Evaluation of the choroidal thickness and retinal nerve fiber layer and visual fields in morbid obesity: Does bariatric surgery affect retinal structure and function?

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Purpose: The study aimed to investigate the changes in choroidal thickness (CT), retinal nerve fiber layer thickness (RNFL), and visual field parameters in morbidly obese patients following bariatric surgery. Methods: The study included 40 morbidly obese patients with body mass indexes (BMI) ≥40 who had undergone bariatric surgery (Group 1) and 40 age-and sex-matched healthy subjects with normal BMI values (Group 2). RNFL and CT measurements by optical coherence tomography (OCT) and visual field test were performed preoperatively and the 1st, 6th, and 12th months postoperatively. CT measurements were obtained from the subfoveal, nasal (N), and temporal (T) regions at distances of 500 µm and 1,000 µm from the fovea. Results: No significant pathology was detected during ophthalmological examinations following bariatric surgery. The BMIs were found to be significantly lower in all of the periods after bariatric surgery (P < 0.0001). The CT measurements decreased significantly in all periods after bariatric surgery (P < 0.0001). No differences were found in terms of the mean RNFL thicknesses in all postoperative periods (P = 0.125). Visual field tests showed no significant changes during scheduled visits. (P = 0.877). No visual field defect was detected in any patient during the follow-up periods after bariatric surgery. Conclusion: These results have suggested that CT is positively correlated with BMI and decreased with a reduction in BMI progressively. Nutritional disorders resulting from malabsorption have not caused any nutritional optic neuropathy and visual field defect for at least the first postoperative year after bariatric surgery.



Key words: Bariatric surgery, choriocapillaris hypoperfusion, choroidal thickness, obesity, optical coherence tomography, retinal nerve fiber layer thickness, visual field

Obesity is an important public health problem, especially in developed countries, and its prevalence is increasing all over the world.^[1] It is also responsible for the development of many chronic diseases such as hypertension, cardiovascular diseases, diabetes mellitus, and certain types of cancers.^[2-4] These secondary disorders are the major risk factors for morbidity and mortality caused by obesity.

Obesity and morbid obesity are defined according to the body mass index (BMI) obtained by dividing the body weight by the square of the height (weight/height²) (kg/m²). The World Health Organization (WHO) identifies cases with BMI values that are more than 40 as morbidly obese. Bariatric surgery in patients with morbid obesity helps them to lose weight, therefore prevents the development of these chronic diseases and improves the quality of life. As a result, the use of bariatric surgery in morbidly obese patients has become widespread.

It is clear that the rapid drop in BMI after bariatric surgery may give rise to some changes in the whole body. Ocular effects of bariatric surgery have been evaluated in a limited number of studies. It has been reported that bariatric surgery can cause a

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Received: 13-Feb-2020 Accepted: 09-Jun-2020 Revision: 19-May-2020 Published: 14-Dec-2020 reduction in systemic blood pressure and intraocular pressure, and can also alter the retrobulbar blood flow.^[5,6] These changes can affect choroidal perfusion and thus retinal function in patients undergoing bariatric surgery. There are only a few studies in the literature that evaluate CT in obese patients, and the results are contradictory.^[7,8] Yumusak *et al.*^[7] reported that the CT was thicker in obese women than in normal women, whereas Teberik *et al.*^[8] reported that the CT was thinner in morbidly obese patients than in normal cases. In addition, there is a unique study that evaluated CT in patients who have undergone bariatric surgery.^[9] However, this study has a 6-month follow-up period, which may not be sufficient to evaluate the effects of bariatric surgery on the ocular structures.

To investigate the effect of rapid BMI decrease with bariatric surgery on ocular structures we designed this study to evaluate the retinal nerve fiber layer thickness (RNFL), choroidal thickness (CT), and visual field changes in morbidly obese patients during 12 months following bariatric surgery.

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Our study is important in that it is the first in the literature to compare the CT in morbidly obese patients to those of normal cases and to evaluate the changes in the CT after bariatric surgery among the same morbidly obese population. The changes on CT may provide further insights to assume how the weight loss achieved by these surgeries might affect the prognosis of some ocular diseases associated with the abnormal choroidal thickness.

