ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Choroidal Vascularity Index Changes in Different Body Mass Index Groups: Case-Control Study

Farklı Beden Kitle İndeksi Gruplarında Koroid Vaskülarite İndeksi Değişiklikleri: Olgu Kontrol Çalışması

Taha SEZER[a], Abdülkadir KAYA[b], Kuddusi TEBERİK[a], Mehmet Tahir ESKİ[c]

[a]Department of Ophthalmology, Düzce University Faculty of Medicine, Düzce, Türkiye
[b]Department of Family Medicine, Düzce University Faculty of Medicine, Düzce, Türkiye
[c]Clinic of Ophthalmology, Erzincan Private Neon Hospital, Erzincan, Türkiye

ABSTRACT Objective: Comparing Choroidal Vascularity Index (CVI) values in groups with different body mass index (BMIs). **Material and Methods:** In this prospective study, we compared choroidal thickness (CT) and CVI values of those with different BMI. The weight and height of all patients were measured, and BMI was calculated. All volunteers were examined with a detailed eye examination. In addition, enhanced depth imaging optical coherence tomography (EDI-OCT) of all individuals was evaluated. **Results:** The study included 157 right eyes of 157 volunteers. Of these, 30 were normal, 30 were overweight, 30 were class 1 obese, 22 were class 2 obese, and 45 were morbidly obese. CVI and CT of all groups were compared with EDI-OCT. There was a statistically significant difference in CT between the groups in the temporal CT 500 µm, temporal CT 1,000 µm, temporal CT 1,500 µm, and nasal CT 500 µm regions ($p<0.005$). The CVI and luminal area/stromal area (LA/SA) groups also found a statistically significant difference ($p<0.005$). In the correlation analysis with BMI, a statistically significant weak negative correlation was found between BMI, CVI, and LA/SA ($r=-0.304$, $p<0.001$ and $r=-0.255$, $p=0.001$, respectively). In addition, a positive correlation was found between BMI in temporal CT 500 µm, temporal CT 1,000 µm and temporal CT 1,500 µm and nasal CT 1,000 µm and nasal CT 1,500 µm measurements. **Conclusion:** There is a negative correlation between BMI and CVI. In addition, a statistically significant difference was found between the morbidly obese group and the normal weight BMI groups regarding choroidal structures.

Keywords: Choroid; optic coherence tomography; obesity

ÖZET Amaç: Farklı beden kitle indeksine (BKİ) sahip bireylerde koroid vaskülarite indeksi (KVİ) değerlerinin karşılaştırılması. **Gereç ve Yöntemler:** Bu prospektif çalışmada, farklı BKİ'ye sahip kişilerin koroid kalınlığı (KK) ve KVİ değerlerini karşılaştırdık. Tüm hastaların kilo ve boyları ölçüldü ve BKİ hesaplandı. Tüm gönüllüler detaylı göz muayenesi ile muayene edildi. Ayrıca tüm bireylerin gelişmiş derinlik görüntülemeli optik koherens tomografisi [enhanced depth imaging optical coherence tomography (EDI-OCT)] değerlendirildi. **Bulgular:** Çalışmaya 157 gönüllünün 157 sağ gözü dâhil edildi. Bunların 30'u normal kilolu, 30'u fazla kilolu, 30'u 1. sınıf obez, 22'si 2. sınıf obez ve 45'i morbid obez idi. Tüm grupların KVİ ve KK'si EDI-OCT ile karşılaştırıldı. KK temporal 500, KK temporal 1.000, KK temporal 1.500 ve KK nazal 500 bölgelerinde gruplar arasında KK açısından istatistiksel olarak anlamlı fark vardı ($p<0,005$). Ayrıca KVİ ve "luminal area/stromal area (LA/SA)" açısından gruplar arasında istatistiksel olarak anlamlı fark bulundu ($p<0,005$). BKİ ile korelasyon analizinde BKİ, KVİ ve LA/SA arasında istatistiksel olarak anlamlı negatif zayıf korelasyon bulundu (sırasıyla $r=-0,304$, $p<0,001$ ve $r=-0,255$, $p=0,001$). Ayrıca BKİ ile KK temporal 500, KK temporal 1.000 ve KK temporal 1.500 ile KK nazal 1.000 ve KK nazal 1.500 ölçümleri arasında pozitif korelasyon bulundu. **Sonuç:** BKİ ve KVİ arasında negatif bir ilişki vardır. Ayrıca morbid obez grup ile normal kilolu BKİ grupları arasında koroid yapıları açısından istatistiksel olarak anlamlı fark bulundu.

