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Original Article

Evaluation of Thyroid Volume in Metabolically Healthy and Unhealthy Obese Patients

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ABSTRACT

Objective: It is known that insulin resistance increases thyroid volume. In our study, we looked at whether thyroid volume differed between metabolically healthy obese and metabolically unhealthy obese patients, along with the relationship between thyroid volume and metabolic syndrome parameters.

Methods: Metabolic syndrome diagnostic criteria were investigated in 116 obese female patients. Two groups were formed such as metabolically healthy obese and metabolically unhealthy obese. Biochemical parameters, thyroid volumes, and carotid intima-media thickness were measured. In addition, the patients were evaluated by grouping them into 2 according to the thyroid volume median value.

Results: When metabolically healthy obese and metabolically unhealthy obese groups were compared, in addition to the metabolic syndrome criteria; a statistically significance difference was realized between thyroid volume ($P < .001$), carotid intima-media thickness ($P = .009$), waist–hip ratio ($P < .001$), insulin resistance-homeostasis model ($P < .001$), insulin ($P < .001$) values. When the patients are divided into 2 according to the thyroid volume there was a statistically significant difference between the 2 groups in terms of body mass index ($P = .004$), weight ($P = .044$), waist circumference ($P = .004$), carotid intima-media thickness ($P = .032$), uric acid ($P = .006$), insulin ($P = .043$), insulin resistance-homeostasis model ($P = .041$), and low-density lipoprotein cholesterol ($P = .043$). In the correlation test with thyroid volume, a significant correlation was found between the presence of metabolic syndrome, the number of metabolic syndrome criteria, systolic and diastolic arterial blood pressure, carotid intima-media thickness, and uric acid.

Conclusion: The statistically significant relationship between thyroid volume and metabolic syndrome parameters indicates that increased thyroid volume in obese people may be a sign of metabolic syndrome and metabolic syndrome-related increased cardiovascular risk.

Keywords: Thyroid gland, cardiovascular disease, metabolic syndrome, obesity, carotid intima-media thickness

INTRODUCTION

Obesity is common worldwide; it is an epidemic disease that causes an increase in the incidence of especially type 2 diabetes, atherosclerotic cardiovascular pathologies, malignancies, and hypertension (HT). The frequency of metabolic syndrome (MS) also increases with obesity.[2]

Metabolic syndrome is an endocrinopathy with high morbidity and mortality, in which systemic disorders such as visceral obesity, carbohydrate metabolism disorders [glucose intolerance and diabetes mellitus (DM)], hyperlipidemia, hypertension, and cardiovascular disease (CVD) are combined with insulin resistance.[1] Studies have shown that there is a difference between obese patients with similar body mass indexes in terms of the risk of causing DM and CVD, and that some obese patients are either protected from or more resistant to obesity-related morbidities, particularly MS.[2] Although these individuals have more body fat than normal; it was observed that cardiometabolic factors such as insulin resistance, dyslipidemia rates, arterial tension, and inflammatory markers were less than expected or not impaired in some patients, and they were evaluated as metabolically healthy obese (MHO)

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individuals. Different MS diagnostic criteria are used in the literature to define metabolically healthy or non-healthy (MNHO) obese individuals.[3] Insulin resistance, the leading cause of MS, has been linked to increased thyroid volume (TV) and nodule prevalence.[3-7] With the increase in insulin levels, insulin-like growth factor-1 (IGF-1) binding protein levels decrease and free IGF-1 levels increase.[3-7] It has been shown that increased free IGF-1 levels as a result of hyperinsulinemia may pave the way for TV increase, nodule development and differentiation.[7] Thyroid hormones also influence energy homeostasis, adipose tissue, lipid and carbohydrate metabolism, and arterial pressure.[8] Because of these effects, it has been presumed that thyroid functional changes may be linked to MS and its components.[9]

Considering the possible effects of MS and insulin resistance on TV, as well as the effects of thyroid hormones on energy metabolism, it has been hypothesized that there may be a difference in thyroid hormone profile and TV in individuals with MHO and MNHO.[4,6,10] In our study, it was aimed to investigate whether there is a difference between MHO and MNHO patient groups in terms of TV and the relationship between TV and MS criteria.

