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Original Article

The Association of Thyroid Volume with Framingham Risk Score and Cardiovascular Risk Factors in Postmenopausal Women

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ABSTRACT

Objective: Insulin resistance contributes to the development of cardiovascular disease by different mechanisms such as atherosclerosis, coronary artery calcification, endothelial dysfunction, and activation of inflammatory processes. Besides functional changes, it has been shown that thyroid volume and the prevalence of thyroid nodules are increased in patients with insulin resistance. Although different studies have shown the relationship between cardiovascular disease and insulin resistance, thyroid morphological abnormalities, and insulin resistance, there is no study showing a possible relationship between thyroid volume and cardiovascular disease. In our study, we aimed to find out whether there was a link between thyroid volume and cardiovascular disease.

Methods: This was a cross-sectional study involving 190 postmenopausal women. Framingham risk scoring was used to estimate the 10-year cardiovascular risk of contributors. In addition to biochemical parameters (parameters of carbohydrate metabolism, lipid profile, and uric acid), carotid intima-media thickness, and thyroid volume were evaluated.

Results: Thyroid volume was associated with parameters closely related to cardiovascular diseases such as increased waist-to-hip ratio, increased arterial systolic blood pressure, increased uric acid level, increased insulin level, and homeostasis model assessment of insulin resistance index. Additionally, the relationship between the thyroid volume and the Framingham risk score was used to reveal the risk of cardiovascular disease. Similarly, there was a significant relationship with CIMT, a predictor of cardiovascular disease.

Conclusion: Present report suggests that patients with high thyroid volume should be evaluated in detail for cardiovascular disease. Thyroid volume can be used to calculate cardiovascular risk and as an indicator for exposure to the risk factors.

Keywords: Cardiovascular disease, goiter, insulin resistance, carotid intima-media thickness, thyroid gland

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death and morbidity throughout the world and has significant human and economic consequences. According to World Health Organization data, CVD causes nearly 18 million deaths per year, accounting for 31% of worldwide deaths.[1] Insulin resistance makes a significant contribution to the development of CVD by different mechanisms such as atherosclerosis, coronary artery calcification, endothelial dysfunction, and activation of inflammatory processes.[2] Furthermore, insulin resistance is associated with metabolic syndrome, carbohydrate metabolism abnormalities, obesity, dyslipidemia, hyperuricemia, as well as elevated thyroid volume and nodule prevalence.[3-5] Increased insulin levels are known to cause increased levels of free insulin-like growth factor-1 (IGF-1) by decreasing IGF-1-binding protein levels. It has also been suggested that elevated free IGF-1 levels as a result of hyperinsulinemia can provide a basis for the thyroid volume increase, nodule development, and differentiation.[5]

Thyroid diseases have also been shown to be at risk for CVD development as well as a number of well-known risk factors such as hypertension, tobacco use, high cholesterol, obesity, poor diet, and sedentary lifestyle.[6]

In different studies, the relationship between CVD and insulin resistance,[1,7] morphological abnormalities of the thyroid, and insulin resistance has been shown,[4,8] and

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there is no study showing a possible association between thyroid volume and CVD. In our study, we tried to find out whether there is a link between thyroid volume and CVD.

METHODS

This was a cross-sectional study involving 190 postmenopausal women. Local ethics committee of Erzincan Binali Yıldırım University, Faculty of Medicine, (Ethics Committee No.: 03/04, dated March 03, 2015) approved the study. A review of their medical records was conducted (age, disease history and duration, medications, menopause age, drug and cigarette use, and family history of premature CVD). Diabetes, thyroid disease, and CVD were all exclusion criteria.

The sample size was calculated in the G Power 3.1.9.2 program (effect size (*d*): 0.5; α: 0.05; power: 0.90) as 86 patients for each group. A total of 190 patients were included in the study, with an excess of 10%, 95 for each group.

The Framingham risk score is calculated according to D'Agostino et al.[9] Participants were divided into groups according to 10-year CVD risk [low (≤10%), moderate (10%-20%), and high (≥20%) risk, respectively]. Since the number of patients in the high-risk group was not sufficient in our study, the high- and intermediate-risk groups were evaluated together.

Waist circumference, height, and weight were measured and recorded appropriately (lightest clothing possible and without shoes) (SECA, Seca GmbH & Co., Hamburg, Germany). Body mass indexes were calculated for the patients by dividing their weight in kilograms by their height in meters squared.

