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Evaluation of the aortic velocity propagation, epicardial fat thickness, and carotid intima-media thickness in patients with subclinical hypothyroidism

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Subclinical hypothyroidism (SH) is associated with hemodynamic and metabolic abnormalities that cause endothelial dysfunction and atherosclerotic cardiovascular diseases. Aortic velocity propagation (AVP), epicardial fat thickness (EFT), and carotid intima-media thickness (CIMT) may provide additional information in SH patients. This study aimed to evaluate thyroid stimulating hormone (TSH), AVP, EFT, and CIMT in SH patients, and determine the associations among these parameters. Eighty patients with SH and 43 euthyroid (EU) individuals were enrolled. Blood samples were collected to measure laboratory parameters. Patients were divided into two groups based on their TSH values (TSH $\geq$10 or TSH $<$10 mIU/L). AVP, EFT, and CIMT were measured and compared between the study groups. A multivariate linear regression model was used for analysis of the independent predictors of AVP (beta = –0.298; 95% confidence interval = –0.946 to –0.287; $p < 0.001$). AVP was significantly lower in SH patients than the control group (43.7 $\pm$ 12.5 and 62.6 $\pm$ 13.8, respectively; $p < 0.001$). EFT values were similar between the SH and control groups (0.7 $\pm$ 0.3 and 0.6 $\pm$ 0.2, respectively; $p = 0.10$). SH patients had higher CIMT values than the control group (0.8 $\pm$ 0.3 and 0.5 $\pm$ 0.2, respectively; $p < 0.001$). In the multivariate linear analysis, TSH was an independent predictor of AVP. AVP was lower and CIMT was higher in SH patients compared to EU individuals. The increased CIMT and decreased AVP levels were significantly associated with TSH levels in SH patients.

Keywords

Subclinical hypothyroidism; Aortic velocity propagation; Epicardial fat thickness; Carotid intima-media thickness

1. Introduction

Subclinical hypothyroidism (SH) is defined as elevated levels of thyroid-stimulating hormone (TSH) and normal levels of free thyroid hormones. SH affects 4–10% of the population [1]. SH is associated with hemodynamic and metabolic abnormalities, which increase the risk for atherosclerotic cardiovascular diseases [2] and endothelial dysfunction [3, 4]. Decreased thyroid hormones are associated with increased arterial stiffness and systemic vascular resistance [5]. SH patients have lower aortic distensibility and higher aortic stiffness index than euthyroid (EU) individuals [6]. Masaki *et al.* [7] demonstrated that the cardio-ankle vascular index was increased in SH patients, suggesting that increased arterial stiffness may be associated with cardiovascular diseases. Moreover, TSH levels were inversely correlated with endothelium-dependent dilatation [8]. Aortic velocity propagation (AVP) is a recently described echocardiography-based measure that reflects aortic stiffness. AVP was negatively associated with coronary and carotid atherosclerosis [9].

Epicardial adipose tissue (EAT) is found between the pericardial visceral layer and myocardium, surrounding the coronary arteries. An increase in EAT is positively associated with coronary artery disease (CAD) [10]. Cytokines released from the EAT are involved in causing atherosclerosis [11]. Previous studies have demonstrated that epicardial fat thickness (EFT) and TSH values are significantly related to SH. Higher EFT values have been reported in SH patients compared to EU individuals [12]. A recent study found that EFT was significantly increased in SH patients with a TSH level $\geq$10 mIU/L compared to SH patients with a TSH level $<$10 mIU/L. However, the EFT values were similar in SH patients and the control group [13].

Carotid intima-media thickness (CIMT) is a marker of subclinical atherosclerosis and was recently found to be associated with CAD [14]. However, the effect of SH on CIMT values is not clear [15, 16]. A recent meta-analysis based on eight studies and 3602 patients demonstrated that the CIMT values were higher in SH patients with TSH $\geq$10 mIU/L compared to EU individuals [17]. CIMT values in SH patients vary with TSH levels, independently of other risk factors.