Anahtar Kelimeler: Koroid; optik koherens tomografi; obezite

Obesity is a health problem that has been increasing in the last century.[1] It is known that the risk of cardiovascular diseases, hypertension, diabetes, dyslipidemia, and stroke increases with high weight.[2-4] As stated by the World Health Organization (WHO), 57.8% of the world's adult population will be considered overweight or obese by 2030.[5] In the United States, due to obesity causing health prob-

Correspondence: Taha SEZER
Department of Ophthalmology, Düzce University Faculty of Medicine, Düzce, Türkiye
E-mail: drtahasezer@gmail.com

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lems, 147 to 210 billion dollars are spent annually.[6] It is necessary to take urgent measures for this epidemic health problem, which has increased three times since 1975.

The ideal used method for diagnosing obesity is body mass index (BMI). It can be easily calculated by the patient's height and weight in the clinic. BMI 18.5 and below are classified as underweight, 18.5 and 24.9 are normal, 25 and 29.9 are overweight, and 30 and above are obese.[7] The higher the obesity class, the higher the comorbidity risk.[8]

In previous studies, the relationship between obesity and cataract, glaucoma, and age-related macular degeneration has been demonstrated.[9] In addition, previous studies evaluated the relationship between obesity and choroidal thickness (CT).[10,11] However, there are not many studies conducted with the Choroidal Vascularity Index (CVI), a new method for obese and overweight patients. It is crucial to evaluate the vascular problems of obese patients non-invasively and quickly in the clinic to take the necessary precautions in the early period. In clinical practice, we can quickly evaluate the choroid layer, which has the wealthiest vascular structure of the eye, with enhanced depth imaging optical coherence tomography (EDI-OCT). The total choroidal area (TCA), luminal area (LA), and stroma area can be calculated by binarizing EDI-OCT images using special software. In addition, CVI is calculated by dividing the lumen area by the TCA.[12] Today, CVI has been evaluated for many different diseases. Changes in the lumen area and CVI have been detected, especially in pathologies that may affect the vascular structure in these diseases.[13-15]

In this study, the choroidal structures of volunteers with different BMI were examined, and the differences between groups were investigated.

MATERIAL AND METHODS

One hundred fifty-seven individuals with different BMIs referred to the ophthalmology clinic by the obesity and family medicine clinics were included in the study (87 women and 70 men). The family physician (K.A) in the obesity policlinic measured the patient's height and weight. The groups were divided into 5 groups normal BMI, overweight BMI, and Stage 1, 2, 3 obese. Furthermore, the groups were created according to the WHO criteria [BMI 18.5-24.99 kg/m^2=normal weight (Group 1); 25.0-29.9 kg/m^2=overweight (Group 2), 30-34.99 kg/m^2=Stage 1 obese (Group 3), 35-39.99 kg/m^2=Stage 2 obese (Group 4) and >40 kg/m^2=Stage 3 obese (Group 5)]. For this study, necessary permissions were obtained from by Düzce University Non-Interventional Health Research Ethics Committee (date: December 20, 2021, no: 2021/240). In addition, in all study processes, the rules of the Declaration of Helsinki have been applied. The informed consent form was read by all individuals participating in the study and obtained their consent. The study did not include volunteers with all factors and diseases that could change the choroidal structure (e.g. smoking history, drugs).

