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The impact of obesity on ocular hemodynamics and choroidal thickness

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Abstract

Background: Obesity affects microvascular structures. The effect of obesity on the ocular vascular system can be evaluated by changes in the choroidal thickness (CT) and retrobulbar blood flow (RBF).

Objectives: To evaluate the CT and RBF parameters in obese patients with various body mass index (BMI) values and compare these parameters with normal weight, healthy subjects.

Design: A prospective study.

Methods: The study included 102 eyes of 102 female patients. Patients were divided into three groups according to BMI as group 1 with a BMI of 18.5–24.99 ($n = 32$), normal weight group; group 2 with a BMI of 30–34.99 ($n = 35$), as obese class I; and group 3 with a BMI of 35–39.99 ($n = 35$), as obese class II. The peak systolic velocity (PSV), end-diastolic velocity (EDV), resistive index, and pulsatility index values of the central retinal artery (CRA) and ophthalmic artery (OA) were evaluated with color Doppler ultrasonography. CT was measured at the subfoveal area and at 500-µm intervals nasal and temporal to the fovea up to a distance of 1500 µm by using the enhanced depth imaging technique of optical coherence tomography. Intraocular pressure (IOP) was measured with a Goldmann applanation tonometry.

Results: There was a significant difference in IOP values within the groups with the highest values in group 3 (17.6 ± 2.1 mmHg) and the lowest in group 1 (12.4 ± 1.7 mmHg). The CT in groups 2 and 3 was found to be statistically significantly lower than that in group 1 at all measurement points ($p < 0.001$). There was a statistically significant negative correlation between CT at all measurement points and BMI ($p < 0.001$). The mean CRA PSV, EDV, and OA EDV values were statistically significantly lower in each obese group than those values in group 1 ($p < 0.001$). The OA PSV values were significantly lower in group 3 (36.5 ± 5.9 cm/s) than those in group 2 (43.8 ± 4 cm/s) and group 1 (44.6 ± 5.2 cm/s) ($p < 0.001$). Also, significant associations were found between BMI and CRA PSV, CRA EDV, and OA PSV values ($p < 0.001$).

Conclusion: Obesity may predispose to eye pathologies by changing the ocular vascular circulation.

Keywords: body mass index, choroidal thickness, intraocular pressure, obesity, retrobulbar blood flow

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Introduction

Obesity is a common life-threatening condition that results in reduced life expectancy in the modern world. The prevalence of being overweight and obesity is increasing in all age groups both in the developing and developed countries.[1]

Overweight status and obesity have been classified by the World Health Organization (WHO) according to the body mass index (BMI) as follows: BMI: 18.5–24.9 kg/m^2 = normal weight; 25–29.9 kg/m^2 = overweight; 30.0–34.9 kg/m^2 = obese class I; 35.0–39.9 kg/m^2 = obese class II;

and >40 kg/m^2 = obese class III.[2] In 2019, obesity prevalence rates ranged from 3.5% in Bangladesh to 32% in the USA.[3] It is emphasized that obesity exacerbates the coronavirus disease 2019 (COVID-19) pandemic, creating a twin pandemic, thus increasing morbidity and mortality.[3] The WHO has just released a report on the state of the obesity pandemic in Europe in May 2022, which states that being overweight and obesity affect approximately 60% of the citizens and approximately one in three children (29% of boys and 27% of girls) in the Europe area.[4] Obesity prevalence in Turkey has been reported as 26% in the latest study, with a prevalence of 34.2% in females and 24.4% in males in the adult age group.[3,4]

Obesity has been associated with ocular disease including cataracts, glaucoma, diabetic retinopathy, and age-related macular degeneration.[5] Although the underlying mechanism is not fully understood, it has been associated with vascular endothelial dysfunction and ocular vascular damage due to the microvascular changes in the retinal vessels and impaired ocular blood flow.[6]

The choroid is very vascular and provides the blood supply of the outer third of the retina. Evaluation of the choroidal thickness (CT) provides important information for the diagnosis and treatment of various ocular and systemic diseases.[7,8] The CT can be measured by using the enhanced depth imaging (EDI) mode of optical coherence tomography (OCT).[9] Considering the vascular structure of the choroid, it could be said that the main reason for the changes in the CT is choroidal blood flow variation.[7] Measuring CT with EDI-OCT could provide information on ocular perfusion.[10]

Color Doppler ultrasound (CDU) is now a widely used non-invasive technique for the evaluation of retrobulbar hemodynamics in ocular diseases; thanks to Doppler technology that provides quantitative data.[11] It provides measurements that are reproducible and reliable between observers.[12] The ophthalmic artery (OA), central retinal artery (CRA) and vein, and the short posterior ciliary arteries (SPCAs) can be measured by CDU.[11]

In obese patients previous studies have focused on retrobulbar ocular blood flow or CT changes, but not both.[13–16] Only two previous studies have evaluated the effect of obesity on retrobulbar ocular blood flow, and these have only included morbidly obese patients. Lower retrobulbar blood flow (RBF) values have been found in morbidly obese patients in these studies.[13,14] The above parameters are clinically important as they are part of the ocular circulation, and they are also essential in guiding the clinical approach to whether subjects suffering from obesity of various degrees have an increased risk of ocular pathology development.

The aims of this study was to evaluate the CT in various regions with EDI-OCT and the systolic and diastolic flow volumes and vascular resistance in the OA and CRA with CDU in obese women from various BMI groups and to compare these parameters with a normal weight group. We also evaluated the relationship between BMI and ocular hemodynamics. To the best of our knowledge, this study is significant as it is the first to evaluate both CT and RBF together in obese patients.