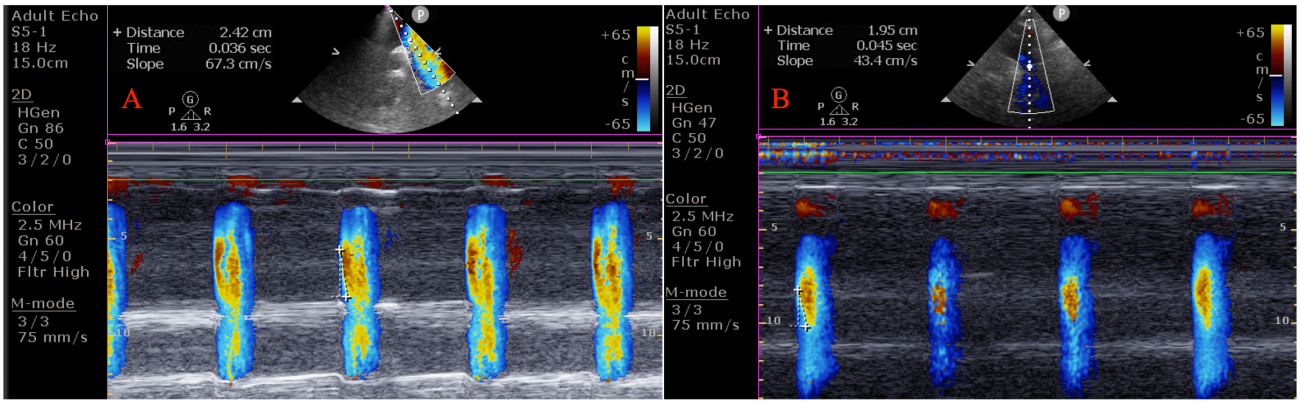

Fig. 1. Aortic velocity propagation (AVP) in an euthyroid subjects (AVP = 67.3 cm/s) (A), and in a patient with subclinical hypothyroidism (AVP = 43.4 cm/s) (B). The AVP was calculated by dividing the distance between points corresponding to the beginning and end of the propagation slope by the duration between corresponding time points.

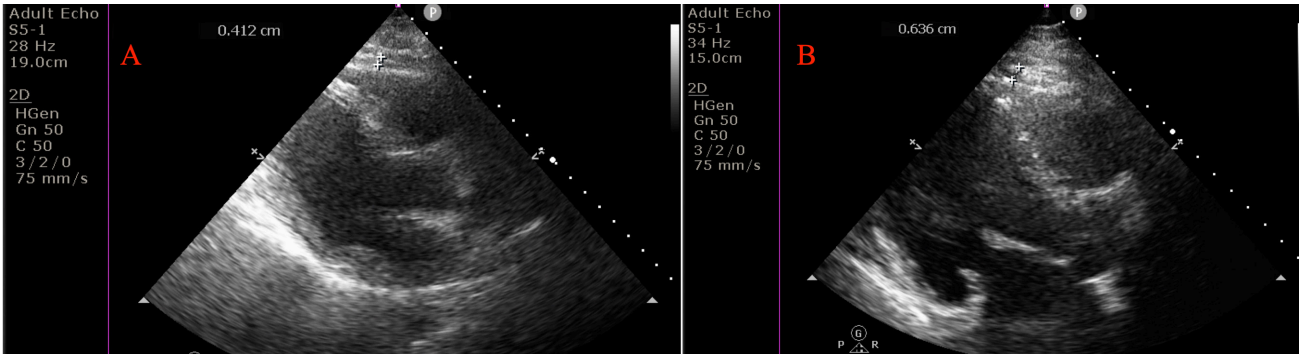

Fig. 2. Measurement of epicardial fat thickness (EFT) in an euthyroid subjects (EFT = 0.4 cm) (A), and in a patient with subclinical hypothyroidism (EFT = 0.6 cm) (B). Epicardial fat thickness (EFT) perpendicular to right ventricular free wall. EFT identified as an echo-free space between the myocardium and visceral pericardium from the parasternal long-axis view on two-dimensional echocardiography, was measured perpendicularly in front of the right ventricular free wall at end-diastole.

AVP, EFT, and CIMT measurements may provide information on subclinical atherosclerosis in SH patients. We hypothesized that TSH may be related to AVP, EFT, and CIMT in SH patients. This study aimed to investigate the associations between TSH, AVP, EFT, and CIMT in SH patients. To the best of our knowledge, this is the first study to evaluate the association of AVP, EFT, and CIMT measurements with subclinical atherosclerosis in SH patients.