OPHTHALMOLOGIC EXAMINATION

The same ophthalmologist performed a detailed eye examination of all groups (TK). Best-corrected visual acuity examination, fundoscopic evaluation after pupil dilation, anterior segment biomicroscopic examination were performed, and non-contact intraocular pressure was measured in all groups. Measures of axial length (AL) were conducted using an Echoscan US 500 system (Nidek Co. Ltd, Aichi, Japan).

Patients with refractive error three diopters and more, those who use eye drops continuously for any reason, those with media opacity problems due to cataract and corneal disease, and those with previously known retinal and choroidal pathology or surgery history were not included in the study.

CT MEASUREMENT

EDI-OCT images of all groups were taken by the same eye specialist (S.T) (Heidelberg Engineering, Heidelberg, Germany). A standard imaging protocol was applied to all patients. An average of 100 B scans per section were performed to obtain a 9 mm horizontal image from the center of the full fovea. These images improved the signal-to-noise ratio. The eye tracking feature was used. OCT images of volunteers were detected after pupil dilation. The hyperreflective line of the retinal pigment epithelium and the hy-

poreflective interface of the sclerochoroidal junction were used to define the CT. Measurements were performed in the center of the fovea and 7 different regions: 500 µm, 1,000 µm, and 1,500 µm nasal and temporal of the fovea. Due to CT and structure can be affected by daily changes, all images were taken before midday (9 a.m. to 11 a.m.). Two independent physicians performed measurements of CT (ST, TK.) The average of the 2 physician's measurements was used for analysis.

CHOROID VASCULARITY INDEX ASSESSMENT

The CVI was first calculated using the method modified by Agrawal et al., the Sonada technique.[12,16] First, the open-source ImageJ program (version 1.47; National Institutes of Health, Bethesda, MD, USA; http://imagej.nih.gov/ij/) was used to process images and detect TCA, LA, and stromal area (SA) areas. The same ophthalmologists processed and evaluated all images (ST, TK.)

The known distance to the ImageJ program was defined with a scale of 200 µm in the OCT image. Images were first converted to 8-bit image quality. Afterward, the 1500 µm area was marked with a special ruler between the RPE and the choroidoscleral junction, with the central fovea in the center (Figure 1). The image was transformed using the Niblack feature in the settings section. Again, the images converted to the TCA area and Niblack were combined using the ImageJ program. The red green blue image property was used to calculate the LA with the color threshold tool (Figure 2). In this way, image binarization was provided. Afterward, TCA and LA values were determined from the measurement settings and SA and CVI values were calculated.

STATISTICAL ANALYSIS

Sample size considering a similar study Type I error (0.05) was calculated considering the target power of 98%.[17] In the study, numerical data in descriptive statistics were given as mean and standard deviation. Categorical data were given as numbers and percentages. The distribution of numerical data was analyzed with Kolmogorov-Smirnov Z test. Analysis of numerical data between more than two independent