Materials and methods

Study population and design

This prospective clinical study included 102 eyes of 102 patients. The research involved 70 eyes of 70 obese patients who were followed up by the Department of Endocrinology being randomly selected and referred consecutively to the Ophthalmology Clinic of Serafeddin Training and Research Hospital between March 2020 and May 2021. The patients who presented to the Endocrinology Outpatient Clinic were classified according to the WHO criteria.[2] The subjects were divided into three groups: group 1 including cases with a BMI of 18.5–24.9 kg/m^2 as normal weight; group 2 including cases with a BMI of 30.0–34.9 kg/m^2 as obese class I; and group 3 including cases with a BMI of 35.0–39.9 kg/m^2 as obese class II. Group 1 consisted of healthy individuals, age- and sex-matched of other two groups without any systemic or ocular disease who consecutively presented to the Ophthalmology Clinic for a routine eye examination. All procedures were conducted in accordance with the Declaration of Helsinki. A written informed consent form was completed by all the participants.

The height was measured in the standing position and the weight by using a digital scale. The body weight and height of all participants were measured with the same scale. The BMI was calculated in both the obese patients and control

subjects by dividing the body mass (kg) into the square of the height (m^2). There were 32 patients in group 1 (31.4%), and 35 each in groups 2 and 3 (34.3% for each).

Participants over 18 years of age, with a refractive error $< \pm 1.50$ diopter (D), and without a history of ocular disease or surgery were included in the study. Exclusion criteria were current systemic disease such as diabetes or hypertension; a history of retinal disease, glaucoma, intraocular surgery, laser treatment, ocular trauma, or any ocular inflammation; a corneal opacity, cataract, or unstable fixation. Subjects with a history of using medication that could affect ocular blood flow (analgesics, decongestants, or antihistamines) in the last 3 months and subjects who were underweight (BMI $\leqslant 18.5$) or morbidly obese (BMI $\geqslant 40$) cases were not included in the present study. The systolic and diastolic blood pressure was measured twice a day for 1 week with an automatic blood pressure device (Omron M2 HEM-7121-E, Japan) before starting the study protocol. A systolic pressure over 140 mmHg and/or diastolic pressure over 90 mmHg resulted in exclusion from the study.

Patient examination protocol and study measurements

All participants underwent a detailed ocular examination including the best corrected visual acuity measurement with a Snellen chart, refraction assessment with an auto-refractor, slit-lamp biomicroscopy, posterior segment examination through the dilated pupil with a 90 diopter (D) lens, intraocular pressure (IOP) measurement with the Goldmann applanation tonometer (Nikon, Tokyo, Japan), central corneal thickness (CCT) measurement with ultrasonic pachymetry (Nidek UP-1000; Nidek Co., Ltd., Aichi, Japan), and axial length (AL) measurement with the Echoscan US 800 system (Nidek Co. Ltd, Aichi, Japan). All measurements were obtained from both eyes, but only the right eye measurements were used for statistical analysis.

The CT was measured with the EDI mode of the spectral domain-OCT device (3D OCT-2000, Topcon, Japan) following pupil dilatation. The central macular thickness (CMT) was measured following EDI-OCT imaging in all subjects. The macular thickness was measured automatically according to the Early Treatment Diabetic Retinopathy Study (ETDRS) map containing nine areas covering an area of $6 \times 6\,mm^2$ as obtained with the software of the device. The CMT was defined as the mean thickness of the neurosensory retina in the central 1 mm diameter using the ETDRS map. The CT was measured at the subfoveal area and at 500 µm intervals nasal and temporal to the fovea up to a distance of 1500 µm. OCT images were taken by the same experienced technician at the same time (at noon) to decrease the effect of diurnal fluctuation. Sections with a signal power index below 6/10 were not included in the evaluation. The CT measurement was performed manually at different times by two independent physicians (MT, NA) and on masked groups, at the outer border of the retinal pigment epithelium hyper-reflectivity and the internal border of the choroid-sclera junction using the measurement tool of the software. The mean value of the two measurements was taken for statistical analysis. The measurements were repeated when there was a difference of more than 10 µm between two values.

The RBF was measured with the 10 MHz linear probe of the CDU device (Toshiba Aplio 500, Tokyo, Japan) by the same radiologist in all cases. The measurements were performed with the patient in the supine position and the eyes closed. Excessive pressure on the eye was avoided during the measurements to prevent artifact formation. An evaluation was performed with the B-mode after applying methylcellulose gel on the eyelids. The eye was screened in the transaxial, sagittal, and oblique planes in the gray scale mode. The color coding of the arterial and venous structure localization was performed with the color Doppler mode. The CRA and OA of the eye to be evaluated were sampled with a Doppler angle of 30–60 degrees. The peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged velocity (TAV), resistive index (RI) [RI = (PSV−EDV)/PSV], and pulsatility index (PI) [PI = (PSV−EDV)/TAV] values were recorded from the CRA and OA. All the measurements of the same patient were taken on the same day.

The SPCAs are known to contribute to the arterial supply of the choroid. It is relatively easy to determine the measurement angle in the CRA and OA, but the angle correction reliability is low[12] and imaging is difficult for SPCAs as they have smaller diameters and are more tortuous with measurements showing more individual variation.[17] We therefore did not include the SPCA measurements in our evaluation.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software for Windows, version 22 (SPSS Inc., Chicago, IL, USA). Sample size was calculated by using G Power 3.1 (version 3.1.9.4, Franz Faul, University of Kiel, Kiel, Germany). With a power of 80%, a significance level of 0.05, and an effect size of 0.80, the sample size for each group was calculated to be 27. Adding a 10% dropout rate, the total of sample size was found to be 30 in each group. The continuous variables were reported as mean ± standard deviation (SD) while the categorical variables were summarized with the use of frequencies. The normality of all data samples was checked with the Kolmogorov–Smirnov test. Since the values obtained from the right and left eyes of the subjects were highly correlated, the right eye values were used in the statistical analysis ($p < 0.001$, $r > 0.90$). Comparisons of the parametric values among the groups were performed with one-way ANOVA, and comparisons of the nonparametric values among the groups were performed with the Kruskal–Wallis test. The CT values and CDU parameters were compared between the groups using univariate analysis of covariance, controlling for potential confounders including the age, IOP, refraction, CCT, and AL, according to the previous studies.[12,18–20] The Bonferroni post hoc test was used for pairwise comparisons. Univariate linear regression followed by multivariate linear regression modeling was used to determine the association of CT and ocular hemodynamics with BMI and other systemic and ocular parameters including the IOP, age, refraction, AL, and CCT. The collinearity statistics were all within accepted limits (BMI, tolerance = 0.87, VIF: 1.14; IOP, tolerance = 0.86, VIF = 1.17; age, tolerance = 0.92, VIF = 1.09; refraction, tolerance = 0.90, VIF = 1.11; AL, tolerance = 0.94, VIF = 1.06; CCT, tolerance = 0.97, VIF = 1.03). A two-tailed p value < 0.05 was considered significant.