After more than 5 minutes of rest, the systolic and diastolic blood pressure (SBP, DBP) were measured using an Erka sphygmomanometer (PMS Instruments Limited, Berkshire, UK) with an appropriate cuff size. For each, 2 readings were taken, and the mean of the 2 readings was used for analysis. Patients on antihypertensive medication or with SBP and DBP greater than 140 mmHg and 90 mmHg, respectively, were assumed to be hypertensive.

The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the formula: HOMA-IR=[glucose (mg/dL) × insulin (μU/mL)/405], using fasting values.

Participants with HbA1C value of 6.5% or more were accepted as diabetic.

Assessment of the Thyroid Volume and Thyroid Nodules

Thyroid volume measurements were made in the supine position with slight neck extension (SIUI/CZ XL-43B (China) Ultrasound System and B mode high-resolution linear probe (8 MHz)). Craniocaudal, mediolateral, and anteroposterior dimensions were measured, and volumes were obtained using the ovoid formula (width × depth × length × π/6) for each lobe. Measurements were made by an operator blinded to all clinical information. All lesions beyond the standard shape and echo features of the thyroid gland greater than 0.3 cm were evaluated as nodules.

Assessment of the Carotid Intima-Media Thickness

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 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 (TC), high-density lipoprotein cholesterol (HDL-C), and plasma triglyceride (TG) concentrations (Oxidation-based technique, Beckman Coulter AU 2700 plus, Missima, Japan); thyroid-stimulating hormone (TSH) (Chemiluminescence assay, UniCel DXi 800 immunoassay system, Beckman Coulter, Fullerton, Calif, USA); insulin, free T3, free T4 measurements (Chemiluminescence, Siemens ADVIA Centaur XP Immun Assay, Germany); and high-sensitivity C-reactive protein (hsCRP) (Nephelometric method, Siemens BN II, Germany) were measured in our hospital's central laboratory after at least 10 hours of fasting in the morning. Low-density lipoprotein cholesterol (LDL-C) was estimated by the Friedewald equation.

Statistical Analysis

IBM's Statistical Package for Social Sciences version 19.0 was used for statistical analyses (IBM SPSS Corp., Armonk, NY, USA). For each variable, descriptive statistics

MAIN POINTS

- Thyroid volume has been found to be associated with the Framingham risk score and some cardiovascular disease risk factors.
- Patients with high thyroid volume should be evaluated in detail for cardiovascular disease.
- Assessing cardiovascular risk with thyroid volume should be addressed in large-scale, advanced research that can assess a large population.

were calculated. The Kolmogorov–Smirnov test was used to determine the distribution of the variables. The mean and standard deviation 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 < .05 was considered significant.

RESULTS

The mean age of the participants was 56.14 ± 7.0 years, and mean menopause age was 47.2 ± 4.8 years. The mean menopause duration was 8.91 ± 8.11 years, and the mean BMI was 31.76 ± 5.92 kg/m^2. Mean CIMT of the patients was calculated as 0.65 ± 0.13 mm. Thyroid nodules were present in 44.21% of the patients, 14.2% of the patients were actively smoking, and 31.6% of the patients were receiving antihypertensive treatment. Twenty percent of the patients participating in the study had a family history of premature CVD. The mean thyroid volume of the patients was found to be 16.36 ± 10.28 mL. Totally, 12.1% of participants had undiagnosed diabetes.

Bivariate correlation test revealed a significant correlation of thyroid volume with BMI, waist-to-hip ratio, SBP, CIMT, uric acid, insulin, HOMA-IR, TSH, and Framingham risk score. Table 1 shows the correlation coefficient and *P* significance value of the parameters that were significantly associated with thyroid volume.

Table 1. Bivariate Correlation Results between Thyroid Volume and Other Significant Parameters

Parameters	Correlation Coefficient (r_s)	*P*
Body mass index (kg/m^2)	0.217	**.003**
Waist-to-hip ratio	0.223	**.002**
Systolic blood pressure (mmHg)	0.278	**<.001**
Carotid intima media thickness (mm)	0.237	**.001**
Uric acid (mg/dL)	0.169	**.020**
Insulin (mU/mL)	0.170	**.019**
HOMA-IR	0.165	**.023**
TSH (μU/mL)	−0.462	**<.001**
Framingham risk score	0.219	**.002**

HOMA-IR, homeostatic model assessment-insulin resistance; TSH, thyroid-stimulating hormone.