METHODS

Patients and Assessments

Ethics committee approval was received for this study from the local ethics committee of Erzincan Binali Yıldırım University (Date: March 28, 2017, Number: 03/06). A total of 116 obese female patients were included in our study. Those with known DM, HT, hyperlipidemia, thyroid pathology, and CVD were excluded. Metabolic syndrome diagnosis criteria were investigated in patients and MHO and MNHO groups were formed according to the presence of MS. The patients' consent was obtained before the study began. Body mass index (BMI) was calculated by making height, weight, and anthropometric measurements of the patients. After resting for 10 minutes, blood pressure measurements were made twice and the average of the values was recorded.

MAIN POINTS

- Insulin resistance increases thyroid volume (TV).
- A significant relationship was found between the presence of metabolic syndrome (MS) and the number of MS criteria and TV.
- A higher TV may be a sign of MS in obese individuals.
- Cheap and practically measurable TV can guide this patient selection for closer patient follow-up and more aggressive treatment modalities.

History of active smoking and the history of early coronary artery disease in first-degree relatives under 55 years of age for men and 65 years of age for women were questioned and recorded.

The diagnosis of MS was made according to the National Cholesterol Education Program-Adult Treatment Panel III criteria.[2] However, the reference values for central obesity of the Turkish Society of Endocrinology and Metabolism were used for waist circumference (≥100 cm in men, ≥90 cm in women). Accordingly, high waist circumference, serum triglyceride (TG) level (≥150 mg/dL), blood pressure (≥130/85 mmHg), serum fasting glucose level (≥100 mg/dL), and low serum high-density lipoprotein (HDL)-C level (<40 mg/dL in men, <50 mg/dL in women) were considered as MS who were positive for 3 or more criteria. Based on the MS criteria, patients were divided into 2 groups: MHO and MNHO.

Those with a glycosylated hemoglobin (HbA1C) value of 6.5% and above were accepted as newly diagnosed diabetes.

The insulin resistance-homeostasis model (HOMA-IR) of the patients was calculated using the following formula: HOMA-IR = (fasting plasma insulin (mU/mL) × fasting plasma glucose (mg/dL))/405. A HOMA-IR value of 2.7 above was considered as insulin resistance.

Assessment of the Thyroid Volume and Thyroid Nodules

Measurements were made with an SIUI/CZ XL-43B (Shantou Institute of Ultrasonic Instruments Co., Ltd., Guangdong, China) model device, and each lobe was measured in 3D with a high-resolution linear probe (8 MHz) in B mode. For each lobe, craniocaudal, mediolateral, and anteroposterior lengths were measured, and right and left lobe volumes were obtained using the ovoid formula (width × depth × length × Π/6). All solitary lesions in the thyroid gland larger than 0.3 cm, other than the normal shape or echo characteristics, were considered nodules.

Assessment of Carotid Intima-Media Thickness

During TV measurements, common carotid artery longitudinal imaging in B mode was performed by ultrasonography and 2 parallel lines between the lumen-intima and media-adventitia were measured to obtain 2 parameters of the right and left carotid intima-media. The mean of both carotid intima-media thickness (CIMT) was used in the evaluation.

Biochemical Measurements

Serum uric acid, glucose (Spectrophotometric analysis, LH 2000 analyzer with Beckman Coulter Inc. kits, Lismeehan, O'Callaghan's Mills Ireland); HbA1c (high-performance liquid chromatography, Adams A1c HA-8160, Arkray

Japan); total cholesterol, HDL cholesterol, and plasma TGs (Oxidation-based technique, Beckman Coulter AU 2700 plus, Mishima, Japan); thyroid stimulating hormone (TSH) (Chemiluminescence study, UniCel DXi 800 immunoassay system, Beckman Coulter, Fullerton CA, USA); insulin, free T3, free T4 measurements (Chemiluminescence method, Siemens ADVIA Centaur XP immunoassay, Germany) were measured in the central laboratory of our hospital after at least 10 hours of fasting in the morning.

