foveal choroidal thickness in TAO cases. There is a significant rise in choroidal thickness in TAO patients either active or inactive in comparison to control group, but did not show a correlation with other studied parameters. OCT has the potential to aid in the definitive diagnosis of TAO by revealing macular and choroidal abnormalities.**

*Keywords:* Choroidal thickness, OCT, Ophthalmopathy, TAO, Thyroid

## 1. Introduction

TAO also known as Graves' ophthlamopathy or dysthyroid opthhalmopathy, is the most frequent extra-ocular manifestation of thyroid dysfunction, most commonly associated with Grave's disease, yet it can also occur with euthyroid or hypothyroid status.[1]

TAO associated with Graves' disease, is an autoimmune disorder in that autoantibodies aim the thyroid-stimulating hormone receptor (TSH-R) present on thyrocytes, resulting in the manufacture of extra thyroid hormone.[2]

The hazard and strictness of ophthalmopathy in cases with Grave's disease might be amplified by many factors including tobacco smoking, genetics, the kind of treatment for hyperthyroidism, TSH receptor antibody levels, advanced age, and worry. For example, cases who smoke has a five times greater threat of developing TAO than those who do not.[3]

Glycosaminoglycan (GAG) deposition (followed by edoema due to their hydrophilic characteristic), fibrosis affecting the extra-ocular muscles, and adipogenesis in the orbit all contribute to the pathophysiology of TAO. This leads to muscle disorder due to inability to relaxation and limitation of movement resulting in diplopia.[4]

This causes an inflammatory eye disease that manifests as exophthalmos, lid retraction, and strabismus. It is characterised by increased volume of the orbital tissues, fat, and extra-ocular muscles.[5]

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In addition, the orbital swelling at the apex results in compression of the orbital structures including the optic nerve (resulting in dysthyroid optic neuropathy), retinal and choroidal microstructures.[6]

In order to assess the disease activity clinically, the VISA score is used, assessing the Vision, Inflammation, Strabismus and Appearance, with vision being the first priority, followed by inflammation as the second priority.[6]

The choroid provides the blood supply to the outer retinal layers, and thus any changes in the choroidal microvasculature from the orbital compression will subsequently affect the retinal function.[7]

One study suggested that the choroidal thickness increase could be an initial indicator of venous congestion, that develops before the elevation of the intraocular pressure (IOP) and thus can be used in monitoring the activity of the disease and allow timely intervention to avoid serious ocular complications.[5]

Purpose of the research was to measure the central choroidal thickness in hyperthyroid cases with active and inactive TAO using Optical Coherence Tomography (OCT) and compare it to control group.

## 2. Patients and methods

The study was a cross-sectionally in Al-Azhar University hospitals and National Institute of Diabetes and Endocrinology. **Patients recruited for the study classified into two groups:** (A): 15 eyes of hyperthyroid cases with TAO. (B): 15 eyes of healthy participants as control group.

### 2.1. Methods

All patients was subjected to the following:

**Complete ocular examination:** Visual acuity: uncorrected visual acuity (UCVA) and corrected distance visual acuity (CDVA), slit-lamb biomicroscope, intra-ocular pressure measurement Using applanation tonometry, fundus examination using indirect ophthalmoscopy and ocular motility and **optical coherence tomography (OCT).**

**Inclusion criteria:** Hyperthyroid patients with TAO and age group 20_50 years.

**Exclusion criteria:** Patients below the age of 20, patients above the age 50, patients with Diabetes Mellitus, patients with dense cataract, patients with corneal opacity, glaucoma patients, patients with vitreous hemorrhage, patients with retinal detachment, patients with high myopia and patients of optic neuropathy.

All participants' eyes were photographed using Spectral Domain Optical Coherence Tomography (SD-OCT) (NIDEK RS-3000 advance) to measure Macula Map and sub foveal choroidal thickness by Macula Line and Macula Radial. Sub foveal choroidal thickness was measured manually by drawing a line from the outer border of the sub foveal RPE to the inner edge of the suprachoroidal space.