When patients were divided into two groups based on the median value of thyroid volume, while there were no significant differences between the groups in terms of age, menopause duration, DBP, glucose, HbA1C, TC, HDL-C, TG, LDL-C, and HsCRP; there were statistically significant differences in terms of menopause age, BMI, waist-to-hip ratio, SBP, CIMT, uric acid, insulin, HOMA-IR, TSH, and Framingham risk score (Table 2).

When participants were divided into two groups as low and moderate/high-risk patients according to the Framingham risk score, while there were no significant differences between the groups according to menopause age, waist-to-hip ratio, insulin, HsCRP, and TSH; there were statistically significant differences in terms of menopause duration, BMI, DBP, CIMT, uric acid, TG, LDL-C, and HOMA-IR parameters (Table 3). The parameters used to calculate the Framingham risk score were not taken into account.

When participants were divided into 2 groups according to the median value of TSH as low and high TSH levels, thyroid volume, TC, and TG levels were significantly different in groups, but no difference was observed regarding other parameters (Table 4).

In the Chi-square test, no significant relationship was found between patients with low and high TSH values and patients with low and medium/high Framingham risk scores. Similarly, no significant relationship was found between nodule presence and Framingham risk score, CIMT, HOMA-IR, active smokers, and premature CVD incidence in the Chi-square test. For these tests, participants were separated into 2 groups as participants with a low and high value according to the median value of the TSH, CIMT, and HOMA-IR parameters.

DISCUSSION

There are 5 main findings of our study. First, the thyroid volume was associated with parameters closely related to CVDs such as increased waist-to-hip ratio, increased arterial systolic blood pressure, increased uric acid level, increased insulin level, and HOMA-IR index. Second, there is a relationship between the thyroid volume and the Framingham risk score used to reveal the risk of CVD. Similarly, there was a significant relationship with CIMT, a predictor of CVD. Third, thyroid volume is shown to be related to menopause age. Fourth, when participants were grouped as low and high TSH according to TSH values, there was a statistically significant difference regarding TG and total cholesterol, but not to other parameters. Finally, when the thyroid volume and Framingham risk score are evaluated inversely, it is statistically significant that the thyroid volume increases in moderate/high-risk patients according to Framingham risk scoring.

Table 2. Demographic, Clinic, and Laboratory Features of the Subjects According to High and Low Thyroid Volume Levels

Parameters	Group 1 (Thyroid Volume <13.85 mL), n = 95	Group 2 (Thyroid Volume ≥13.85 mL), n = 95	*P*
Age (years)*	54 (50-59)	56 (52-61)	.118
Age of menopause (years)*	47 (45-50)	49 (46-51)	**.035**
Menopause duration (years)*	6 (2-13)	7 (3-14)	.468
Body mass index (kg/m^2)*	29.76 (26.92-33.32)	32.47 (29.30-36.96)	**.001**
Waist-to-hip ratio**	0.88 ± 0.06	0.91 ± 0.08	**.009**
Systolic blood pressure (mmHg)*	120 (110-130)	130 (115-140)	**.006**
Diastolic blood pressure (mmHg)*	70 (70-80)	70 (70-80)	.860
Carotid intima media thickness (mm)*	0.60 (0.55-0.70)	0.70 (0.60-0.75)	**.007**
Glucose (mg/dL)*	94 (87-102)	93 (86-102)	.931
HbA1c (%)*	5.8 (5.5-6.1)	5.9 (5.6-6.3)	.136
Uric acid (mg/dL)*	4.3 (3.8-5.1)	4.7 (4,0-5.7)	**.005**
Cholesterol (mg/dL)**	222.5 ± 46.4	220.1 ± 47.5	.727
HDL-cholesterol (mg/dL)*	53 (46-62)	51 (44.9-59)	.236
Triglyceride (mg/dL)*	137 (105-179)	151 (114-199)	.079
LDL-cholesterol (mg/dL)*	134 (112-158)	129 (111-163)	.389
Insulin (mU/ml)*	7.55 (5.80-13.00)	11.90 (6.56-16.95)	**.014**
HOMA-IR*	1.93 (1.28-3.09)	2.69 (1.47-4.18)	**.022**
Hs-CRP (mg/L)*	2.29 (0.75-4.67)	2.80 (1.06-5.40)	.237
TSH (uU/mL) *	1.91 (1.36-2.97)	1,26 (0.91-1.86)	**<.001**
Framingham risk score (10 year)*	6.3 (3.9-10)	8.6 (5.3-13.7)	**.008**