Statistical Analysis

IBM Statistical Package for the Social Sciences version 20 (IBM SPSS Corp., Armonk, NY, USA) was used for all statistical analyses. For each variable, descriptive statistics were calculated. The Kolmogorov–Smirnov test was used to determine the distribution of the variables. The mean and SD of normally distributed data were calculated. For variables that did not have a normal distribution, median and interquartile range values were used. The Student's *t*-test was used to compare data with a normal distribution, while the Mann–Whitney *U*-test was used to compare continuous variables without a normal distribution. For categorical variables, the chi-square test was used to determine statistically significant differences between groups. The Spearman's rho method was used to investigate the relationships between the variables for data that were not normally distributed. A *P*-value less than .05 was considered significant.

RESULTS

The mean age of 116 obese female patients included in our study was 37.2 ± 7.9 years. The mean BMI of the patients was calculated as 35.0 ± 4.5 kg/m^2. 57.76% of the patients were recorded as stage 1, 26.72% as stage 2, and 15.52% as stage 3 obese. The mean TV of the patients was 13.71 ± 6.90 mL. The mean CIMT of the patients was calculated as 0.48 ± 0.10 mm. Thyroid nodules were present in 12.93% of the patients. 19.83% of the patients were active smokers. According to the history of the patients participating in the study, 37% had a family history of early coronary artery disease.

Table 1 shows the clinical, demographic, and laboratory characteristics of the study groups. When MHO and MNHO groups are compared; in addition to the MS criteria (waist circumference, systolic and diastolic blood pressure, arterial, fasting glucose, HDL cholesterol, and TG) which naturally expected a significant difference; a statistically significant difference was found between TV, CIMT, waist–hip ratio, HOMA-IR, and insulin values. There was no statistically significant difference between age, height, weight, BMI, hip circumference, HbA1c, uric acid, total cholesterol, LDL cholesterol, creatinine, and TSH values.

When the patients are divided into 2 groups such as patients with low and high TV according to the median value of the TV as presented in Table 2, there was no significant difference between the 2 groups in terms of age, height, hip circumference, waist–hip ratio, systolic and diastolic blood pressure, arterial, fasting glucose, HbA1c, total cholesterol, HDL cholesterol, TG, creatinine, and TSH parameters. However, in terms of BMI, weight, waist circumference, CIMT, uric acid, insulin, HOMA-IR, and LDL cholesterol, a statistically significant difference was found between the 2 groups.

As shown in Table 3, when the patient groups with and without thyroid nodules were compared, there was a significant difference in terms of age and CIMT values and no statistically significant difference between the 2 groups in terms of other parameters.

In the correlation test performed to determine the parameters related to the TV, the presence of MS ($r = .311$, $P = .001$), the number of MS criteria ($r = .313$, $P = .001$), systolic arterial blood pressure ($r = .206$, $P = .026$), diastolic arterial blood pressure ($r = .192$, $P = .039$), CIMT ($r = .308$, $P = .001$), and uric acid ($r = .202$, $P = .003$) values were significantly correlated (weak to moderate positive correlation). Table 4 shows the correlation coefficient and *P* significance value of the parameters that were found to be significantly correlated with TV.

When the patients with a family history of early CVD and active smokers were evaluated separately, no statistically significant difference was found in terms of TV.

DISCUSSION

It is important to evaluate obese individuals in terms of MS, as the risk of CVD increases in MS.[1,11] In obesity; it is important to choose patients who will be treated more conservatively because they do not have MS criteria and patients who will be treated more aggressively because they are metabolically unhealthy. It has also been shown that MS and its components are linked to thyroid gland functional changes.[4,6,9,10]

Therefore, we aimed to evaluate the usability of TV, which can be evaluated non-invasively, cheaply, easily, and practically, in the differentiation of metabolically healthy and unhealthy obese patients.