### 2.2. Statistical methods

Investigation of statistics was done using software MedCalc v. 20.110. Researchers looked into the numbers. For normality using Kolmogorov-Smirnov test of normality. Since the majority of the data were normally distributed (parametric data), the results of the Kolmogorov-Smirnov test suggested that parametric tests should be employed for the majority of comparisons One way analysis of variance (ANOVA), which was used to examine the difference between the means of various subgroups of a variable, was used to compare quantitative variables. $\chi^2$ was used to compare qualitative variables and find out how significant the differences were between one set of classifications and another set, or between two sets of classifications and another set (two-way classification).

## 3. Results

There was no significant difference in demographic data of sex, age, among case and control groups of the study ($P < 0.05$) (Table 1), Fig. 1.

*Table 1. Demographic data of the research group.*

| Demographic data | Case (hyperthyroidism) ($n = 15$) | Control ($n = 15$) | $P$ value |
|---|---|---|---|
| Males | | | |
| $N$ (%) | 5 (33.3%) | 10 (66.7%) | 0.0726 |
| Females | | | |
| $N$ (%) | 10 (66.7%) | 5 (33.3%) | |
| Age (y) | | | |
| Mean ± SD | 35.3 ± 6.1 | 35.2 ± 4.9 | 0.974 |
| Range | 28–48 | 29–48 | |

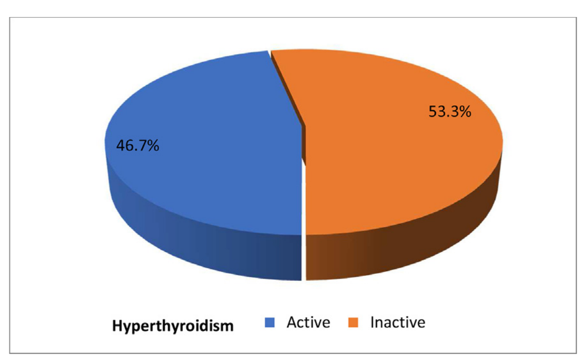


*Fig. 1. Grouping of case group according to activity.*

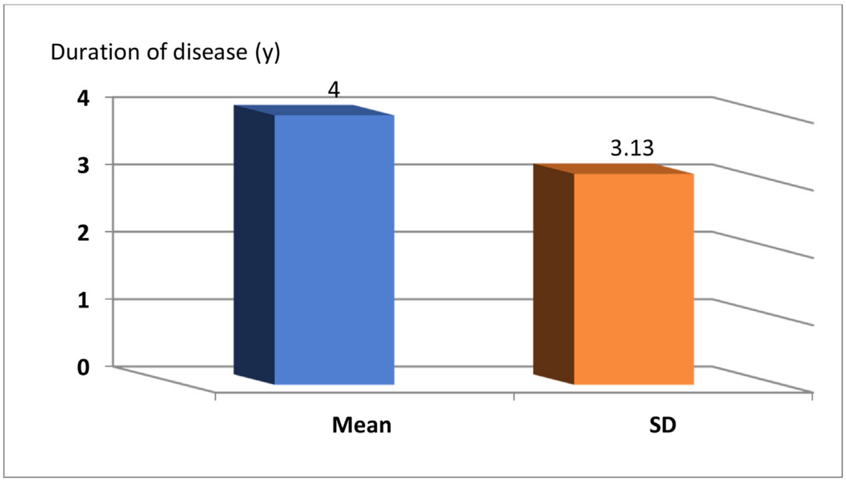


*Fig. 2. Duration of disease in case group.*

*Table 2. Comparing ocular measurements between case group and control group.*

| Ocular measurement | Case ($n$ = 15) | | Control ($n$ = 15) | | $P$ value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Vision | 0.89 | 0.17 | 0.92 | 0.13 | 0.724 |
| IOP | 12.53 | 2.09 | 13.87 | 1.84 | 0.075 |
| CT | 331.93 | 86.23 | 268.57 | 56.58 | 0.024* |
| CMT | 230.10 | 46.54 | 257.50 | 34.41 | 0.077 |

*$P \leq 0.05$ is considered significant.