Results

Our study included 70 obese patients and 32 normal weight healthy subjects. There was no significant difference among the groups for age, CCT values, refractive errors, and AL ($p = 0.316$, $p = 0.877$, $p = 0.976$, $p = 0.751$, respectively). The mean IOP value was 12.4 ± 1.7 mmHg in group 1, 16.5 ± 1.5 mmHg in group 2, and 17.6 ± 2.1 mmHg in group 3. A significant difference in terms of the mean IOP values was found among the groups ($p < 0.001$). While the mean IOP values were significantly different among the groups, they were highest in group 3 and lowest in group 1 (the Bonferroni post hoc test result was $p < 0.001$ for groups 1 and 2, $p < 0.001$ for groups 1 and 3, and $p = 0.195$ for groups 2 and 3). The demographic clinical characteristics of the groups are shown in Table 1.

The CT was significantly lower in groups 2 and 3 than in group 1 ($p < 0.001$) at subfoveal (FCT); nasal 500, 1000, and 15,000 µm (N500, N1000, and N1500) and temporal 500, 1000, and 1500 µm (T500, T1000, and T1500) measurement points. Furthermore, the mean CT was significantly lower in group 3 than that in group 2 at FCT, N500, T500, T1000, and T1500 µm ($p < 0.001$, $p = 0.03$, $p = 0.01$, $p = 0.05$, $p = 0.04$, respectively) (Table 2).

Regarding the CRA parameters, the mean PSV and EDV values were significantly lower in groups 2 and 3 than in group 1 ($p = 0.01$, $p < 0.001$, respectively). The mean CRA PSV values were found to be significantly lower in group 3 than in group 2 ($p < 0.001$). However, there was no significant difference between the mean CRA EDV values of groups 2 and 3 ($p = 0.11$).

Evaluation of the OA parameters revealed that the mean PSV and EDV values were significantly lower in group 3 than in group 1 ($p < 0.001$, $p < 0.001$, respectively). The mean OA PSV and EDV values were also significantly lower in group 3 than in group 2 ($p < 0.001$, $p = 0.02$, respectively). Besides, the mean OA EDV values were statistically significantly lower in group 2 than in group 1 ($p = 0.04$).

In addition, no significant difference was found between the groups in terms of the CRA RI and PI values ($p = 0.15$, $p = 0.45$, respectively) and OA RI and PI values ($p = 0.46$, $p = 0.52$, respectively) (Table 3).

Results of univariate and multivariate regression analyses for the association of systemic and ocular variables and CT are shown in Table 4, and the results for the ocular hemodynamics with BMI and other clinical variables are summarized in Table 5. Multivariate regression using these variables showed that only BMI had an association with CT ($p < 0.001$). The scatter plots illustrating the relationship of the CT with BMI and other clinical variables are presented in Figure 1. For the ocular hemodynamic parameters, significant

Table 1. The demographic and clinical characteristics of participants.

Parameters		Group 1 ($n=32$)	Group 2 ($n=35$)	Group 3 ($n=35$)	p Value
Age, years	Mean ± SD	33.6 ± 8.1	32.7 ± 7.6	35.7 ± 9.2	0.316*
	(Range)	(20–51)	(19–50)	(18–57)	
IOP (mmHg)	Mean ± SD	12.4 ± 1.7	16.5 ± 1.5	17.6 ± 2.1	**<0.001****
	(Range)	(16–21)	(14–19)	(11–21)	
CCT (μm)	Mean ± SD	545.6 ± 17.3	543.8 ± 19.2	546.2 ± 20	0.877*
	(Range)	(519–598)	(510–587	(510–589)	
Refractive error (D)	Mean ± SD	−0.05 ± 0.5	0.02 ± 0.04	0.02 ± 0.6	0.976**
	(Range)	(−1.50 to 1.00)	(−1.00 to 1.00)	(−1.00 to 1.00)	
Axial length (mm)	Mean ± SD	22.2 ± 0.9	22 ± 1.05	22.1 ± 0.7	0.751**
	(Range)	(20.10–23.68)	(20.15–23.90)	(20.48–23.44)	
BMI (kg/m^2)	Mean ± SD	21.6 ± 1.7	32.7 ± 1.5	37.6 ± 1.3	**<0.001****
	(Range)	(18.60–24.80)	(30.1–34.7)	(35.0–39.9)	

*One-way ANOVA test. **Kruskal–Wallis test.
BMI, body mass index; CCT, central corneal thickness; D, diopter; IOP, intraocular pressure. Boldfaced values are statistically significant ($p<0.05$).

associations were found between BMI and CRA PSV ($\beta=-0.66$, $B=-0.46$, 95% CI: −0.56 to −0.36, $p<0.001$), CRA EDV ($\beta=-0.49$, $B=-0.15$, 95% CI: −0.20 to −0.10, $p<0.001$), and OA PSV ($\beta=-0.39$, $B=-0.42$, 95% CI: −0.60 to −0.25, $p<0.001$). In addition, OA PI was significantly associated with the age on multivariate regression ($\beta=-0.31$, $B=-0.01$, 95% CI: −0.02 to −0.01, $p<0.01$) (Table 5). The scatter plots illustrating the relationship of the ocular hemodynamics with BMI and other clinical variables are presented in Figure 2.