There are 3 important findings of our study. First, a significant difference was found between the groups formed by MHO and MNHO individuals in terms of TV. Second, TV was found to be associated with the following parameters; MS criteria number, uric acid, insulin value, HOMA-IR index, LDL cholesterol, and BMI. Third, a statistically

Table 1. Demographic, Clinical, and Laboratory Data of Patients in Metabolically Healthy and Non-healthy Obese Patient Groups

Parameters	Group 1 (Metabolically Healthy), n = 64	Group 2 (Metabolically Non-healthy), n = 52	*P*
Age (years)**	36.6 ± 7.4	37.9 ± 8.5	.387
Height (cm)**	159.8 ± 6.6	159.3 ± 5.6	.706
Weight (kg)*	85.0 (79.0-95.5)	88.5 (80.0-100.0)	.380
Body mass index (kg/m^2)*	33.9 (31.0-36.7)	34.9 (31.6-37.7)	.202
Waist circumference (cm)**	104.5 ± 10.8	110.0 ± 9.9	**.006**
Hip circumference (cm)**	120.6 ± 9.5	120.1 ± 12.4	.812
Waist/hip ratio**	0.87 ± 0.06	0.92 ± 0.08	**<.001**
Systolic blood pressure arterial (mmHg)*	110 (100-120)	120 (100-140)	**.006**
Diastolic blood pressure arterial (mmHg)*	70 (60-80)	80 (70-90)	**.003**
Thyroid volume (mL)*	11.73 (9.36-14.05)	14.16 (11.12-19.04)	**.001**
Carotid intima-media thickness (mm)*	0.45 (0.40-0.50)	0.50 (0.40-0.60)	**.009**
Glucose (mg/dL)*	91.0 (85.3-95.8)	99.0 (90.0-104.0)	**<.001**
HbA1c (%)*	5.4 (5.2-5.7)	5.5 (5.3-5.8)	.172
Uric acid (mg/dL)**	4.4 (3.9-5.3)	4.5 (3.9-5.3)	.324
Total cholesterol (mg/dL)**	189.5 ± 33.2	191.2 ± 45.0	.811
HDL cholesterol (mg/dL)*	52.5 (47.0-60.0)	44.0 (39.0-53.5)	**.001**
Triglyceride (mg/dL)*	101.0 (83.3-131.8)	165.0 (125.5-223.0)	**<.001**
LDL cholesterol (mg/dL)**	113.4 ± 30.1	107.5 ± 33.2	.317
Insulin (mU/mL)*	10.6 (7.2-17.0)	17.3 (12.6-25.4)	**<.001**
HOMA-IR*	2.4 (1.5-3.8)	4.1 (3.0-5.8)	**<.001**
Creatinine (mg/dL)*	0.8 (0.7-0.8)	0.8 (0.7-0.9)	.236
TSH (μU/mL)*	1.9 (1.4-2.9)	1.9 (1.3-2.4)	.403

Criteria used in the diagnosis of metabolic syndrome.
*Mann–Whitney *U*-test [median (Q1-Q3)].
***t*-Test (mean ± SD).
HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, insulin resistance-homeostasis model evaluation; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

significant relationship was found between TV and CIMT, a predictor of CVD.

in the last decades, many studies have been published suggesting that MS and/or insulin resistance are linked to functional and morphological changes in the thyroid.[4,6,10] Several explanations for the interaction of MS and thyroid morphology have been proposed.[7,12,13]

The most important point of view to explain these reasons is the relationship between hyperinsulinemia/insulin resistance and thyroid morphological changes, and previous studies have shown the presence of insulin-like growth factor-1 (IGF-1R) and insulin receptors (IRs) in human thyroid tissue.[13] TSH is the main regulator of thyroid cell proliferation and positively regulates IR expression via cAMP and additionally increases IR and IGF-1R autophosphorylation. In human thyrocyte cultures, IR induction by TSH has been shown to allow the proliferative activity of TSH at physiological concentrations of insulin. In human thyroid cells, IGF-1 is required for the mitogenic activity of TSH or epidermal growth factor (EGF), but alone is not a stimulator of proliferation.[13] A study by Malaguarnera et al[12] shows that insulin receptor isoforms, IGF-1 receptor, IGF-1, and IGF-2 are highly expressed in thyroid follicular cell precursors and decreased in differentiated cells. In addition, it is known that increasing insulin levels cause an increase in free IGF-1 levels by decreasing IGF-1 binding protein levels, and it is suggested that increased free