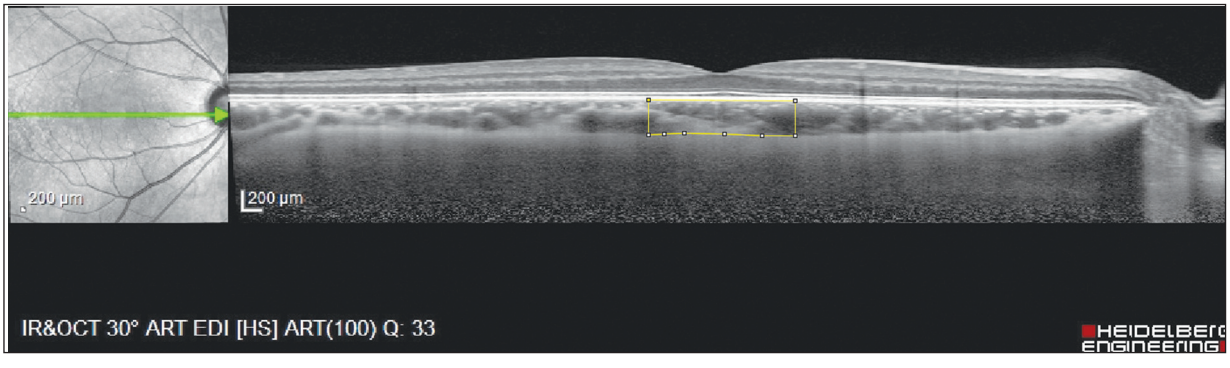

FIGURE 1: The manual plotting polygonal tool selected a width of 1.5 mm centered at the fovea.

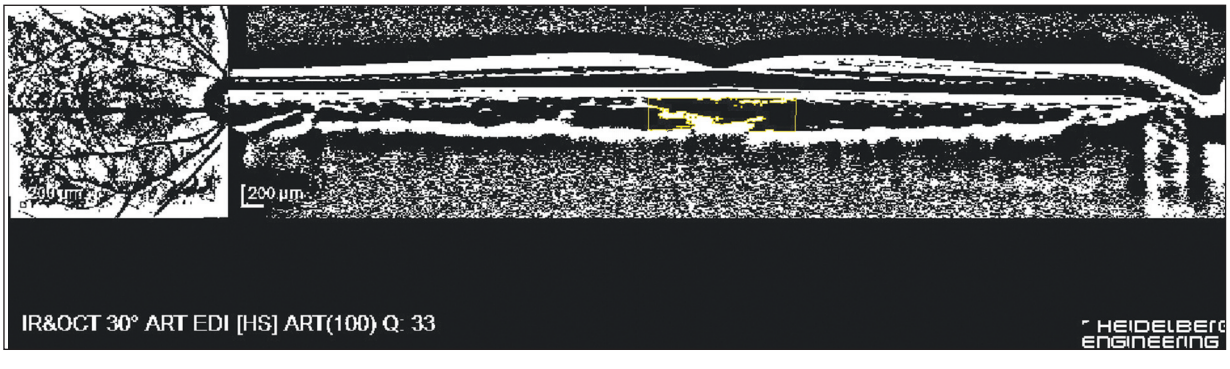

FIGURE 2: Superimposed binarized image showing segmentation of choroidal luminal and stromal structures.

groups was performed using the one-way ANOVA and Kruskal-Wallis tests. In addition, Tukey and Tamhane tests were used in intra-group post hoc analyses. P significance value was accepted as <0.05. SPSS V23.0 package program (SPSS Inc., IBM Corp., Chicago, IL) was used in the analysis.

RESULTS

One hundred fifty-seven right eyes of 157 volunteers participated in the study. Thirty volunteers were normal, 30 were overweight, 30 were 1st class obese, 22 were 2nd class obese, and 45 were morbidly obese. There was no significant difference between the groups in the mean age and mean AL measurements. Demographic and ocular parameters are shown in Table 1.

There was a statistically significant difference in CT between the groups in the CT temporal 500 µm, CT temporal 1,000 µm and CT temporal 1,500 µm, and CT nasal 500 µm region (p<0.005). In the post hoc Tukey analysis at CT temporal 500 µm, no significant difference was detected within the group. In post hoc Tukey analysis at CT temporal 1,000 µm and CT temporal 1,500 µm, the BMI 25-29.9 group was significantly lower than those in the BMI over 40 groups. There was no significant difference within the group in the measurements of CT nasal 500 µm, CT nasal 1,000 µm, and CT nasal 1,500 µm. A statistically significant difference was found between CVI and LA/SA groups (p<0.005) (Table 2). In the CVI post hoc Tamhane analysis, the BMI of group 5

TABLE 1: Demographic and clinical features of BMI groups.