*Mann–Whitney *U* test.
***t*-test.
HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; HsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

Although there has been a decrease in the rate of death due to coronary heart disease since 1980,[10] CVDs are still among the leading causes of all deaths.[1] Despite improvements in protection from CVD, early diagnosis, and treatment, it still causes approximately 17.6 million deaths annually, accounting for 31.43% of all deaths.[11] Although three-fourths of all cardiovascular deaths are in middle-income countries, cardiovascular deaths are also the leading cause of death in developed Western societies.[1]

The relationship between hyperinsulinemia and atherosclerosis is known. Insulin resistance contributes to the development of CVD by different mechanisms such as atherosclerosis, coronary artery calcification, endothelial dysfunction, and activation of inflammatory processes.[2,12,13] Human and animal studies have shown a relationship between insulin resistance and endothelial dysfunction, an early finding of atherosclerosis.[14] Insulin resistance leads to inactivation of endothelial nitric oxide synthase and decreases nitric oxide in the endothelial cell, by leading to an abnormality in the phosphatidylinositol 3-kinase/Akt pathway.[12] Increased vascular cell adhesion molecule expression, increased leukocyte interaction with endothelial cells, abnormal PI3K response, and increased mitogen-activated protein kinase signaling exacerbate the process of atherosclerosis by increasing impaired vascular function.[12] Supporting this data, insulin infusion has been shown to stimulate vasodilatation in healthy human studies and to increase peripheral blood flow.[12] Insulin resistance is also closely related to other risk factors for CVD such as metabolic syndrome, carbohydrate metabolism abnormalities, obesity, dyslipidemia, hyperuricemia, and hypertension.[2,12]

Metabolic syndrome and its components, obesity, hypertension, insulin resistance, lipid, and glucose metabolism disorders have been shown to be related to functional changes in the thyroid gland.[15] In addition to functional changes, it has been shown that thyroid volume and the prevalence of thyroid nodules are increased in patients with insulin resistance.[3-5,16] It is known that TSH stimulates cell cycle progression and proliferation in thyroid cell

Table 3. Demographic, Clinical, and Laboratory Features of the Subjects According to 10-Year Cardiovascular Risk by Framingham Risk Scoring (Low and Medium/ High-risk Groups)

Parameters	Group-1 (FRS ≤ 10), n = 133	Group-2 (FRS > 10), n = 57	*P*
Age of menopause (years)*	47 (45-50)	50 (45-51)	.062
Menopause duration (years)*	5 (1-11)	12 (5-20.5)	**<.001**
Body mass index (kg/m^2)*	30.8 (27.1-34.5)	32.8 (28.9-37.8)	**.034**
Waist-to-hip ratio**	0.89 ± 0.07	0.91 ± 0.07	.114
Diastolic blood pressure (mmHg)*	70 (70-80)	80 (70-90)	**<.001**
Thyroid volume (mL)*	13.10 (8.88-18.23)	17.47 (10.16-23.40)	**.024**
Carotid intima media thickness (mm)*	0.60 (0.55-0.70)	0.70 (0.60-0.88)	**<.001**
Uric acid (mg/dL)*	4.30 (3.80-5.05)	5.20 (4.05-6.65)	**<.001**
Triglyceride (mg/dL)*	134.00 (94.50-179.50)	163.00 (123.15-242.00)	**.001**
LDL-cholesterol (mg/dL)*	130.0 (109.7-152.9)	144.2 (116.1-177.7)	**.036**
Insulin (mU/mL)*	8.63 (6.05-14.60)	12.30 (7.10-16.68)	.064
HOMA-IR*	1.97 (1.29-3.32)	2.80 (1.84-4.38)	**.021**
Hs-CRP (mg/L)*	2.41 (0.96-4.74)	3.20 (1.10-5.47)	.295
TSH (μU/mL)*	1.57 (1.06-2.26)	1.66 (1.04-2.50)	.808

*Mann–Whitney *U* test.
***t*-test.
FRS, 10-year cardiovascular risk by Framingham risk scoring; HsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostatic model assessment-insulin resistance; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

Table 4. Demographic, Clinical, and Laboratory Features of Patients with Low and High TSH levels