Discussion

The chronic inflammation seen in some disorders such as systemic lupus erythematosus, rheumatoid arthritis, and obstructive apnea syndrome can decrease CT by altering the microvascular structures.[21–23] Obesity is known to be a cause of low-grade systemic or chronic inflammation resulting in cytokine, adipokine, and chemokine release.[24] The inflammatory mediators secreted to the blood in obese patients are believed to increase oxidative stress and hypoxia, and the accompanying chronic low-grade inflammation creates a predisposition for vascular endothelial damage and microvascular changes, as in other systemic disorders.[25,26]

The aim of this study was to evaluate the ocular perfusion by investigating both the RBF and choroidal circulation in order to determine microvascular changes. Our study showed that ocular perfusion was affected by the lower CT and decreased RBF values detected in obese patients.

The retrobulbar circulation was evaluated with color Doppler imaging. Impaired ocular perfusion is reflected by low PSV and EDV values while the RI and PI parameters indicate vascular resistance. There is an acceptance of the fact that RI is more reliable to determine resistance in small diameter vessels such as the retrobulbar vessels while PI shows the resistance for large diameter vessels.[27] In this study, the CRA PSV, CRA EDV, and OA EDV values were lower in each obese patient group than in the healthy group. In addition, the OA PSV values were significantly lower in the obese class II group than both the obese class I group and normal weight subjects. Besides, there was signification negative correlation between the BMI and the OA PSV, CRA PSV, and CRA EDV values on multivariate regression analysis. These results were found

Table 2. Comparison central macular thickness and choroidal thickness measurements between groups.

Parameters		Group 1 ($n=32$)	Group 2 ($n=35$)	Group 3 ($n=35$)	p Value	Pairwise comparisons		
CMT (μm)	Mean ± SD	218.8 ± 10.2	215.6 ± 10.1	218.6 ± 11.1	0.14			
	(Range)	(204–242)	(200–237)	(203–249)				
FCT (μm)	Mean ± SD	361.5 ± 13.5	319.8 ± 13.5	308.7 ± 14.5	**<0.001**	**<0.001**[a]	**<0.001**[b]	**<0.001**[c]
	(Range)	(335–399)	(295–346)	(290–346)				
N 500 μm	Mean ± SD	351.8 ± 14.4	308.7 ± 12.4	301 ± 14.6	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0,03** [c]
	(Range)	(325–380)	(275–333)	(280–334)				
N 1000 μm	Mean ± SD	343.5 ± 12.6	301.9 ± 12.1	297.9 ± 15.9	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0,30** [c]
	(Range)	(318–364)	(269–328)	(275–328)				
N 1500 μm	Mean ± SD	335.68 ± 13.78	294.94 ± 17.60	292.14 ± 19.63	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0.49** [c]
	(Range)	(310–370)	(233-328)	(246–340)				
T 500 μm	Mean ± SD	356.1 ± 15	314.8 ± 13.4	305 ± 15.7	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0.01** [c]
	(Range)	(329–399)	(285–339)	(275–340)				
T 1000 μm	Mean ± SD	351.4 ± 16.7	309.4 ± 11.1	302 ± 15.88	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0.05** [c]
	(Range)	(311–387)	(283–328)	(269–340)				
T 1500 μm	Mean ± SD	346.5 ± 16.4	305.5 ± 11.6	298.5 ± 16.5	**<0.001**	**<0.001**[a]	**<0.001**[b]	**0.04** [c]
	(Range)	(318–399)	(275–322)	(272–341)				

Boldfaced values are statistically significant.
[a]p Value between groups 1 and 2.
[b]p Value between groups 1 and 3.
[c]p Value between groups 2 and 3.
CMT, central macular thickness; FCT, foveal choroidal thickness; N, nasal; T, temporal.

without a statistically significant difference between the groups for the vascular resistance index.

Ocular blood flow changes are correlated with the amount of retrobulbar adipose tissue. Çekiç et al.[13] have reported significantly decreased IOP levels and increased OA PSV and EDV values in the postoperative period after bariatric surgery, as related to the decreased BMI values in morbidly obese patients. Lopez et al. have evaluated the effects of decompression surgery on RBF in patients with Graves' ophthalmopathy and found a significantly decreased CRA and OA RI values together with increased OA PSV and EDV values after decompression surgery.[28] We can therefore speculate that an increased severity of obesity leads to an alteration in the vascular resistance and OA flow parameters in parallel to the increase in the retrobulbar adipose tissue, and it can also lead to decreased ocular perfusion as reflected in the OA parameters. Another study that included morbidly obese patients has found a decrease only in the OA PSV and EDV values together with decreased CRA PI.[14] The retina and optic nerve head vessels also have an autoregulation system that enables the maintenance of blood flow velocity even when the perfusion pressure is changed. Changes in both the OA and CRA were monitored in the current study while other studies on morbidly obese patients have only found changes in the OA parameters.[13,14] It is possible that autoregulatory mechanisms become effective in protecting the retinal arteriole perfusion when the OA velocity decreases in association with the increasing retrobulbar fat tissue in the morbidly obese. At the morbid obesity level, only the OA flow has been found to decrease with an attempt to protect the retinal arteriole flow in the presence of increased vascular resistance, with the autoregulatory mechanism required to protect the optic

Table 3. Comparison of color Doppler ultrasonography parameters among groups.