	BMI 18-24.9 (n=30)	BMI 25-29.9 (n=30)	BMI 30-34.9 (n=30)	BMI 35-39.9 (n=22)	BMI over 40 (n=45)
Female n (%)	19 (21.8%)	12 (13.8%)	16 (18.4%)	10 (11.5%)	30 (34.5%)
Male n (%)	11 (15.7%)	18 (25.7%)	14 (20.0%)	12 (17.1%)	15 (21.4%)
Age±SD	35.70±16.48	37.57±12.59	44.57±13.21	37.50±12.22	36.78±11.32
(Range)	(19-81)	(20-71)	(21-70)	(14-53)	(16-63)
AL±SD	22.74±1.21	22.80±1.08	22.89±1.23	23.23±0.84	22.92±0.90
(Range)	(21.24-25.43)	(21.01-25.01)	(21.24-25.76)	(21.89-25.65)	(21.33-25.16)
Height±SD	165.97±9.12	169.10±9.50	165.70±8.92	168.73±8.91	164.62±9.07
(Range)	(147-185)	(151-186)	(150-185)	(155-183)	(147-186)
Weight±SD	61.32±8.82	73.76±9.33	88.73±11.92	108.50±10.07	131.08±16.43
(Range)	(49-83)	(57-95)	(70-118)	(90-125)	(103-188)
BMI±SD	22.18±1.92	25.71±1.37	32.15±1.54	38.08±1.51	48.46±5.65
(Range)	(18.73-27.70)	(22.77-28-39)	(30.06-34.85)	(33.52-39.90)	(41.26-66.61)

BMI: Body mass index; SD: Standard deviation; AL: Axial length.

TABLE 2: The mean CT measurements and TCA, LA, SA, CVI and LA/SA values of different BMI groups.

	BMI 18-24.9 (n=30)	BMI 25-29.9 (n=30)	BMI 30-34.9 (n=30)	BMI 35-39.9 (n=22)	BMI over 40 (n=45)	p value*
SCT	308.00±74.87	303.50±73.81	313.23±60.34	326.09±57.73	328.78±78.07	0.518
T500	289.60±72.71	283.63±66.18	300.63±48.71	332.23±61.00	325.47±77.29	0.018
T1000	284.90±62.26	273.00±64.44	285.80±50.89	320.59±58.77	320.53±76.14	0.006
T1500	276.07±65.30	256.93±59.84	284.13±50.86	317.09±49.79	310.22±72.96	0.001
N500	272.13±65.23	283.63±79.93	283.03±54.36	317.32±53.83	315.07±83.75	0.036
N1000	266.00±67.34	274.27±79.80	277.67±57.16	302.50±59.54	302.93±83.27	0.135
N1500	259.53±65.62	265.53±77.82	262.93±54.74	287.32±47.80	284.27±82.04	0.381
TCA	0.73±0.22	0.74±0.21	0.73±0.19	0.72±0.20	0.72±0.18	0.997
LA	0.48±0.14	0.48±0.14	0.46±0.13	0.45±0.12	0.44±0.11	0.632
SA	0.25±0.08	0.25±0.08	0.26±0.07	0.27±0.08	0.27±0.08	0.659
CVI	0.66±0.05	0.65±0.05	0.63±0.05	0.62±0.04	0.61±0.05	0.001
LA/SA	2.03±0.46	1.92±0.47	1.80±0.41	1.71±0.28	1.66±0.40	0.006

*p values calculated with one-way ANOVA and Kruskal-Wallis tests; CT: Choroidal thickness; TCA: Total choroidal area; LA: Luminal area; SA: Stromal area; CVI: Choroidal Vascularity Index; BMI: Body mass index; SCT: Subfoveal choroidal thickness; CT nasal 500 µm (N500), CT temporal 500 µm (T500), CT nasal 1,000 µm (N1000) and CT temporal 1,000 µm (T1000) in the groups, CT nasal 1,500 µm (N1500), CT temporal 1,500 µm (T1500).