2. Methods

This cross-sectional study included 80 SH patients and 43 controls (matched by age and sex) who presented to our clinic between May and August 2020. SH was diagnosed on the basis of TSH levels >4.2 mIU/L (normal range: 0.27–4.2 mIU/L) and normal free T4 (normal range: 0.93–1.7 ng/dL), measured twice at a 3-month interval [1]. SH patients were categorized into those with mildly elevated TSH (4.2 < TSH <10 mIU/L) or those with markedly elevated TSH (≥10 mIU/L). Patients with the following conditions were excluded from the study: left ventricular systolic dysfunction, valvular pathology, history of CAD, chronic lung disease, hepatic dysfunction, renal failure, malignancy, tobacco use, hypertension, diabetes mellitus, systemic infections or inflammatory disorders, secondary or postoperative hypothyroidism, pregnancy, or age <18 years or >65 years. None of the participants were using any lipid-lowering or thyroid-altering medications. Informed consent was obtained from all participants before the study. This study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of the Van Training and Research Hospital.

Patient evaluation included physical examinations (including anthropometric measurements), medical history, and basic laboratory tests. Following a fast of ≥8 hours, blood samples were obtained from the antecubital vein through an atraumatic puncture and sent for laboratory analysis. The hospital laboratory performed complete blood count and biochemical testing, including total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL), high-density lipoproteins (HDL), C-reactive protein (CRP), and creatinine. Serum TSH and free T4 levels were measured using chemiluminescence-based methods. Each patient underwent transthoracic echocardiography using an echocardiographic device (Vivid S6, General Electric, Horten, Norway) with a

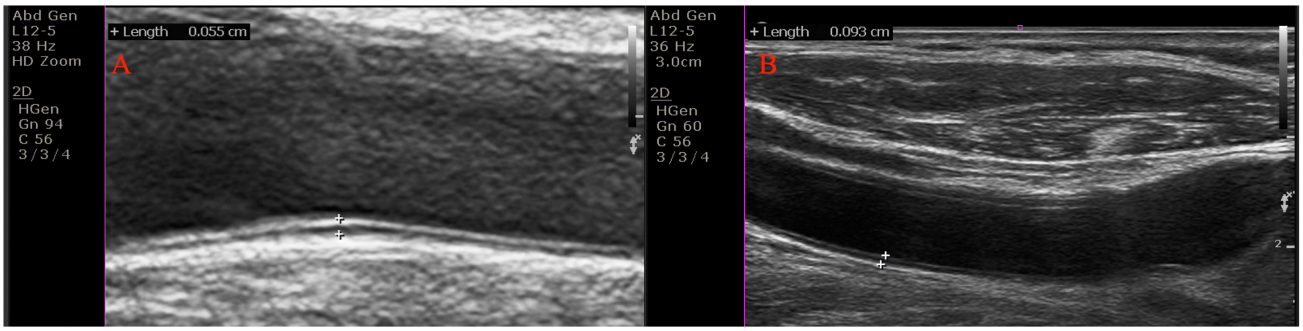

Fig. 3. Carotid intima-media thickness (CIMT) in an euthyroid subjects (CIMT = 0.5 mm) (A), and in a patient with subclinical hypothyroidism (CIMT = 0.6 mm) (B). The CIMT was computed on the far wall at 1–2 cm from the common carotid artery's bifurcation as the interval between the lumen-intima and the media-adventitia borders.

3.0-MHz transducer. Two cardiologists who were blinded to clinical data performed the echocardiography. Echocardiographic images were recorded and measured offline. Left ventricular ejection fractions were measured using the modified Simpson method.

Color M-mode Doppler recordings were obtained using the suprasternal window in supine position. The cursor was placed parallel to the direction of main flow in the descending aorta. The Nyquist limit was 30–50 cm/s, and a recorder sweep rate of 200 mm/s was used during M-mode. AVP was defined as the velocity of flow in the artery, calculated by dividing the distance between the points corresponding to the beginning and end of the propagation slope by the duration between the corresponding time points. At least three measurements were obtained, and their mean was recorded as the AVP (Fig. 1).