Parameters		Group 1 ($n=32$)	Group 2 ($n=35$)	Group 3 ($n=35$)	p Value	Pairwise comparisons		
CRA PSV (cm/s)	Mean ± SD	19.9 ± 3.1	15.9 ± 4.1	12.3 ± 2.5	<**0.001**	**0.01**[a]	<**0.001**[b]	<**0.001**[c]
	(Range)	(11.5–24.6)	(8.7–23.5)	(7.3–16.36)				
CRA EDV (cm/s)	Mean ± SD	6.6 ± 1.5	4.8 ± 1.6	4.3 ± 1.6	<**0.001**	**0.01**[a]	<**0.001**[b]	**0.11**[c]
	(Range)	(3.7–9.1)	(2.0–9.4)	(2.3–7.63)				
CRA RI	Mean ± SD	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.15			
	(Range)	(0.57–0.79)	(0.52–0.82)	(0.42–0.80)				
CRA PI	Mean ± SD	1.1 ± 0.2	1.2 ± 0.3	1.1 ± 0.3	0.45			
	(Range)	(0.78–1.45)	(0.79–1.72)	(0.61–1.72)				
OA PSV (cm/s)	Mean ± SD	44.6 ± 5.2	43.8 ± 4.0	36.5 ± 5.9	<**0.001**	**0.82**[a]	<**0.001**[b]	<**0.001**[c]
	(Range)	(37–56.4)	(31.60–50.60)	(20.92–45)				
OA EDV (cm/s)	Mean ± SD	12.5 ± 3.1	11.1 ± 2.6	9.7 ± 2.9	<**0.001**	**0.04**[a]	<**0.001**[b]	**0.02**[c]
	(Range)	(5.7–18.3)	(6.7–14.9)	(5.30–13.20)				
OA RI	Mean ± SD	0.7 ± 0.9	0.7 ± 0.8	0.7 ± 0.1	0.46			
	(Range)	(0.54–0.89)	(0.56–0.87)	(0.44–0.87)				
OA PI	Mean ± SD	1.43 ± 0.4	1.5 ± 0.3	1.5 ± 0.3	0.52			
	(Range)	(0.89–2.35)	(0.94–2.04)	(0.68–2.08)				

Boldfaced values are statistically significant.
[a]p Value between groups 1 and 2.
[b]p Value between groups 1 and 3.
[c]p Value between groups 2 and 3.
CRA, central retinal artery; EDV, end-diastolic velocity; OA, ophthalmic artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistive index.

nerve head perfusion.[13,14] These results suggest that the decreased OA and CRA flow and the lower ocular perfusion pressure in obese patients without a change in vascular resistance could be because they have not yet reached the level that activates the autoregulatory mechanism.

A decreased blood flow rate was found in this study, as indicated by our results related to both the retrobulbar and choroidal circulation. The ciliary artery, a branch of the OA, plays a role in the choroidal circulation, and any OA velocity decrease could therefore indicate choroidal circulation changes. This study found significantly decreased OA PSV and EDV values in the obese group compared to the healthy group and this finding was supported with decreased CT in the two obese groups. A statistically significant negative correlation was also found between the CT at all measurement points and the BMI on multivariate analysis, in support of this result. High BMI values were found to decrease capillary density and tissue perfusion, and this finding was one of the earliest microvascular changes seen during weight gain.[29] Boillet et al. have shown that patients with high BMI have narrower retinal arterioles and wider retinal venules.[30] Dogan et al.[31] have found the CT to be significantly thinner in the morbid obese group compared to the non-obese group, while Yilmaz et al.[15] have detected a negative correlation between BMI and CT. In addition, Dogan et al.[32] have reported a persistent increase in the thickness of the subfoveal choroid at the postoperative 3rd and 6th months following sleeve gastrectomy in morbidly obese patients.

Several studies have reviewed the underlying mechanisms of the microvascular changes as related to obesity.[26,33–35] The choroidal blood flow decreases with the activation of the choroidal

Table 4. Univariate and multivariate regression analysis results for the association of the choroidal thickness with BMI and other clinical variables.

	FCT (µm)		N 500 (µm)		N 1000 (µm)		N 1500 (µm)		T 500 (µm)		T 1000 (µm)		T 1500 (µm)	
Correlation parameters	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***
Univariate linear regression														
BMI (kg/m^2)	***–0.85***	***<0.001***	***–0.83***	***<0.001***	***–0.80***	***<0.001***	***–0.72***	***<0.001***	***–0.83***	***<0.001***	***–0.81***	***<0.001***	***–0.80***	***<0.001***
IOP (mmHg)	***–0.70***	***<0.001***	***–0.66***	***<0.001***	***–0.69***	***<0.001***	***–0.62***	***<0.001***	***–0.65***	***<0.001***	***–0.63***	***<0.001***	***–0.59***	***<0.001***
Age (years)	–0.06	0.54	–0.02	0.82	0.01	0.93	0.03	0.76	–0.08	0.44	–0.09	0.36	–0.09	0.37
Refraction (D)	–0.07	0.47	–0.07	0.47	–0.11	0.29	–0.13	0.18	–0.08	0.44	–0.08	0.43	–0.04	0.68
Axial length (mm)	0.04	0.67	0.01	0.89	0.02	0.81	0.04	0.70	0.01	0.94	0.01	0.94	0.04	0.72
CCT (µm)	0.02	0.81	0.02	0.87	0.01	0.90	0.11	0.28	0.07	0.50	0.08	0.43	0.09	0.37
Multivariate linear regression														
BMI (kg/m^2)	***–0.73***	***<0.001***	***–0.75***	***<0.001***	***–0.64***	***<0.001***	***–0.59***	***<0.001***	***–0.77***	***<0.001***	***–0.76***	***<0.001***	***–0.81***	***<0.001***
IOP (mmHg)	***–0.16***	***0.05***	0.77	0.24	***–0.21***	***0.02***	–0.17	0.10	–0.08	0.37	–0.07	0.46	0.01	0.90
Age (years)														
Refraction (D)														
Axial length (mm)														
CCT (µm)														

Boldfaced values are statistically significant ($p<0.05$).
BMI, body mass index; CCT, Central corneal thickness; D, diopter; IOP, Intraocular pressure.