Parameters	Group-1 (TSH < 1.63 μU/mL), n = 95	Group-2 (TSH ≥ 1.63 μU/mL), n = 95	*P*
Age (years)*	55 (51-60)	55 (51-60)	.668
Age of menopause (years)*	48 (45-50)	48 (45-50)	.455
Menopause duration (years)*	6 (2-14)	7 (3-13)	.765
Body mass index (kg/m^2)*	31.11 (27.37-35.34)	31.11 (27.92-34.72)	.993
Waist-to-hip ratio**	0.90 ± 0.07	0.89 ± 0.07	.394
Systolic blood pressure (mmHg)*	120 (110-140)	120 (110-135)	.249
Diastolic blood pressure (mmHg)*	70 (70-80)	80 (70-80)	.768
Carotid intima media thickness (mm)*	0.65 (0.55-0.75)	0.60 (0.50-0.65)	.908
Glucose (mg/dL)*	93 (87-102)	95 (86-103)	.868
HbA1c (%)*	5.8 (5.6-6.2)	5.9 (5.6-6.2)	.960
Uric acid (mg/dL)*	4.4 (3.9-5.3)	4.5 (3.9-5.3)	.509
Cholesterol (mg/dL)**	213.9 ± 44.3	228.8 ± 48,4	**.028**
HDL-cholesterol (mg/dL)*	51 (45-60)	52 (45-62)	.738
Triglyceride (mg/dL)*	133.40 (91.00-179.00)	148.00 (118.00-210.60)	**.038**
LDL-cholesterol (mg/dL)*	129.4 (106.4-154.6)	136.3 (116.0-170.6)	.73
Insulin (mU/mL)*	9.70 (6.16-16.30)	9.26 (6.43-14.20)	.564
HOMA-IR*	2.41 (1.35-3.88)	2.04 (1.33-3.27)	.499
Hs-CRP (mg/L)*	2.58 (1.02-4.76)	2.41 (0.98-4.80)	.960
Thyroid volume (mL)*	17.47 (12.23-24.33)	10.43 (7.71-16.52)	**<.001**
Framingham risk score (10 year)*	7.3 (4.5-11.7)	7.3 (4.5-13.7)	.285

*Mann–Whitney *U* test.
***t*-test
HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; Hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

cultures with insulin or/and IGF-1.[17] In addition, it is known that the insulin/IGF-1 signaling pathway regulates thyroid gene expression and has been suggested as an additional contribution to thyroid cell proliferation and differentiation.[17] Furthermore, increased insulin levels lead to an increase in free IGF-1 levels by decreasing IGF-1-binding protein levels. It has also been suggested that elevated levels of free IGF-1 as a result of hyperinsulinemia may be the basis for volume increase, nodule development, and differentiation.[5,18] It has also been shown that the prevalence of insulin resistance is higher in patients with differentiated thyroid carcinoma.[19] In our study, insulin resistance was associated with thyroid volume as reported in the literature.[3-5] In our study, there was no relationship of thyroid volume with fasting blood glucose and HbA1c, unlike studies revealed association of thyroid volume with glucose metabolism disorders and diabetes.[3-5] This result can be explained by the fact that patients with known diabetes are not included in the study, and the number of patients diagnosed with diabetes during the evaluation is low in our sample.

Several studies have shown that serum uric acid levels are associated with cardiovascular risk factors.[20,21] Like other components of metabolic syndrome, the relationship between serum uric acid levels and dyslipidemia is well defined.[20,22] A number of reasons have been proposed to explain the relationship between hyperuricemia and cardiovascular risk factors. Decreased renal clearance of uric acid or increased reabsorption from the proximal tubule due to increased insulin levels and insulin resistance, increased fructose consumption which is associated with obesity, and elevated leptin levels have been identified among possible causes.[23] On the other hand, in some studies, it has been shown that hypertriglyceridemia reduces renal clearance of uric acid, and reduction in TG levels results in increased urinary uric acid levels.[24] Although the cause/effect relationship cannot be established because of the cross-sectional nature of our study, the fact that thyroid volume is statistically significant with uric acid in our study can be explained by the relation of insulin resistance-uric acid-atherogenic dyslipidemia. However, in this study, no correlation was found between the lipid parameters assessed and the thyroid volume. These findings support that the relationship of thyroid volume with CVD may be explainable with an underlying pathogenic mechanism, which is associated with many, such as insulin resistance instead of separately each CVD risk factors.