EFT was measured for the right ventricle's free wall using the parasternal long-axis view with aortic annulus as the anatomic reference. EFT was measured during the end-systolic period. Epicardial fat was identified as the space without an echogenic view between the visceral pericardium and myocardium. EFT was measured at the thickest area, preferably the right supraventricular area (Fig. 2).

Both carotid arteries were analyzed at plaque-free sites. CIMT was defined as the interval between the lumen-intima and the media-adventitia borders at the far wall 1–2 cm away from the common carotid artery bifurcation (Fig. 3) [18].

Data were analyzed with SPSS Statistics software (version 25.0 for Windows; IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to confirm the normal distribution of continuous variables. Normally distributed variables were expressed as means ± standard deviations (SDs). Categorical variables were presented as percentages. Differences between the two groups in parameters with a normal distribution were evaluated using unpaired *t*-tests. A one-way analysis of variance (ANOVA) followed by a Tukey post hoc test were used for normally distributed continuous data to perform multiple comparisons. The frequencies of nominal variables were compared using Fisher's exact test or chi-square test. Pearson test was used for evaluating the correlation between variables. A multivariate linear regression model was used to determine the independent predictors of AVP. Additionally, 15 patients were randomly selected to assess intra- and inter-observer reliability for AVP and EFT, expressed as intraclass correlation coefficients (ICCs). Statistical significance was defined at a p-value ≤ 0.05.

3. Results

Table 1 summarizes the demographic and laboratory characteristics of the study population. There were no differences between the groups in terms of age, sex, body mass index ($p > 0.05$), TC, LDL, HDL, TG, or ejection fraction. AVP was significantly lower in SH patients compared to the control group (43.7 ± 12.5 and 62.6 ± 13.8, respectively; $p < 0.001$). EFT values were similar between the SH and control groups (0.7 ± 0.3 and 0.6 ± 0.2, respectively; $p = 0.10$). SH patients had higher CIMT values than the control group (0.8 ± 0.3 and 0.5 ± 0.2, respectively; $p < 0.001$). SH patients had higher TSH and free T4 values compared to the control group (14.2 ± 6.8 and 3.1 ± 0.7, respectively; $p < 0.001$ for TSH; 1.4 ± 0.1 and 1.3 ± 0.1, respectively; $p < 0.001$ for free T4).

SH patients were divided into two groups based on their TSH values and compared with the control group (Table 2). AVP values were significantly lower in SH patients with TSH <10 or TSH ≥10 mIU/L compared to the control group (46.7 ± 14.5, 41.4 ± 10.2, and 62.6 ± 13.8, respectively; $p < 0.001$). EFT values were similar between SH patients with TSH <10 or TSH ≥10 mIU/L ($p > 0.05$). SH patients with TSH <10 or TSH ≥10 mIU/L had higher CIMT values compared to the control group (0.8 ± 0.3, 0.7 ± 0.3, and 0.5 ± 0.2, respectively; $p < 0.001$).

Table 3 summarizes the correlation between TSH and clinical parameters. TSH levels had a weak positive correlation with EFT (r = 0.188; $p = 0.038$) and CIMT (r = 0.236; $p = 0.009$) values (Fig. 4). However, AVP had a significant negative correlation with TSH levels (r = –0.424; $p < 0.001$) (Fig. 5).

There was no significant correlation of TSH levels with TC or LDL levels ($p > 0.05$). Table 4 shows the linear regression analysis for AVP using TSH, CRP, and TC. In the

Table 1. Baseline demographic features and laboratory parameters of the study population.