The secondary aim of this study is to investigate the ocular side effects of malabsorption related to bariatric surgery. As to our knowledge, this surgery can cause malnutrition, hypoalbuminemia, B1, B12, folate, C, A, and D vitamin deficiencies, and deficiencies in trace elements such as iron, selenium, copper, and zinc.^[10,11] Metabolic and nutritional optic neuropathy^[12-14] and retinopathy^[15,16] can develop as a result of these complications. Regarding these, we have aimed to find out any optic nerve damage related to bariatric surgery, and compared visual fields and RNFL thickness before and after bariatric surgery. Our study is also unique in the literature in terms of investigating the long-term effect of bariatric surgery on the visual field and RNFL.

Methods

This study was conducted at the departments of Ophthalmology and General Surgery and was approved by the local ethics committee of our University (Meeting date; 26.09.2013, decision number: 2013-49). The study included 40 morbidly obese patients (Group 1) who had undergone bariatric surgery at our University General Surgery Clinic between 2013 and 2017 and 40 healthy volunteers (Group 2) with normal BMI who had been examined at the ophthalmology department. The protocol of the study adhered to the tenets of the Declaration of Helsinki.

Patients who had undergone bariatric surgery and been diagnosed as having morbid obesity based on body mass indexes (BMI) \geq 40 were included in the study, along with patients who had best-corrected visual acuity of 20/20 or more, patients with less than ± 2.00 spherical equivalence refraction, and patients with an axial length between 21 and 24 mm. These inclusion criteria were valid for the control group except for BMI values. Exclusion criteria were patients with diabetes mellitus, diabetic retinopathy or other retinopathy, systemic hypertension, ocular hypertension, glaucoma and other optic neuropathies, histories of coffee, alcohol, and cigarette dependence, cataracts, and other media opacities that could affect the measurements obtained from imaging through optical coherence tomography (OCT) and patients who had had ocular trauma, intraocular surgery, or retinal laser photocoagulation.

Preoperative BMIs and values at the first, sixth, and 12th months after surgery were calculated using the standard (WHO) formula (kg/m²). All patients and healthy volunteers were evaluated using the Snellen chart for uncorrected and corrected visual acuities. Intraocular pressures were measured by Goldmann applanation tonometry. Anterior segment examination was performed with a biomicroscope. Tropicamide 1% was administered through drops, and pupil dilatation was achieved. Indirect ophthalmoscopy was performed with a 90 diopter lens. RNFL thicknesses and CTs were measured preoperatively and at one, six, 12 months postoperatively, using OCT (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany). The SITA 30-2

program was used for the visual field test in all cases (Humphrey Field Analyzer, Carl Zeiss Meditech, Inc., Dublin, CA, USA). Evaluation of the visual fields was done using reliable visual field results with loss of fixation and false-positive and false-negative ratios below 30%. The results obtained before bariatric surgery were compared to the values obtained after the surgery and the values of the control group.

The RNFL thickness measurements were obtained using the OCT's automatic standard peri-papillary RNFL measurement mode. Enhanced deep imaging-optical coherence tomography (EDI-OCT) was used for choroidal imaging. The CT measurements were determined from five points on the axis passing through the center of the fovea. CT values were obtained from the fovea, nasal (N), and temporal (T) areas at a distance of 500 µm and 1000 µm from the fovea. CT measurements were taken by two ophthalmologists who took manual measurements of the vertical line drawn from the outer edge of the hyper-reflective retinal pigment epithelium (RPE) to the choroid-sclera connection [Fig. 1]. The mean of the values measured by the two ophthalmologists was used to reduce measurement errors. To reduce diurnal variation, all choroidal imaging was performed between one and three o'clock p.m. Data from the right eyes of all subjects were used for analysis.