TABLE 3: Correlation between BMI and all parameters.

BMI	r value	p value
Axial length	0.059	0.461
SCT	0.122	0.128
T500	0.226	0.004
T1000	0.238	0.003
T1500	0.256	0.001
N500	0.209	0.009
N1000	0.184	0.021
N1500	0.137	0.087
TCA	-0.027	0.740
LA	-0.120	0.134
SA	0.079	0.324
CVI	-0.304	<0.001
LA/SA	-0.255	0.001

r: Correlation coefficient; BMI: Body mass index; SCT: Subfoveal choroidal thickness; CT nasal 500 µm (N500), CT temporal 500 µm (T500), CT nasal 1,000 µm (N1000) and CT temporal 1,000 µm (T1000) in the groups, CT nasal 1,500 µm (N1500), CT temporal 1,500 µm (T1500); TCA: Total choroidal area; LA: Luminal area; SA: Stromal area; CVI: Choroidal Vascularity Index.

was lower than Group 1 and Group 2. On the other hand, LA/SA was also found to be significantly higher than Group 1, Group 4, and Group 5.

In the correlation analysis with BMI, a statistically significant weak negative correlation was found between BMI, CVI, and LA/SA (r=-0.304, p<0.001 and r=0.255, p=0.001 respectively). In addition, a weak positive correlation was found between BMI in CT temporal 500 µm, CT temporal 1,000 µm and CT temporal 1,500 µm and CT nasal 1,000 µm and CT nasal 1,500 µm measurements (Table 3).

DISCUSSION

This study evaluated five different BMI groups regarding CVI and CT for the first time. CT and CVI of 5 different BMI groups were evaluated in the study conducted on 157 volunteers. There was a statistically significant difference between the groups in the CT temporal 500 µm, CT temporal 1,000 µm and CT temporal 1,500 µm, and CT nasal 500 µm regions between the groups (p<0.005). In the CT temporal 1,000 µm region, Group 1 was significantly lower than Group 5. At the same time, in the CT temporal 1,500 µm region, Group 1 was significantly lower than in Group 4 and Group 5.

CT is a parameter that is affected by many drugs and diseases. Many studies have shown that drugs, inflammatory diseases, and central serous chorioretinopathy cause changes in CT.[18,19] Moreover, CT changes depending on age and AL.[20] Öncül et al., comparing 5 different BMI groups, found thinner CT in 5 choroid regions in the morbidly obese group (p<0.001).[17] On the other hand, Teberik et al. compared 101 morbidly obese volunteers and 95 healthy volunteers. In this study, it was found that the CT in the obese patient group was significantly thinner than the group with normal weight BMI, except for temporal 1500 mm (p<0.05).[21] They stated that the sympathetic and parasympathetic regulation that regulates the choroidal vascular structure might be caused by the deterioration of the nitric oxide and noradrenaline balance in obese groups. Unlike these studies, Yumusak et al. compared CT scans of 72 female volunteers with a BMI of 30 and above and 68 female patients with a BMI of 25 and below, CT was found to be thicker in the obese group in all regions. Significant thickening was detected, especially in CT foveal, CT nasal 500 µm, and CT nasal 1,000 µm (p<0.05).[22] Likewise, with this study, the baseline CT of morbidly obese patients who will receive bariatric surgery and diet therapy due to morbid obesity was found to be thicker, although it was not statistically significant (p=0.91).[23] Another remarkable point in this study is that the CT was thicker in the obese group. However, it was not statistically significant, while the CVI was lower. However, we could not find clear pathophysiology to explain why CVI decreases as CT increases. However, it is seen that the data we obtained in our study are compatible with this study. In another study, Gonul et al. compared the preoperative CT of 40 morbidly obese patients who underwent bariatric surgery for morbid obesity with the CT of the normal weight control group and found that the CT was thicker in the morbidly obese group. Especially foveal, CT nasal 500 µm and CT temporal 500 µm regions were statistically significant (p<0.05). In these studies, obese individuals stated that CT might increase due to increased venous congestion.[24] The variability of CT in different studies may be caused by many conditions. The different results in all these studies may be the sample size, the different BMIs of the groups compared, and the age and demographic characteristics of the groups. For