	Control (n = 43)	Patients (n = 80)	*p* value
Age (years)	46.7 ± 8.3	44.0 ± 13.1	0.22
Body mass index (kg/m^2)	26.2 ± 2.4	26.5 ± 2.4	0.51
Male (%)	27 (63)	36 (45)	0.06
White blood cell count (10^3/mm^3)	7.9 ± 1.8	7.2 ± 2.0	0.10
Hemoglobin (g/dL)	14.5 ± 1.8	14.8 ± 1.5	0.12
Platelet count (10^3/mm^3)	249.3 ± 76.8	235.3 ± 71.8	0.32
Creatinine (mg/dL)	0.7 ± 0.1	0.7 ± 0.1	0.89
Sodium (mEq/L)	137.3 ± 4.2	137.0 ± 2.9	0.65
albumin (g/dL)	3.5 ± 0.4	3.8 ± 0.7	0.11
C-reactive protein (mg/L)	6.9 ± 2.4	6.5 ± 2.3	0.16
Triglyceride (mg/dL)	205.2 ± 22.0	201.9 ± 39.1	0.42
High density lipoprotein (mg/dL)	42.3 ± 11.4	44.7 ± 8.3	0.12
Low density lipoprotein (mg/dL)	119.2 ± 28.5	118.6 ± 35.6	0.92
Total cholesterol (mg/dL)	196.7 ± 36.5	187.0 ± 32.6	0.15
Ejection fraction (%)	60.8 ± 2.6	58.9 ± 5.8	0.06
AVP (cm/s)	62.6 ± 13.8	43.7 ± 12.5	<0.001
EFT (mm)	0.6 ± 0.2	0.7 ± 0.3	0.10
CIMT (mm)	0.5 ± 0.2	0.8 ± 0.3	<0.001
T4 (μg/dL)	1.3 ± 0.1	1.4 ± 0.1	<0.001
TSH (mIU/L)	3.1 ± 0.7	14.2 ± 6.8	<0.001

AVP, aortic velocity propagation; EFT, Epicardial fat thickness; CIMT, carotid intima-media thickness; T4, Thyroxine 4; TSH, Thyroid stimulant hormone. Differences between the two groups were evaluated using Unpaired *t*-test for parameters with a normal distribution. $p < 0.05$ was considered statistically significant.

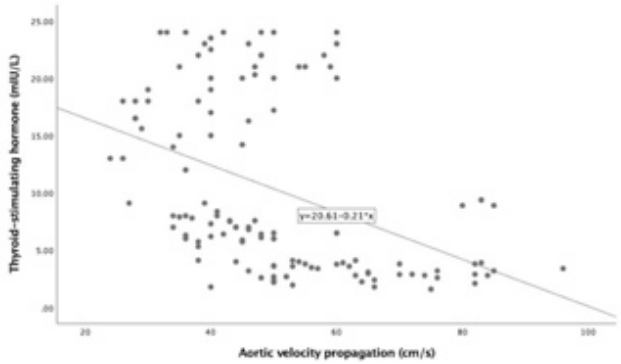

Fig. 4. Correlation between Thyroid stimulating hormone and Aortic velocity propagation (AVP) (r = –0.424, $p < 0.001$).

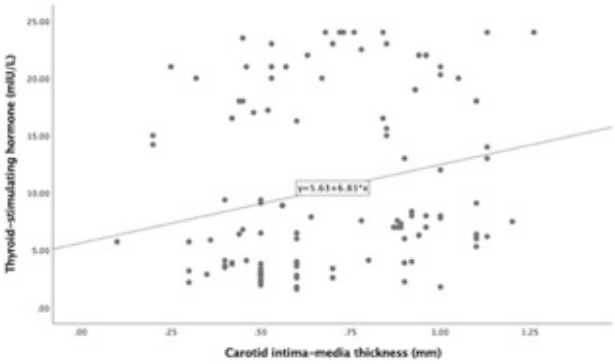

Fig. 5. Correlation between Thyroid stimulating hormone and carotid intima-media thickness (r = 0.236, $p = 0.009$).

multivariate linear analysis, TSH was an independent predictor of AVP (beta = –0.298; 95% CI = –0.946 to –0.287; $p < 0.001$).

ICCs for intra- and inter-observer reliability for AVP among 15 randomly selected patients were 0.92 (95% CI = 0.86–0.95) and 0.88 (95% CI = 0.82–0.94), respectively. ICCs for intra- and inter-observer reliability for EFT were 0.92 (95% CI = 0.85–0.94) and 0.90 (95% CI = 0.84–0.96), respectively.

4. Discussion

This study investigated the AVP, EFT, and CIMT values in SH patients and EU individuals. AVP was lower in SH patients compared to the control group, and AVP decreased significantly with an increase in TSH levels. SH patients had significantly higher CIMT values compared to EU individuals. In addition, TSH levels had a significant negative correlation with AVP as well as a positive correlation with CIMT and EFT. TSH levels were independently associated with AVP. These findings may explain the pathological mechanisms of cardiovascular diseases in SH patients.