*Table 3. Comparing ocular measurements between active and inactive subgroups.*

| Ocular measurement | Active cases ($n$ = 7) | | Inactive cases ($n$ = 8) | | $P$ value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Vision | 0.95 | 0.040 | 0.85 | 0.22 | 0.260 |
| IOP | 13.14 | 0.89 | 12.00 | 2.72 | 0.310 |
| CT | 341.14 | 25.79 | 323.87 | 118.92 | 0.714 |
| CMT | 243.21 | 15.55 | 218.62 | 61.65 | 0.325 |

Cases of hyperthyroidism classified according to activity into 7 active cases (46.7%) and 8 inactive cases (53.3%) Fig. 2.

Within case group, duration of disease ranged from 1.5 to 10 years with mean 4 ± 3.13 and median 2 years Table 2.

There was significant increase of CT in case group (331 ± 86.23) in comparison to control group (268.57 ± 56.58) ($P.\leq0.05$). No significant difference of vision, IOP and CMT among two groups ($P.>0.05$) Table 3.

There was no significant difference amongst active and inactive cases as regards vision, IOP, CT and CMT ($P > 0.05$) Fig. 3.

There was no significant difference among control, active and inactive cases regarding vision, IOP, CT and CMT ($P.>0.05$) Table 4.

Within active cases, vision had significant positive correlation with age, disease duration, IOP (R + ve,

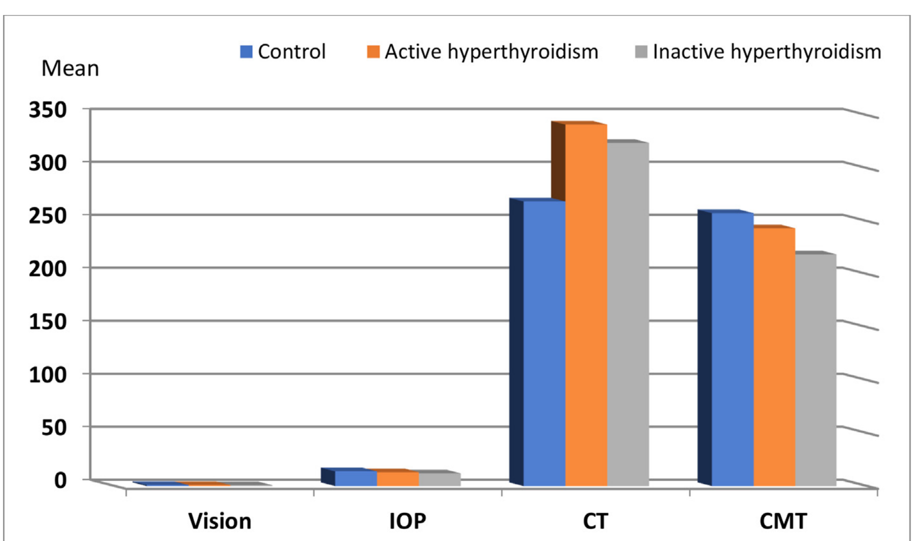


*Fig. 3. Comparing ocular measurements between control and cases subgroups according to activity.*

*Table 4. Correlation among vision and other parameters in case group.*

| Ocular measurement | Vision | | | |
|---|---|---|---|---|
| | Active cases ($n = 7$) | | Inactive cases ($n = 8$) | |
| | R | $P$ value | R | $P$ value |
| Age | 0.994 | <0.0001* | −0.779 | 0.0227* |
| Disease duration | 0.837 | 0.0189* | −0.720 | 0.0441* |
| IOP | 0.907 | 0.0048* | 0.809 | 0.0151* |
| CT | −0.965 | 0.0004* | 0.946 | 0.0004* |
| CMT | −0.223 | 0.6307 | 0.999 | <0.0001* |

*$P \leq 0.05$ is regarded to be of great importance.