this reason, we think that the choroid vascularity index, defined by Sonoda et al. and modified by Agrawal et al., is a more reliable parameter of the choroidal structure.[12,16] There may be deficiencies in evaluating a rich vascular structure, such as the choroid with only the CT. For this purpose, we evaluated the CVIs of groups with different BMIs in this study.

In our study, a significant difference was found between the groups in CVI. In the post hoc Tamhane analysis between the groups, it was found that the Stage 3 obese group was significantly lower CVI than Group 1 and Group 2. Additionally, the LA/SA ratio was significantly higher in Group 1 than in Stage 2 and Stage 3 obese groups. We could not find a study that would include all groups, especially the morbid obesity group, and compare the CVI. In a study comparing the Stage 1 obese group with underweight BMI, normal weight BMI groups, and overweight BMI group, Temel et al. found a significant decrease in CVI, TCA, and LA in Stage 1 obese group compared to the overweight BMI group. At the same time, it was determined that the mean CVI values of the overweight BMI group and Stage 1 obese group were significantly decreased compared to the underweight BMI group and normal weight group.[25] Although the group with underweight BMI was included in the study, unlike our study, we think that the exclusion of the clinically Stage 2 and Stage 3 obese groups, which is the morbidly obese class, is a crucial shortcoming compared to our study. For this reason, we have included the Stage 2 and Stage 3 obese groups in our study, unlike the previous study.

This study detected a statistically significant negative correlation between BMI and CVI. In addition, we found that this decrease was statistically significant compared to Stage 3 and Stage 2 obese groups and Group 1. A statistically significant negative correlation was also detected in the LA/SA ratio in the study. However, no statistically significant correlation was found with BMI in TCA, LA, and SA values. When the LA/TCA and LA/SA ratios are examined, it is seen that LA significantly decreases compared to SA. Therefore, it can be said that the vascular area decreases with weight gain. This suggests that these findings are compatible with the pathophysiology of morbidly obese patients with cardiovascular diseases and perfusion disorders. However, a study with more volunteers and evaluating all disease data is needed for CVI to be used as a cardiovascular marker, especially in morbidly obese patients.

This study has some limitations. First of all, different hormonal and systemic factors in obese individuals were not evaluated in the study. The study did not evaluate diseases such as obstructive apnea syndrome and obesity hypoventilation syndrome, often seen in severely obese individuals. As it is known from previous studies on CT, manual measurement of CT is another limitation of the study. Another limitation is that obesity, which is an increasing health problem all over the world, should be evaluated with more volunteers. So more studies and data are needed on this subject.

CONCLUSION

In conclusion, this study shows a negative correlation between CT, CVI, and BMI. More studies are needed to use CVI as a clinical indicator for systemic diseases, especially in morbidly obese individuals.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Taha Sezer, Abdülkadir Kaya, MehmetTahir Eski;* ***Design:*** *Taha Sezer, Kuddusi Teberik;* ***Control/Supervision:*** *Taha Sezer, Kuddusi Teberik;* ***Data Collection and/or Processing:*** *Abdülkadir Kaya, Taha Sezer;* ***Analysis and/or Interpretation:*** *Abdülkadir Kaya, Mehmet Tahir Eski;* ***Literature Review:*** *Taha Sezer, Abdülkadir Kaya;* ***Writing the Article:*** *Taha Sezer, Abdülkadir Kaya, Kuddusi Teberik;* ***Critical Review:*** *Taha Sezer, Mehmet Tahir Eski;* ***References and Fundings:*** *Abdülkadir Kaya;* ***Materials:*** *Taha Sezeri Abdülkadir Kaya.*

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