Table 2. Demographic, Clinical, and Laboratory Data of Patients in Low and High Thyroid Volume Patient Groups

Parameters	Group 1 (Thyroid Volume < 12.27 cm^3), n = 58	Group 2 (Thyroid Volume ≥ 12.27 cm^3), n = 58	*P*
Age (years)**	37.1 ± 7.4	37.3 ± 8.4	.879
Height (cm)*	160 (155-164)	160 (155-165)	.938
Weight (kg)*	84.5 (77.8-94.0)	88.5 (81.0-100.3)	**.044**
Body mass index (kg/m^2)*	32.9 (30.6-36.1)	35.4 (32.0-37.8)	**.004**
Waist circumference (cm)**	104.9 ± 10.7	109.1 ± 10.5	**.038**
Hip circumference (cm)**	118.7 ± 10.6	122.0 ± 10.9	.104
Waist/hip ratio**	0.89 ± 0.07	0.90 ± 0.08	.453
Systolic blood pressure arterial (mmHg)*	110 (100-120)	115 (100-136)	.224
Diastolic blood pressure arterial (mmHg)*	70 (67-80)	70 (70-85)	.183
Carotid intima-media thickness (mm)*	0.45 (0.40-0.50)	0.50 (0.40-0.60)	**.032**
Glucose (mg/dL)*	92 (86-98)	94 (89-103)	.098
HbA1c (%)*	5.5 (5.2-5.6)	5.5 (5.3-5.7)	.278
Uric acid (mg/dL)**	4.7 ± 0.8	5.7 ± 0.9	**.006**
Cholesterol (mg/dL)**	195.6 ± 39.7	184.9 ± 37.5	.140
HDL cholesterol (mg/dL)**	50.8 ± 10.3	50.3 ± 12.5	.827
Triglyceride (mg/dL)*	121.0 (95.8-165.8)	132.0 (86.8-179.3)	.871
LDL cholesterol (mg/dL)**	116.6 ± 34.4	104.8 ± 27.5	**.043**
Insulin (mU/mL)*	12.3 (7.4-17.7)	15.5 (10.3-22.9)	**.035**
HOMA-IR*	2.8 (1.6-4.2)	3.5 (2.3-4.9)	**.041**
Creatinine (mg/dL)*	0.8 (0.7-0.8)	0.8 (0.7-0.9)	.866
TSH (μU/mL)*	1.9 (1.4-2.6)	1.9 (1.3-2.7)	.365

*Mann–Whitney *U*-test [median (Q1-Q3)].
**t*-Test (mean ± SD).
HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, insulin resistance-homeostasis model evaluation; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone;.

IGF-1 levels as a result of hyperinsulinemia may predispose to TV increase, nodule development, and differentiation.[7]

In addition, studies have suggested that some hormonal or humoral mediators originating from adipose tissue stimulate the hypothalamus–pituitary–thyroid axis and increase TSH secretion.[14,15] The main suspected mechanism is the relationship between leptin and thyroid hormones.[14,15] Leptin secretion increases sharply with enhancing fat mass, and insulin raises total leptin levels as well.[14,15] It is thought that leptin modulates TRH gene expression in the paraventricular nucleus of the hypothalamus and may increase TSH levels by stimulating TRH.[14,15] In adipose tissue, TSH has been shown to induce differentiation and adipogenesis from preadipocytes to adipocytes via TSH receptors. TSH also directly induces the synthesis and release of adipokines from adipose tissue.[14,15] In conclusion, the positive relationship between TSH and adipose tissue is thought to be important in terms of TV. Thus, insulin resistance together with increased fat mass in MS may contribute to TSH increase by affecting serum leptin concentrations. It has also been reported that increased cytokines in the circulation due to MS may suppress thyroid function at the hypothalamic, pituitary, or thyroid level.[14,15]

Rezzenico et al[6] showed that increased insulin levels stimulate thyroid proliferation and that the TV and prevalence of thyroid nodules increase in individuals with insulin resistance. In another study, IR overexpression was shown in the early stage of thyroid carcinogenesis.[16] In the study of Aytürk et al.[4] an increase in TV was found in euthyroid patients with MS. In our study, a statistically significant difference was found between MHO and MNHO patient groups in terms of TV, which is consistent with the literature. As in a study conducted by Kır et al.[10] we also found that there was a significant correlation between the number of metabolic syndrome criteria present in patients and TV.