Table 2. The demographic and clinical data of the patients with subclinical hypothyroidism and control group.

	Control (n = 43)	TSH <10 (n = 45)	TSH ≥10 (n = 35)	*p* value
Age (years)	46.7 ± 8.3	46.4 ± 15.7	42.2 ± 10.6	0.13
Body mass index (kg/m^2)	26.2 ± 2.4	26.6 ± 2.1	26.4 ± 2.6	0.71
White blood cell count (10^3/mm^3)	7.9 ± 1.8	6.7 ± 2.4	7.7 ± 1.6	0.02
Hemoglobin (g/dL)	14.5 ± 1.8	14.1 ± 1.6	14.6 ± 1.3	0.24
Platelet count (10^3/mm^3)	249.3 ± 76.8	244.4 ± 80.8	228.2 ± 64.0	0.38
Creatinine (mg/dL)	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.64
Sodium (mEq/L)	137.3 ± 4.2	137.5 ± 3.0	136.6 ± 2.7	0.46
albumin (g/dL)	3.5 ± 0.4	3.8 ± 0.6	3.8 ± 0.7	0.09
C-reactive protein (mg/L)	6.9 ± 2.4	6.3 ± 2.7	6.6 ± 2.1	0.12
Triglyceride (mg/dl)	205.2 ± 22.0	191.9 ± 39.8	209.6 ± 37.2	0.59
High density lipoprotein (mg/dL)	42.3 ± 11.4	43.6 ± 7.8	45.6 ± 8.6	0.18
Low density lipoprotein (mg/dL)	119.2 ± 28.5	118.9 ± 27.5	118.4 ± 41.1	0.99
Total cholesterol (mg/dL)	196.7 ± 36.5	190.5 ± 34.6	184.4 ± 31.1	0.24
Ejection fraction (%)	60.8 ± 2.6	60.1 ± 5.2	58.0 ± 6.2	0.02
AVP (cm/s)	62.6 ± 13.8	46.7 ± 14.5^a	41.4 ± 10.2^a	<0.001
EFT (mm)	0.6 ± 0.2	0.7 ± 0.3	0.7 ± 0.3	0.16
CIMT (mm)	0.5 ± 0.2	0.8 ± 0.3^a	0.7 ± 0.3^a	<0.001
T4 (µg/dL)	1.3 ± 0.11	1.4 ± 0.12^a	1.4 ± 0.13^a	0.001
TSH (mIU/L)	3.1 ± 0.7	7.2 ± 1.2^a	19.6 ± 3.5^{a,b}	<0.001

AVP, aortic velocity propagation; EFT, Epicardial fat thickness; CIMT, carotid intima-media thickness; T4, Thyroxine 4; TSH, Thyroid stimulant hormone. ^{a}Control vs other groups. ^{b}TSH <10 vs TSH ≥10. One-way analysis of variance (ANOVA) test followed by the Tukey post hoc test was used for multiple comparisons. $p < 0.05$ was considered statistically significant.

Table 3. Correlation between thyroid stimulant hormone (TSH) and clinical parameters in the study population.

AVP	r	–0.424
	p	<0.001
EFT	r	0.188
	p	0.038
CIMT	r	0.236
	p	0.009
TC	r	–0.126
	p	0.16
LDL	r	0.067
	p	0.46

TSH, Thyroid stimulant hormone; AVP, aortic velocity propagation; EFT, Epicardial fat thickness; CIMT, carotid intima-media thickness; TC, Total cholesterol; LDL, Low density lipoprotein.

Table 4. Independent predictors for Aortic velocity propagation (AVP) by multivariate linear regression analysis.

	B	t	*p*	95% CI
TSH	–0.298	–3.702	<0.001	–0.946–(–)0.287
CRP	0.078	0.996	0.321	–2.003
TC	0.128	1.628	0.106	–0.144

TSH, Thyroid stimulant hormone; CRP, C-reactive protein; TC, Total cholesterol. B, Regression coefficient; t, Degree of freedom; CI, confidence interval. $p < 0.05$ was considered statistically significant.