SPSS program (SPSS for Windows 16, Chicago, IL, USA) was used for the statistical analysis. Descriptive statistics were shown as mean ± standard deviation. Probability-probability (PP)-plot analysis was used to test the normality of the variables used in the study, and it was observed that the data did not deviate much from the normal distribution. Analysis of variance in repetitive measurements that are robust to the distortion of normality assumptions (repeated measures ANOVA) was used to compare the mean values of the variables measured before and after bariatric surgery. In cases where the result was P < 0.05 after Mauchly's sphericity test had been conducted, Greenhouse-Geisser correction was performed. When the difference between variables was meaningful at the end of the analysis, multiple comparisons were done using the Bonferroni adjustment test, to determine in which period or periods this difference had occurred.

The independent t-test was used to compare the mean of the variables in Group 1 and Group 2, and Levene's test was performed for the homogeneity assumption of this test. If the variances were not homogeneous after doing Levene's test, the corrected degree of freedom was used. The Pearson correlation coefficient was calculated for correlations, and the significance of the relationship was tested. The degree

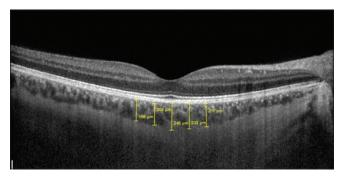


Figure 1: Determination of choroidal thickness measurements from five points on the axis passing through the center of the fovea

of association between choroidal thickness and each factor including BMI, axial length, age, and sex was calculated using multiple regression analyses in Group 1. The significance level was defined as P < 0.05.

Results

The sexes and the mean age of the 40 patients (32 females, 8 males) in Group 1, which was 38.50 ± 11.14 years, matched those of Group 2 (the control group). The mean BMI values were 48.45 ± 9.25 in Group 1 and 22.41 ± 1.44 in Group 2. There was a statistically significant difference in BMI values (P < 0.0001).

In terms of the CTs of the two groups, the measurements obtained from the fovea, N500, and T500 points were significantly higher in Group 1 (P = 0.0459, 0.0465, 0.0328, respectively) [Table 1].

A positive correlation was determined between the BMIs and CT values of the fovea and T1000 in Group 1 (r = 0.313, P = 0.0492 and r = 0.346, P = 0.029, respectively) [Table 2]. Multivariate regression analysis showed that BMI is the only factor that significantly affects the CT values of the fovea and T1000 in Group 1 ($\beta = 3.41$, 95% Cl = 0.11 to 6.70, P = 0.043 and $\beta = 3.13$, 95% Cl = 0.41 to 5.85, P = 0.025, respectively).

The BMIs were found to be significantly lower in all of the periods after bariatric surgery (P < 0.0001, for all pairwise comparisons). There was also a significant decrease in the CT values in all postoperative periods (for all pairwise comparisons, Table 3). However, no changes in the RNFL thickness values were observed in any period after bariatric surgery (P = 0.125) [Table 3 and Fig. 2].

When the results of the visual field tests were evaluated, the mean deviation (MD) values of the preoperative, and the postoperative first, sixth, and 12^{th} months were 0.07 ± 1.27 dB, 0.03 ± 1.33 dB, 0.12 ± 1.31 dB, and -0.004 ± 1.25 dB, respectively. There was no statistically significant difference between the groups (*P* = 0.877). Also, no visual field defects were detected during the follow-up in patients who underwent bariatric surgery.

Discussion

This study evaluated primarily the CT in morbidly obese patients who had undergone bariatric surgery. The results

of this study showed that the preoperative CT values of these morbidly obese patients were higher than those of the control group, and there was a moderate correlation between the BMIs and the preoperative CT values. Obesity can cause primary microvascular dysfunction in many tissues, including the eyes.^[17,18] The choriocapillaris hypoperfusion that results from these microvascular changes may explain the abnormal choroidal thicknesses found in our study. A recent study that used optic coherence tomography-angiography (OCT-A) in patients with central serous chorioretinopathy also demonstrated a reduction in choriocapillaris microvascular flow and choriocapillaris hypoperfusion in patients with the thick choroids. In this study, it was shown that choriocapillaris hypoperfusion might be an indicator of primary choroidal vasculopathy in patients with central serous chorioretinopathy.^[19] Therefore, we believe that there is a need for further studies that use OCT-A to evaluate choriocapillaris perfusion disorder and CT together in obese patients.