$P \leq 0.05$), and significant negative correlation with CT (R-ve, $P \leq 0.05$). Within inactive cases, vision had significant negative correlation with age, disease duration (R-ve, $P$.≤0.05) and significant positive correlation with IOP, CT and CMT (R + ve, $P$£0.05) Figs. 4 and 5.

## 4. Discussion

(TAO) is the most prevalent extrathyroidal manifestation of Graves' disease and is an ocular condi-

*Fig. 4. A patient with active TAO, showing bilateral proptosis, conjunctival chemosis, lid retraction and oedema.*

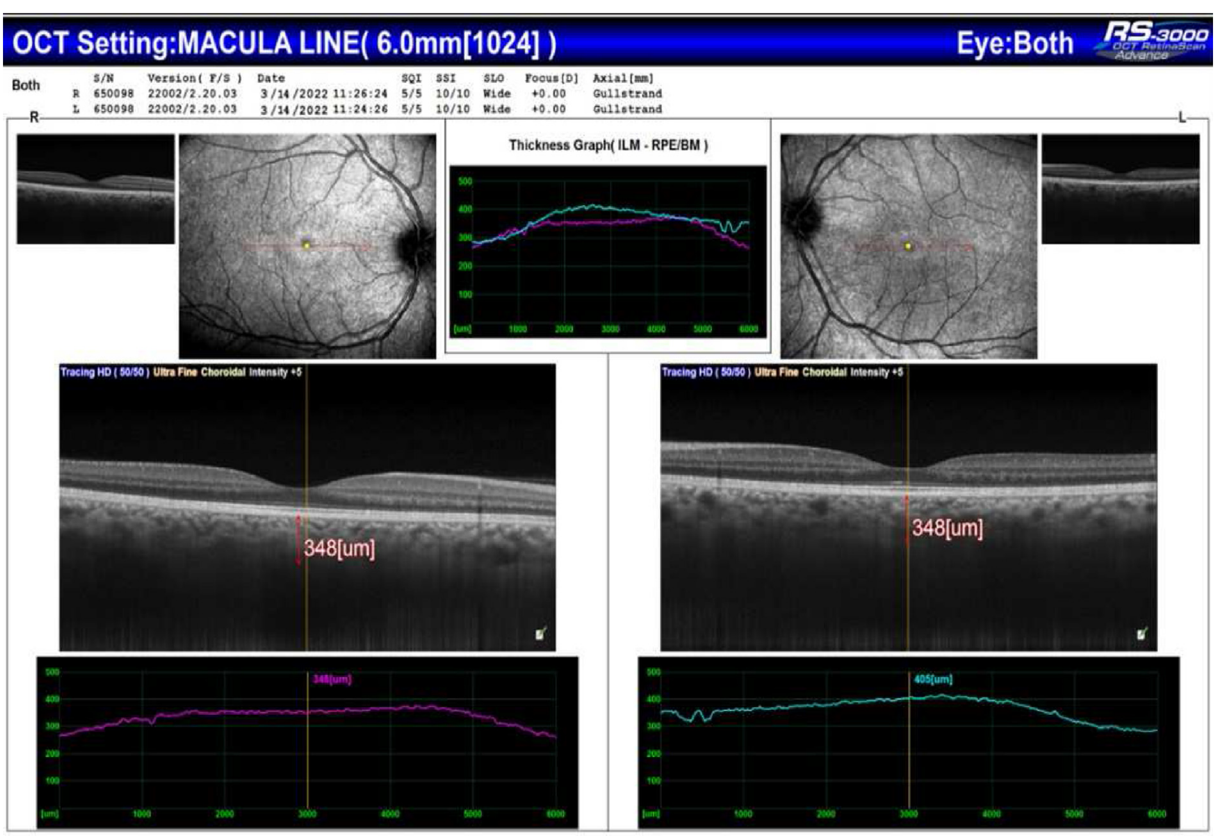


*Fig. 5. OCT, Macula Line of the previously shown in patient. Sub-foveal choroidal thickness measured 348 μm and 348 μm in right and left eye respectively.*

tion often associated with thyroid failure. TAO is mostly associated with a hyperthyroid status, However, it can occur with hypothyroid or euthyroid status.[8]