The association of BMI with thyroid volume is known.[5] However, according to our detailed literature review, this study is the first study revealing a significant association between waist-to-hip ratio and thyroid volume. The fact that waist-to-hip ratio is indicative of visceral obesity, which is more closely related to CVD risk, supports the idea that thyroid volume is associated with CVD. In addition, a significant difference in thyroid volume between low and moderate/high-risked patient groups with no difference in waist-to-hip ratio and high sensitivity CRP values suggests that thyroid volume may be more valuable than these parameters.

Thyroid dysfunction and consequently thyroid volume is known to be related to arterial tension. The arterial systolic blood pressure values were increased as the thyroid volume increased in our study, as supported by the report of Zheng et al[25] which evaluates the association of metabolic syndrome and thyroid volume. However, a similar relationship could not be established with diastolic blood pressure.

In our detailed literature review, there are no studies showing an association between thyroid volume and CIMT or CVD risk scores. The demonstration of the relationship between CVD markers and thyroid volume, such as the CIMT and Framingham risk score, which has proven efficacy and reliability in many studies, is striking. Also, the thyroid volume and CIMT were increased in the Framingham risk score moderate/high patient group.

On the other hand, subclinical and apparent hypothyroidism is known to be important factor in the development of metabolic syndrome and CVD.[6] In many studies, serum TSH levels have been shown to be closely associated with atherogenic lipid profile.[6] Similarly, hypothyroidism and high TSH levels have been shown to increase CVD risk in association with increased blood pressure,[26] HbA1c,[27] BMI,[27] insulin resistance,[27] and endothelial dysfunction.[28] Thyroid stimulating hormone has also been shown to be closely related to CIMT, a sign of early atherosclerotic changes.[28] However, in our study, no statistically significant difference was observed between the low TSH value group and the high TSH value group among the CVD risk factors except cholesterol and TG levels. Considering our results, it is thought that the relation of the risk factors/markers of CVD and thyroid volume we detect may be explained by insulin value/insulin resistance rather than TSH value. In addition, exclusion of participants with known thyroid disease minimizes the effects of thyroid dysfunction and reduces the effect of TSH. Furthermore, the negative effects of metformin and 3-hydroxy-3-methyl-glutaryl-coenzyme (HMG-CoA) reductase inhibitors on thyroid volume, which are known to have positive effects on CVD, are important in supporting the outcome of this report.[17]

It is probably necessary to ask the following question: Should CVD risk factors and thyroid volume association be linked only to hyperinsulinemia and insulin resistance?

Factors that increase thyroid volume such as smoking,[29] selenium deficiency,[30] vitamin A deficiency,[31] iodine deficiency,[32] high amount of alcohol consumption,[33] and iron deficiency[34] are also associated with CVD. These factors should be considered as factors contributing to the CVD–thyroid volume association in addition to insulin resistance.

The prevalence of goiter has been reported to be higher in women than in men.[29] The high prevalence of thyroid disease in women has been claimed to be linked to high estrogen levels. Estrogen has been shown to increase proliferation and mitogenic activity in thyroid cells.[35] In our study, the age of menopause was found to be lower in the patient group with low thyroid volume to support this information.

Some limitations of our work need to be revealed. Our results may not reflect the general population because the study is single centered, and only postmenopausal female participants are accepted to work to ensure homogeneity. Due to the cross-sectional nature of our study, no causal relationship can be established in the interpretation of our findings. Past consumption of cigarettes was not questioned, and only active cigarette consumption was questioned. Effects of iodine, selenium, vitamin A levels, and alcohol consumption on thyroid volume have not been evaluated.

This study reports a significant statistical relationship between thyroid volume and Framingham risk score, CVD risk factors such as uric acid, waist-to-hip ratio, insulin, insulin resistance, CIMT, systolic blood pressure, BMI, and TSH. Additionally, this is the first study revealing this relationship for uric acid, waist-to-hip ratio, CIMT, and a CVD risk score. This statistical relationship suggests that the thyroid volume may be a candidate for calculating cardiovascular risk exposure. Our study showed that patients with high thyroid volume should be evaluated in detail for CVD. Thyroid volume measurement is noninvasive, inexpensive, easily accessible process, and the usefulness of assessing cardiovascular risk with thyroid volume should be addressed in large-scale, advanced research that can assess a large population.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erzincan Binali Yıldırım University (Date: March 3, 2015 Number: 03/04).

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

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