AVP is a parameter for aortic stiffness that can be measured during echocardiography. AVP had a significant correlation with aortic strain and distensibility in CAD patients [19]. Many studies have demonstrated increased vascular stiffness in patients with SH. However, a number of other studies did not find such an association.

Different mechanisms may be responsible for the change in arterial wall properties in SH patients. These mechanisms include endothelial dysfunction, increased angiotensin receptor expression, inflammation, and dyslipidemia [4, 20, 21]. In our study, SH patients had greater aortic stiffness than EU individuals. Moreover, AVP had a significant negative correlation with TSH levels, probably because TSH directly affects the arterial wall. We assumed that high TSH values may predispose SH patients to endothelial dysfunction and increased angiotensin receptor expression, leading to decreased blood velocity in the descending aorta. Previous studies have reported that TSH levels are negatively associated with endothelium-dependent dilatation [22]. Dardano *et al.* [20] reported that recombinant human TSH reduced vascular nitric oxide levels and induced inflammation leading to endothelium-dependent vasodilation in patients with thyroid disorders. TSH levels affect the aortic wall tension in SH patients. Yurtdaş *et al.* [6] demonstrated that SH patients

had higher aortic stiffness index, lower aortic distensibility, and reduced systolic aortic velocity compared to the control group.

Previous studies reported that SH patients had higher brachial-ankle pulse wave velocity, cardio-ankle vascular index, and flow-mediated dilatation compared to EU individuals [7, 23, 24]. Tian *et al.* [21] demonstrated that SH was associated with increased carotid arterial stiffness, likely to be due to increased high-sensitivity CRP levels. Arterial wall thickness, arterial stiffness, and endothelial dysfunction in SH patients was associated with increased cardiovascular risk [25]. Itterman *et al.* [26] reported that hypothyroidism (clinical or subclinical) was associated with atherosclerosis. Additionally, thoracic aortic wall thickness increased with increasing levels of TSH. However, Nagasaki *et al.* [23] did not find a correlation of brachial-ankle pulse wave velocity with TSH, T3, or T4 levels. Another study found normal arterial stiffness in SH patients [27]. The brachial-ankle pulse wave velocity was decreased in SH patients treated with thyroid hormone replacement [28]. In addition, thyroid hormone replacement reduces atherosclerosis by its direct effect on the blood vessels in SH patients [29]. This study demonstrated that AVP could be used to determine aortic stiffness in SH patients. In the regression analysis, TSH levels were independently associated with AVP in SH patients. We assumed that higher TSH levels caused endothelial dysfunction and increased arterial stiffness. Therefore, AVP decreased significantly with an increase in TSH values. Decreased AVP may indicate atherosclerosis in SH patients, and AVP decreases prior to clinically apparent vascular diseases.

EAT induces paracrine and vasocrine secretion of pro-inflammatory and pro-atherogenic cytokines into the myocardium that affect the cardiac function [11]. EAT may also contribute to the pathogenesis and development of CAD due to the production of several inflammatory adipokines [30]. Besides, the mechanical effects of EAT may also contribute to the development of atherosclerosis [31]. A previous study reported that there was increased TSH receptor expression in EAT, which may affect the cardiac function and pathology [32]. The relationships between EFT and TSH levels in SH patients are controversial. Korkmaz *et al.* [12] demonstrated the EFT values in 61 newly diagnosed SH patients and 24 controls. SH patients had higher EFT values that correlated with the TSH levels. Additionally, SH patients with TSH $\geq$10 mIU/L had higher EFT values compared to SH patients with TSH $<$10 mIU/L. The EFT increased with increasing severity of SH. A recent study found that EFT was increased in SH patients, and correlated significantly with TSH levels. However, this study only included SH patients with TSH $\geq$10 mIU/L [33]. Arpaci *et al.* [34] found similar EFT values between 41 SH patients and 35 EU individuals, and there was no correlation between TSH and EFT values. Santos *et al.* [13] observed similar EFT values between SH patients with TSH $<$10 mIU/L and the control group. However, TSH was significantly correlated with EFT in SH patients. In contrast to the studies conducted by Santos and Aşık, our study evaluated SH patients with TSH $\geq$10 or TSH $<$10 mIU/L and found similar EFT values between SH patients and EU individuals. However, in the correlation analyses, TSH levels were correlated with EFT values.