Table 3. Demographic, Clinical, and Laboratory Data of the Patients in the Patient Groups With and Without Nodules

Parameters	Group 1 (Non-nodule), n = 101	Group 2 (With Nodule), n = 15	*P*
Age (years)*	37 (30-42)	41 (37-50)	**.014**
Waist circumference (cm)**	107.3 ± 11.1	105.1 ± 7.5	.475
Hip circumference (cm)**	120.8 ± 11.1	117.5 ± 8.8	.284
Waist/hip ratio*	0.89 (0.84-0.93)	0.89 (0.85-0.95)	.687
Systolic blood pressure arterial (mmHg)*	110 (100-130)	120 (90-140)	.505
Diastolic blood pressure arterial (mmHg)*	70 (70-80)	70 (70-95)	.149
Carotid intima-media thickness (mm)*	0.45 (0.40-0.53)	0.55 (0.50-0.60)	**.040**
Glucose (mg/dL)*	93.0 (86.5-99.5)	94.0 (91.0-99.0)	.422
HbA1c (%)*	5.5 (5.2-5.7)	5.6 (5.4-5.7)	.133
Uric acid (mg/dL)**	5.0 ± 0.8	4.8 ± 1.2	.528
Cholesterol (mg/dL)**	188.1 ± 37.1	204.5 ± 47.7	.127
HDL cholesterol (mg/dL)**	50.3 ± 11.1	52.1 ± 13.4	.569
Triglyceride (mg/dL)*	128 (89-165)	173 (99-217)	.152
LDL cholesterol (mg/dL)**	110.1 ± 32.1	115.1 ± 28.2	.558
Insulin (mU/mL)*	13.4 (8.4-20.2)	13.5 (9.1-17.1)	.554
HOMA-IR*	3.0 (2.1-4.8)	3.3 (2.1-4.2)	.720
Creatinine (mg/dL)*	0.8 (0.7-0.8)	0.8 (0.7-0.9)	.218

*Mann–Whitney *U*-test [median (Q1-Q3)].
***t*-Test (mean ± SD).
HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, insulin resistance-homeostasis model evaluation; LDL, low-density lipoprotein.

Table 4. Parameters With Significant Correlation With Thyroid Volume

Parameters	Correlation Coefficient (*rs*)	*P*
MS by NCEP-ATP III criteria	0.311	**.001**
Number of metabolic syndrome criteria	0.313	**.001**
Systolic blood pressure arterial (mmHg)	0.206	**.026**
Diastolic blood pressure arterial (mmHg)	0.192	**.039**
Uric acid (mg/dL)	0.202	**.003**
Carotid intima-media thickness (mm)	0.308	**.001**

MS, metabolic syndrome; NCEP-ATP III, National Cholesterol Education Program-Adult Treatment Panel III.

It is also known that insulin resistance has an important role in the development of hypertension in obese patients.[1] Hypertension is one of the components of MS and is a risk factor for cardiovascular disease.[1] The causes of insulin resistance leading to hypertension can be listed as follows; decreased peripheral vasodilator effect of insulin and related vasoconstriction, stimulation of renal sodium reabsorption, stimulation of sympathetic nervous system activity, increase in arterial wall thickness and stimulation of the renin-angiotensin system.[1] The association of increased arterial blood pressure values with thyroid dysfunction and TV has been reported. Similar to the study conducted by Aytürk et al[4] evaluating the relationship between MS TV., in our patients, arterial systolic and diastolic blood pressure values increased as TV increased.