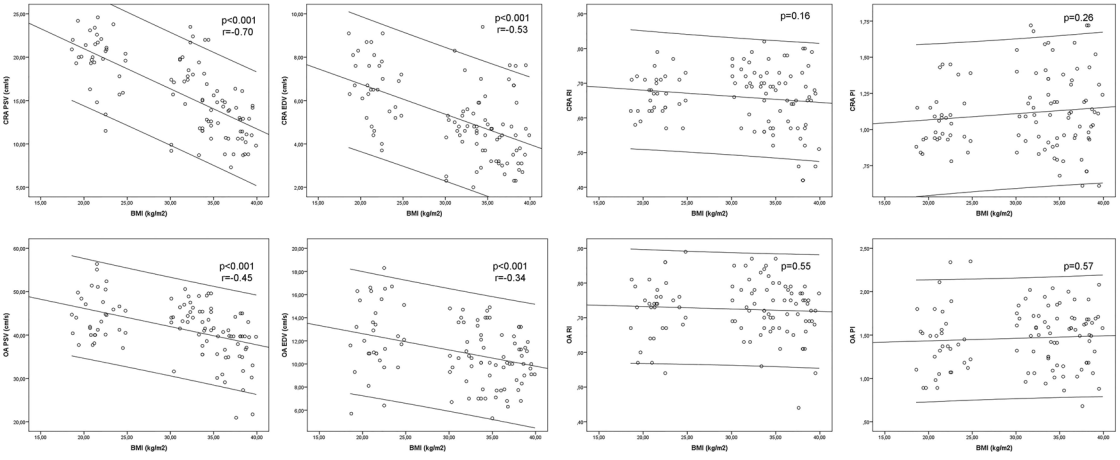

Figure 1. Relationship of the choroidal thickness with BMI and other clinical variables.
BMI, body mass index.

circulation-related sympathetic efferent nerves and the secretion of noradrenaline, while increasing with nitrous oxide (NO) secretion by the parasympathetic efferent nerves, both under the regulation of the autonomic nervous system.[36] The level of NO, a vasodilator molecule of endothelial origin that regulates the ocular blood flow and has a positive effect on IOP regulation,

Table 5. Univariate and multivariate regression analysis results for the association of the ocular hemodynamics with BMI and other clinical variables.

	CRA PSV (cm/s)		CRA EDV (cm/s)		CRA RI		CRA PI		OA PSV (cm/s)		OA EDV (cm/s)		OA RI		OA PI	
Correlation parameters	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***	**β**	***p***
Univariate linear regression																
BMI (kg/m²)	***−0.70***	***<0.001***	***−0.53***	***<0.001***	−0.14	0.16	0.11	0.26	***−0.45***	***<0.001***	***−0.34***	***<0.001***	−0.06	0.55	0.06	0.57
IOP (mmHg)	***−0.54***	***<0.001***	***−0.41***	***<0.001***	−0.03	0.75	0.10	0.31	***−0.37***	***<0.001***	***−0.33***	***<0.001***	−0.07	0.46	−0.05	0.64
Age (years)	0.05	0.64	0.11	0.27	−0.02	0.87	−0.09	0.37	−0.12	0.21	0.06	0.54	***−0.24***	***0.01***	***−0.34***	***<0.001***
Refraction (D)	−0.09	0.35	−0.01	0.96	−0.01	0.92	0.05	0.60	0.15	0.13	0.07	0.46	0.00	1.00	−0.16	0.11
Axial length (mm)	−0.06	0.55	−0.02	0.85	−0.06	0.55	0.10	0.30	0.04	0.69	0.12	0.25	−0.10	0.33	−0.06	0.56
CCT (μm)	0.13	0.19	0.10	0.34	0.03	0.79	−0.06	0.57	0.10	0.32	0.01	0.93	0.16	0.10	***0.22***	***0.03***
Multivariate linear regression																
BMI (kg/m²)	***−0.66***	***<0.001***	***−0.49***	***<0.001***					***−0.39***	***<0.001***	−0.20	0.15				
IOP (mmHg)	−0.05	0.62	−0.05	0.69					−0.09	0.52	−0.18	0.20				
Age (years)															***−0.31***	***<0.001***
Refraction (D)																
Axial length (mm)																
CCT (μm)															0.18	0.06

Boldfaced values are statistically significant ($p<0.05$).
BMI, body mass index; CCT, central corneal thickness; D, diopter; IOP, intraocular pressure.

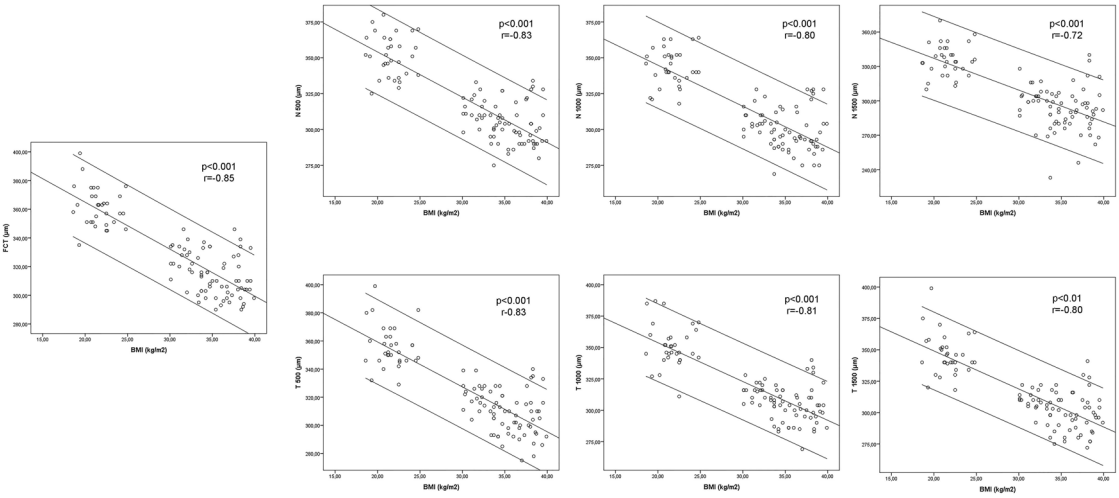

Figure 2. Relationship of the ocular hemodynamics with BMI and other clinical variables.
BMI, body mass index.

is low in obese patients[26,33] while the level of vasoconstrictor molecules such as endothelin-1 and angiotensin-II have been found to increase in the serum in correlation with the BMI.[34,35] We believe that the decreased thickness of the choroid, which is rich in vascular supply, in our cases is due to the balance between the vasodilator and vasoconstrictor agents shifting toward vasoconstriction.