In another study that investigated the diameters of obesity-related retinal vascular structures, high BMI values were reported to be associated with the existence of narrow retinal arteries but large retinal vein diameters.^[20] There is no study in the literature that examines the diameters of vascular structures in the choroid. However, if there are indications that these microvascular changes developed in the entire body and retina due to obesity may also develop in the choroid, we can postulate that vascular congestion in the venous structures may explain the larger CT in morbidly obese patients. In addition, Tanabe et al. reported that the diameters of the choroidal veins showed good correlations with the CT.[21] Studies that are consistent with our study are those conducted by Bulus et al. as they reported that the subfoveal CT were thicker than normal among obese pediatric subjects and the BMI values were well correlated with the subfoveal CT in the obese subjects. This study reported that larger CT might be associated with increased levels of leptin and obesity-related inflammatory factors in obese subjects.^[22] Yumusak et al.^[7] also reported that CT was higher in obese women than in the control group, and the CTs were moderately correlated with the BMIs in these cases. This study is consistent with our study as it reported that changes in ocular circulation may be the cause of the larger CT in obese patients.

Table 1: Comparison of the choroidal thicknesses between groups on the fovea, N500, T500, N1000, and T1000						
	Fovea	N500	T500	N1000	T1000	
Grup 1 (µm)	366.50±97.41	337.80±98.20	340.00±87.90	319.17±94.67	318.40±81.29	
Grup 2 (µm)	324.37±88.03	296.40±84.34	298.30±83.70	288.72±84.67	295.70±84.29	
Ρ	0.0459	0.0465	0.0328	0.1335	0.2239	

N500: Nasal area at a distance of 500 µm from the fovea, T500: Temporal area at a distance of 500 µm from the fovea, N1000: Nasal area at a distance of 1000 µm from the fovea, T1000: Temporal area at a distance of 1000 µm from the fovea

Table 2: Evaluation of the relationships between BMI and CT values in Group 1							
	Fovea	N500	T500	N1000	T1000		
r	0.313	0.311	0.294	0.299	0.346		
Ρ	0.0492	0.0509	0.0652	0.0605	0.029		

N500: Nasal area at a distance of 500 µm from the fovea, T500: Temporal area at a distance of 500 µm from the fovea, N1000: Nasal area at a distance of 1000 µm from the fovea, T1000: Temporal area at a distance of 1000 µm from the fovea

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Table 3: Comparison of parameters after bariatric surgery							
	Preoperatif	1 month	6 month	12 month	Р		
BMİ (kg/m²)	48.45±9.25	42.41±7.45	35.11±6.43	29.93±5.58	<0.0001 ¹ <0.0001 ^{2*}		
Fovea (µm)	366.50±97.41	346.25±94.34	338.60±93.87	331.27±93.78	<0.0001 ¹ <0.0001 ^{2†}		
N500 (µm)	337.80±98.20	323.70±95.29	316.17±92.55	312.65±91.57	<0.0001 ¹ , <0.0001 ^{2‡}		
T500 (µm)	340.00±87.90	326.75±87.68	319.20±87.52	313.60±84.31	<0.0001 ¹ , <0.0001 ^{2*}		
N1000 (µm)	319.17±94.67	305.12±90.73	297.00±90.75	290.75±90.58	<0.0001 ¹ , <0.0001 ^{2§}		
T1000 (µm)	318.40±81.29	307.82±83.68	302.82±83.05	298.12±80.59	<0.0001 ¹ , <0.0001 ^{2*}		
RSLT (µm)	98.25±10.11	98.12±10.30	97.97±9.89	97.90±9.98	0.125 ¹		