CIMT can be safely measured using ultrasound images, and it may indicate subclinical atherosclerosis. Carotid plaques are an early surrogate marker of systemic atherosclerosis and predict major cardiovascular events [35]. Hypothyroidism is associated with accelerated atherosclerosis. A previous study showed that CIMT was an objective sign of accelerated atherosclerosis in patients with primary hypothyroidism [36]. Saif *et al.* [37] demonstrated that CIMT was higher in overt hypothyroidism and SH patients compared to the controls. Additionally, endothelial dysfunction was associated with increased CIMT values in patients with SH or overt hypothyroidism [37]. A recent meta-analysis reported similar CIMT values in SH patients with TSH $\geq$10.0 mIU/L and EU individuals. However, the CIMT values were higher in SH patients with TSH $\geq$10.0 mIU/L compared to SH patients with TSH $<$10.0 mIU/L [24]. Another meta-analysis reported that CIMT was significantly higher in SH patients with TSH $\geq$10.0 mIU/L compared to EU individuals. However, there was significant heterogeneity in CIMT values between SH patients with TSH $<$10.0 mIU/L and EU individuals [17]. ELSA-Brasil was the largest study to evaluate the association between CIMT values and SH. In that study, SH was associated with higher CIMT values than in EU individuals [38]. Cabral *et al.* [27] demonstrated higher CIMT values in 21 female SH patients with positive serum anti-thyroid peroxidase antibodies (anti-TPO-Ab) compared to 21 female patients with negative anti-TPO-Ab. However, this difference was not statistically significant [27].

Other studies did not report any significant association between SH and CIMT. Almeida *et al.* demonstrated that CIMT values were similar between SH patients with TSH $\geq$8 or TSH $<$8 mIU/L and positive or negative anti-TPO-Abs. They did not find an association of mild SH (in the absence of relevant metabolic changes) with the cardiovascular risk. Delitala *et al.* [39] demonstrated that the thyroid hormone levels were not associated with carotid artery plaque or increased CIMT. Additionally, Valentina *et al.* [15] reported that TSH levels were associated with higher CIMT values, independently of other risk factors such as dyslipidemia, hypertension, and age. They concluded that TSH may be responsible for increased CIMT in SH patients [15]. Our study showed that TSH had a weak and positive correlation with CIMT values. The CIMT values were increased in SH patients independently of traditional risk factors. We assumed that higher CIMT values in SH patients were related to endothelial dysfunction. Our findings are consistent with those of previous studies, which are that the increase in CIMT values in SH patients began in the subclinical stage.

5. Limitations

There were a few limitations to this study. This was a single-center study based on a relatively small group of patients. The sample size may not be large enough to generalize the results of this study. Women are more prone to thyroid diseases than men. There were more female patients in the SH group than the control group. However, this difference was not statistically significant ($p = 0.06$). This difference in the sex ratio may explain the absence of sex differences in our study. We did not evaluate the autoimmune antibodies, such as anti-thyroglobulin antibody or anti-TPO-Ab, or their relationship with aortic stiffness. Pulse wave velocity is the gold standard for measuring arterial stiffness. However, we did not measure it in our study. We did not use magnetic resonance imaging or computed tomography to measure EFT. However, the use of echocardiography for the measurement of EFT is less costly and widely accepted. TC levels were similar between the study groups, probably because of the small number of patients and unknown duration of SH. A large randomized clinical trial is needed to validate these findings.

6. Conclusions

In conclusion, we found that AVP was lower and CIMT was higher in SH patients compared to EU individuals. Different mechanisms may be responsible for the role of TSH in aortic stiffness and subclinical atherosclerosis in SH patients. These mechanisms should be investigated further. The present study suggested that AVP, EFT, and CIMT should be routinely measured in SH patients.

Author contributions

EA, RA—conception and design of the study, provision of study material and patients. EA, ZD, TA—data collection and analysis, provision of study material and patients. EA, ZD—study oversight and critical revision of the article, provision of study material and patients. EA, TA, RA—analysis and interpretation of data, drafting of the article.

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Van Training and Research Hospital (approval number: 2020/25).

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Conflict of interest

The authors declare no conflict of interest.

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