Obesity has been found to be an independent risk factor in IOP elevation.[37,38] The IOP was found to be statistically significantly higher in the obese patients compared to the control group in this study (although still within the normal range). These results are consistent with the literature. Khan et al.[37] have shown that a high BMI level was associated with increased IOP; Stojanov et al.[39] have found that high retrobulbar adipose tissue volume was correlated with high IOP values in obese patients; and Gunes et al.[40] have reported a positive relationship between BMI and increased IOP. Similarly, IOP elevation that was parallel to the increased BMI in obese patients has been observed in this study. IOP elevation in obese patients is explained with vascular and mechanical mechanisms. The elevation has also been associated with increased oxidative stress that damages the trabecular meshwork,[41] and the increased episcleral venous pressure related to the increased orbital fat mass with the resultant decreased aqueous outflow.[39]

This study had various limitations. The first one was the small size of our groups. The second limitation was the lack of information on the obesity duration of the subjects and the blood levels of the inflammatory cytokines named adipokines. In addition, the inability to evaluate SPCAs with CDU, which is a good indicator of choroidal circulation, is another limitation of our study.

Conclusion

In conclusion, it was found that obese patients had higher IOP values with decreased CT and ocular blood flow, which were affected by vascular perfusion before reaching the morbid obesity level as well. These changes were related to the severity of the obesity. The results indicate that obesity creates ocular perfusion changes by influencing the microvascular structures. These vascular changes can create a foundation for ocular disorders that can develop in the presence of decreased ocular perfusion. Clinicians should therefore be more careful in the diagnosis and follow-up of ocular pathologies in obese patients.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Tokat Gaziosmanpasa University Medical School (approval date: 29.09.2015; approval no: 2015/15). All procedures were conducted in accordance with the Declaration of Helsinki. Written informed consent form was obtained from each patient.

Consent for publication

Not applicable.

Author contributions

Melek Tufek: Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Visualization; Writing – original draft; Writing – review & editing.

Pinar Nalcacioglu: Conceptualization; Investigation; Visualization; Writing – original draft; Writing – review & editing.

Mustafa Capraz: Data curation; Investigation; Project administration; Software; Writing – review & editing.

Kenan Varol: Conceptualization; Data curation; Formal analysis; Methodology; Visualization; Writing – review & editing.

Ahmet Turan Kaya: Conceptualization; Formal analysis; Supervision; Writing – review & editing.

Nihat Aydın: Conceptualization; Data curation; Formal analysis; Visualization; Writing – review & editing.

Caner Kara: Conceptualization; Software; Validation; Visualization; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author (MT) on request.

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References

1. Shetty P and Schmidhuber J. Introductory lecture the epidemiology and determinants of obesity in developed and developing countries. *Int J Vitam Nutr Res* 2006; 76: 157–162
2. World Health Organization. *Obesity: Preventing and managing the global epidemic*. Report of a WHO Consultation. WHO Technical Report Series 894. 2000. www.who.int/nutrition/publications/obesity//WHO_TRS_894/en/ (accessed 12 July 2017).
3. Boutari C and Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. *Metabolism* 2022; 133: 155217
4. World Health Organization. *WHO European Regional Obesity Report 2022*. Copenhagen: WHO Regional Office for Europe 2022, 2022.
5. Cheung N and Wong TY. Obesity and eye diseases. *Surv Ophthalmol* 2007; 52: 180–195.
6. Grieshaber MC and Flammer J. Blood flow in glaucoma. *Curr Opin Ophthalmol* 2005; 16: 79–83.
7. Nickla DL and Wallman J. The multifunctional choroid. *Prog Retin Eye Res* 2010; 29: 144–168.
8. Sezer T, Altınışık M, Koytak İA, *et al*. The choroid and optical coherence tomography. *Turk J Ophthalmol* 2016; 46: 30–37.
9. Tian J, Marziliano P, Baskaran M, *et al*. Automatic measurements of choroidal thickness in EDI-OCT images. *Annu Int Conf IEEE Eng Med Biol Soc* 2012; 2012: 5360–5363.
10. Kim M, Kim SS, Kwon HJ, *et al*. Association between choroidal thickness and ocular perfusion pressure in young, healthy subjects: enhanced depth imaging optical coherence tomography study. *Invest Ophthalmol Vis Sci* 2012; 53: 7710–7717.
11. Pauk-Domańska M and Walasik-Szemplińska D. Color Doppler imaging of the retrobulbar vessels in diabetic retinopathy. *J Ultrason* 2014; 14: 28–35.
12. Stalmans I, Vandewalle E, Anderson DR, *et al*. Use of colour Doppler imaging in ocular blood flow research. *Acta Ophthalmol* 2011; 89: e609–e630.
13. Çekiç B, Dogan B, Toslak EI, *et al*. The effect of bariatric surgery on the retrobulbar flow hemodynamic parameters in patients with obesity: color Doppler evaluation. *Int Ophthalmol* 2018; 38: 1845–1850.
14. Çekiç B, Toslak İE, Doğan B, *et al*. Effects of obesity on retrobulbar flow hemodynamics: color Doppler ultrasound evaluation. *Arq Bras Oftalmol* 2017; 80: 143–147.
15. Yilmaz I, Ozkaya A, Kocamaz M, *et al*. Correlation of choroidal thickness and body mass index. *Retina* 2015; 35: 2085–2090.
16. Yumusak E, Ornek K, Durmaz SA, *et al*. Choroidal thickness in obese women. *BMC Ophthalmol* 2016; 16: 48.