BMI: Body mass index, N500: Nasal area at a distance of 500 µm from the fovea, T500: Temporal area at a distance of 500 µm from the fovea, N1000: Nasal area at a distance of 1000 µm from the fovea, T1000: Temporal area at a distance of 1000 µm from the fovea 1: Repeated measure ANOVA 2: Multiple Comparison with Bonferroni Adjustment, *for all pairwise comparisons, [†]all pair wise comparisons except for sixth and 12th month comparison (0.001 for 6 and 12 month comparison), [‡]all pairwise comparisons except for 6 and 12 month comparison), [§]all pairwise comparisons except for sixth and 12th month comparison), [§]all pairwise comparisons except for sixth and 12th month comparison), [§]all pairwise comparisons except for sixth and 12th month comparison), [§]all pairwise comparisons (0.019 for 6 and 12 month comparison)

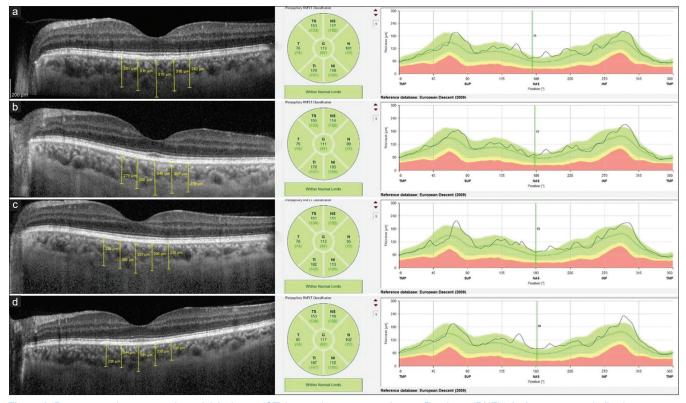


Figure 2: Progressive decrease in choroidal thickness (CT) but no change in retinal nerve fiber layer (RNFL) thickness in a morbidly obese patient after bariatric surgery (a = Preoperative, b = Postoperative first month, c = Postoperative 6th month, d = Postoperative first year)

In addition to the studies indicating that the CT among obese subjects is not different from those of the normal population,^[23] contrasting studies are postulating that CT is thinner in obese subjects.^[8,9,24] CT measurements can be affected by many factors, such as age, gender, ethnicity, axial length, diurinal variations, and coffee and cigarette dependence, which may account for the differences between the studies.^[7] In our study, to investigate the strength of significance of these confounding factors on choroidal thickness, we performed the multivariate regression analysis in the patient group, and it showed that the only factor affecting the CT is BMI values. This may show that confounding factors such as age, sex, and axial length do not affect CT values in our study. In addition, the prospective design of our study eliminates the majority of these confounding factors, and the

decreased CT was confirmed in the first, sixth, and 12th month follow-ups after bariatric surgery. Our study group had no ethnic variations, and all choroidal imaging was performed between one and three o'clock p.m. to reduce the diurnal variation of the CT.

A similar study by Doğan *et al.*^[9] evaluating CT after bariatric surgery with a shorter follow-up reported increases in the CT. This discrepancy between studies may be due to differences between the patient characteristics including preoperative CT values, gender distribution, and follow-up schedule. In our study, the mean preoperative subfoveal CT was 366.50 ± 97.41 µm and 32 of the 40 morbidly obese patients were female. In the study conducted by Dogan *et al.*, the mean preoperative subfoveal CT was $309.8 \pm 71.8 \,\mu\text{m}$ and the ratio of male to female was not specified. It is also important to note that obese women are predominant in studies reporting that the CT is higher than those of the normal population. As an example, in the study done by Yumusak et al.,[7] all cases were female, and in the studies by Bulus et al., [22] 27 out of 44 subjects were women. Therefore, further studies are needed to investigate the differences between the genders. In addition, our study has a longer follow-up period than the study conducted by Doğan et al., which has a 6 months follow-up period. Therefore, long term changes in the orbital tissue after bariatric surgery may explain the reduction of the CT in our study. Obesity can cause excessive intraorbital adipose tissue by causing increased venous pressure at the veins draining choroidal vasculature.^[25] After bariatric surgery, intraorbital pressure decreases as well as the pressure on the veins draining the choroidal vasculature. As discussed earlier, the diameters of the choroid veins are closely related to CT.^[21] Therefore, these changes may cause reduced CT after bariatric surgery, and explain the discrepancy between the studies as long term changes.