Increased fatty acid levels, which are closely associated with insulin resistance, contribute to insulin resistance by increasing glucose output from the liver, decreasing glucose transport, phosphorylation, muscle glycogen synthesis, and glucose oxidation.[1,11] Increased free fatty acid levels also contribute to the development of insulin resistance by increasing radical oxygen species.[1,11] Dyslipidemia associated with insulin resistance is characterized by high TG, apolipoprotein (a), small dense LDL cholesterol, and low HDL cholesterol and has been described to be more atherogenic.[1,11] However, in our study, only a significant relationship between LDL cholesterol and TV was found among lipid parameters. The inability to detect the relationship between atherogenic dyslipidemia (high TG and low HDL) and TV in our study suggests that the relationship between TV and MS cannot be explained solely by insulin resistance. In a study, it was shown that insulin resistance alone cannot affect TV in the absence of MS, and that MS components have a cumulative effect on TV and nodule.[10]

It has been determined that increased serum uric acid levels are associated with cardiovascular disease and MS parameters such as obesity, dyslipidemia, hypertension, and impaired glucose metabolism.[17] As a result of increased insulin levels and insulin resistance, decreased renal clearance of uric acid or increased reabsorption from the proximal tubule, increased fructose consumption, which is closely related to obesity, and increased

leptin levels have been identified as possible causes of hyperuricemia.[17] In addition, some studies have shown that increased uric acid levels lead to insulin resistance.[18] On the other hand; some studies have shown that hypertriglyceridemia reduces the renal clearance of uric acid and that the decrease in TG levels results in increased urinary uric acid levels.[17] In our study, while there was no statistically significant difference in terms of uric acid in the obese group with and without MS, the significant difference between the obese groups with high TV and low TV could not be explained by the relationship between insulin resistance and uric acid alone. It is suggested that there may be additional mechanisms to explain the relationship between volume and volume.

Central obesity, one of the MS criteria, is an important risk factor for cardiovascular diseases. The type of obesity in which waist circumference or waist/hip ratio increases is defined as "central obesity."[19] Secretion of tissue factor, plasminogen activator inhibitor-1 (PAI-1), fibrinogen, and various cytokines by adipocytes contribute to the progression of atherosclerosis and the risk of CVD.[1,9,11,17,20] In many studies, it has been shown that there is a positive relationship between increased BMI and TV, which is another CVD risk factor.[3-5] In our study, a statistically significant relationship was found between TV, waist circumference, and BMI.

It has been shown that increased CIMT can be used as a marker of atherosclerosis.[20] It has also been shown that TSH increases the risk of cardiovascular disease and is closely related to CIMT, which is an indicator of early atherosclerotic changes.[21] In our study, a statistically significant difference was found in terms of CIMT between the MHO and MNHO groups, as well as between the obese groups with high TV and low TV, in line with the literature.

In our study, in contrast to studies showing the relationship between TV and MS, glucose metabolism disorders, and diabetes,[3-7] no relationship was found between fasting blood glucose and HbA1c values and TV. This result can be explained by the fact that patients with known diabetes were not included in the study and the number of patients diagnosed with diabetes was low.

In some studies, it has been reported that patients with insulin resistance have an increased risk for thyroid nodule formation and larger TV, and it has been suggested that increased circulating insulin levels may cause an increase in thyroid nodules and thyroid proliferation.[4,6] In our study, no significant relationship was found between insulin resistance and thyroid nodule.

Some limitations of our study need to be pointed out. Our results may not reflect the entire population, as the study was single-center and only included obese young-middle-aged female participants to ensure homogeneity. Because of the cross-sectional character of our study, a cause–effect association in the analysis of the results cannot be established. Since blood pressure measurements were made in the outpatient setting in our study, white coat hypertension may have affected the results of our study. Iodine, selenium, vitamin A levels, and alcohol consumption that affect TV were not evaluated.

The statistically significant relationship between TV and MS parameters indicates that higher TV may be a sign of MS in obese individuals and could be used to determine increased CVD risk. Due to the difficulty of obesity treatment, it is important to choose patients who will be approached aggressively in treatment. We think that cheap and practically measurable TV can guide this patient selection.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erzincan Binali Yıldırım University (Date: March 28, 2017, Number: 03/06).

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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