17. Németh J, Kovács R, Harkányi Z, *et al.* Observer experience improves reproducibility of color Doppler sonography of orbital vessels. *J Clin Ultrsound* 2002; 30: 332–335.

18. Zhang X, Cole E, Pillar A, *et al.* The effect of change in intraocular pressure on choroidal structure in glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2017; 58: 3278–3285.

19. Xie J, Ye L, Chen Q, *et al.* Choroidal thickness and its association with age, axial length, and refractive error in Chinese adults. *Invest Ophthalmol Vis Sci* 2022; 63: 34.

20. Modrzejewska M, Siesky B, Amireskandari A, *et al.* Parameters characterizing age-dependent retrobulbar circulation in healthy subjects measured by color Doppler ultrasonography. *Curr Eye Res* 2015; 40: 729–736.

21. Duru N, Altinkaynak H, Erten Ş, *et al.* Thinning of choroidal thickness in patients with rheumatoid arthritis unrelated to disease activity. *Ocul Immunol Inflamm* 2016; 24: 246–253.

22. Akay F, Gundogan FC, Yolcu U, *et al.* Choroidal thickness in systemic arterial hypertension. *Eur J Ophthalmol* 2016; 26: 152–157.

23. Karalezli A, Eroglu FC, Kivanc T, *et al.* Evaluation of choroidal thickness using spectral-domain optical coherence tomography in patients with severe obstructive sleep apnea syndrome: a comparative study. *Int J Ophthalmol* 2014; 7: 1030–1034.

24. Xue W, Fan Z, Li L, *et al.* The chemokine system and its role in obesity. *J Cell Physiol* 2019; 234: 3336–3346.

25. Karti O, Nalbantoglu O, Abali S, *et al.* The assessment of peripapillary retinal nerve fiber layer and macular ganglion cell layer changes in obese children: a cross-sectional study using optical coherence tomography. *Int Ophthalmol* 2017; 37: 1031–1038.

26. Stapleton PA, James ME, Goodwill AG, *et al.* Obesity and vascular dysfunction. *Pathophysiology* 2008; 15: 79–89.

27. Mulhern M, Hulsmans F, Geijssen HC, *et al.* Resistivity indices in CDI of ocular vessels. *Ophthalmology* 1996; 103: 1333–1334.

28. Pérez-López M, Sales-Sanz M, Rebolleda G, *et al.* Retrobulbar ocular blood flow changes after orbital decompression in Graves' ophthalmopathy measured by Color Doppler imaging. *Invest Ophthalmol Vis Sci* 2011; 52; 5612–5617.

29. Askarizadeh F, Heirani M, Khorrami-Nejad M, *et al.* Is there any connection between choroidal thickness and obesity? *Ther Adv Ophthalmol* 2022;14: 25158414221100649.

30. Boillot A, Zoungas S, Mitchell P, *et al.* Obesity and the microvasculature: a systematic review and meta-analysis. *PLoS ONE* 2013; 8: e52708.

31. Doğan B, Erol MK, Doğan U, *et al.* The retinal nerve fiber layer, choroidal thickness, and central macular thickness in morbid obesity: an evaluation using spectral-domain optical coherence tomography. *Eur Rev Med Pharmacol Sci* 2016; 20: 886–891.

32. Dogan B, Dogan U, Erol MK, *et al.* Optical coherence tomography parameters in morbidly obese patients who underwent laparoscopic sleeve gastrectomy. *J Ophthalmol* 2016; 2016: 5302368.

33. Pang IH, Jonhson EC, Jıa L, *et al.* Evaluation of inducible nitric oxide synthase in glaucomatous optic neuropathy and pressure-induced optic nerve damage. *Invest Ophthalmol Vis Sci* 2005; 46; 1313–1321.

34. Baretella O, Chung SK, Barton M, *et al.* Obesity and heterozygous endothelial overexpression of prepro-endothelin-1 modulate responsiveness of mouse main and segmental renal arteries to vasoconstrictor agents. *Life Sci* 2014; 118: 206–212.

35. Stepp DW, Boesen EI, Sullivan JC, *et al.* Obesity augments vasoconstrictor reactivity to angiotensin II in the renal circulation of the Zucker rat. *Am J Physiol Heart Circ Physiol* 2007; 293: H2537–H2542.

36. Reiner A, Fitzgerald MEC, Del Mar N, *et al.* Neural control of choroidal blood flow. *Prog Retin Eye Res* 2018; 64: 96–130.

37. Khan S, Kirubarajan A, Lee M, *et al.* The correlation between body weight and intraocular pressure. *Aerosp Med Hum Perform* 2021; 92: 886–897.

38. Akinci A, Cetinkaya E, Aycan Z, *et al.* Relationship between intraocular pressure and obesity in children. *J Glaucoma* 2007; 16: 627–630.

39. Stojanov O, Stokić E, Sveljo O, *et al.* The influence of retrobulbar adipose tissue volume upon intraocular pressure in obesity. *Vojnosanit Pregl* 2013; 70: 469–476.

40. Gunes A, Uzun F, Karaca EE, *et al.* Evaluation of anterior segment parameters in obesity. *Korean J Ophthalmol* 2015; 29: 220–225.

41. Caballero M, Liton PB, Epstein DL, *et al.* Proteasome inhibition by chronic oxidative stress in human trabecular meshwork cells. *Biochem Biophys Res Commun* 2003; 308: 346–352.