In our study, the reduction of CT after bariatric surgery can be explained by both the mechanical and vascular changes. Mechanical changes might be related to decreased adipose tissue in the orbita, as mentioned above. Vascular changes can be associated with leptin levels and obesity-related inflammatory factors. Obese patients have markedly increased leptin production due to resistance to its actions.^[26] It has been reported that leptin receptors are commonly found on vascular cells, which suggest that leptin plays a significant role in vascular pathophysiology. It has been also reported that leptin has angiogenic activity and increases oxidative stress in endothelial cells.[22,27] Therefore, an increased level of leptin in morbidly obese patients may explain changes in choroidal vasculature and increased CT. Terra et al.^[28] have shown that bariatric surgery markedly reduces the fasting leptin level, which may explain the reduction in CT after bariatric surgery in our study. In addition, vascular changes due to morbid obesity may result from obesity-related inflammatory factors. Codoñer-Franch et al.[29] have shown that obese patients have a higher concentration of all plasmatic parameters of nitric oxide metabolism, and there is a positive correlation between plasma nitrate and proinflammatory cytokine levels. In this study, it has been postulated that an increase the nitric oxide metabolism is associated with the early stages of oxidative stress and inflammation. This inflammatory condition in morbidly obese patients may cause increased CT, and bariatric surgery might have relieved the inflammatory condition and thus reduced the CT.

After bariatric surgery, macro- and micro-nutritional disorders resulting from malabsorption are frequently encountered. The most common deficiencies are protein, iron, calcium and vitamin D, vitamin B12, and nutrients such as folic acid, thiamine, vitamin C, vitamin E, selenium, zinc, magnesium, and vitamin A. To prevent such conditions, it is recommended that after bariatric surgery micro-nutritional supplements to be given and blood tests are done to test for certain nutritional disorders during specific periods both preoperatively and postoperatively. Although these disorders may be clinically obvious, they could also be subclinical and therefore overlooked.^[30] For this reason, in the postoperative period, our study investigated changes in RNFL thicknesses and visual fields that resulted from metabolic and nutritional optic

neuropathy and retinopathy. The main retinal complication is nyctalopia (night blindness), which is caused by vitamin A deficiency. In addition, vitamin E deficiency may affect the retina, and cause pigmentary retinopathy.^[15,16,31,32] No changes were observed in the visual field mean deviations (MDs) or RNFL thicknesses after bariatric surgery. Also, no additional visual field defects were detected in any case. These results may indicate that during the first year after bariatric surgery, patients are not at risk for neuropathies and retinopathies that might develop metabolically and nutritionally. However, since changes in gastrointestinal structure and function that result from bariatric surgery may continue over time, further studies with longer-term follow-up are needed.

The relatively small number of cases can be shown as a limitation in our study. In addition, women dominated the study group because most of the patients who underwent bariatric surgery were women. Therefore, further studies are required to investigate gender differences and more cases are needed to confirm our results and eliminate potential gender effects on the parameters that are studied. Finally, this study evaluated only CT in morbidly obese patients. However, further studies using OCT-A are needed to demonstrate any choroidal microvascular disorder that is due to morbid obesity and to evaluate its relationship to CT.

Conclusion

In conclusion, this study showed that the CT values were greater in morbidly obese patients than in the normal population, there was a moderate correlation between the BMIs and CTs, and thinning occurred in the CTs after bariatric surgery. This result may show that in morbidly obese patients, especially those with disorders in the pachychoroid spectrum, bariatric surgery may have positive effects on the prognosis of these eye diseases. In addition, these results may indicate that bariatric surgery is a safe method that is not associated with any risk of nutritional neuropathies for the first year following surgery.

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Conflicts of interest

There are no conflicts of interest.

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