Proptosis, upper eyelid retraction, periorbital edoema, and erythema are the most frequent clinical signs. Throughout the 40−60 age range, the disease has a bimodal incidence and affects women more frequently than men.[9]

TAO results in compression of the orbital contents, impairment of the blood flow and thus affects the choroidal and retinal microstructure and function.[5]

OCT-based choroidal thickness measurement is increasingly being used to evaluate eye disorders. This research sought to determine if there was a correlation between TAO and variations in subfoveal choroidal thickness (CT).

We found that CT was significantly rised in cases with TAO matched with normal subjects. The significant increase in CT was revealed in many studies done by Del Noce et al.[10]; Lai et al.[11]; Gul et al.[12]; Yu et al.[13]; Çalõşkan et al.[9] and Özkan et al.[14]

In **Del Noce** ***et al.***,[10] The sub foveal CT was significantly thicker in TAO cases than the control eyes (285.6275 ± 32.5 μm matched with 135.89 ± 19.8 μm, respectively; $P = 0.0089$). In Gul et al. (2019), the sub foveal CT was 262.04 ± 63.46 in stable cases, and 304.79 ± 75.19 in active cases; $P = 0.04$. In Yu et al. (2018), the sub foveal CT was 313.47 ± 100.32; $P = 0.003$. In **Çalõşkan** ***et al.***,[9] the mean sub foveal CT was significantly higher in active GO group (395.84 ± 9.68 μm) than that in inactive GO group and healthy subjects' group (319.76 ± 7.07 μm and 314.22 ± 5.74 μm, respectively; $P < 0.001$).

The previously mentioned studies proposed that the pathological extension of the extraocular muscles and orbital soft tissues that happen in patients with TAO will significantly reduce the orbital venous drainage (as a consequence of the vascular compression within the orbital space) and as a result, will lead to choroidal venous congestion and increased choroidal thickness.

**Del Noce** ***et al.***[10] was the first study to investigate the possible changes in choroidal vascular blood flow in TAO cases using OCT-Angiography. Their study revealed a significant reduction of the vascular flow at the choriocapillary layer in subjects with TAO matched with healthy subjects, while in the deeper choroidal layer; there was an increase in vascular flow in TAO patients compared with normal subjects. They suggested that these vascular changes can be explained by the concept of a hindered orbital venous outflow at the level of the ophthalmic veins by the increased volume of the extraocular muscles and orbital soft tissues.

In our study we found no significance regarding macular thickness between hyperthyroidism patients and normal subjects.

**Eissa**,[15] also found no significant changes in macular thickness between hyperthyroidism cases and normal subjects as we found in our study.

We did not find a significant difference regarding age, gender, vision and IOP between TAO patients (either active or inactive) and normal subjects. Many studies as **Del Noce** ***et al.***[10]; **Gul** ***et al.***[12]; **Çalõşkan** ***et al.***[9] and **Özkan** ***et al.***[14] agreed with us about these findings. In addition, our study also revealed no significant correlation between CT and other studied parameters other than the activity score.

Finally, another researches are essential to confirm our results and reach judgements about the role played by OCT during the various stages of TAO.

### 4.1. Conclusion

Results from this research recommend that there is a significant affection of sub-foveal choroidal thickness in (TAO) patients. There is a significant rise in choroidal thickness in TAO cases either active or inactive in comparison to control group, but did not show a correlation with other studied parameters. OCT might allow an correct identification of macular and choroidal changes in established TAO cases.

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Authorship

All authors have a substantial contribution to the article.

### Conflicts of interest

The authors declared that there were no conflicts of interest.

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