

Aortic Wall Stiffness in Obese Children: Evaluation of Its Relationship with Subclinical Hypothyroidism – A Cross-Sectional Study

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Abstract

Background

Childhood obesity predisposes to early cardiovascular risk, and subclinical hypothyroidism — elevated thyroid-stimulating hormone with normal free thyroxine — is more prevalent in obese children and may compound vascular risk. We aimed to evaluate its association with echocardiographic aortic elasticity in obese children aged 5–18 years. We hypothesized that subclinical hypothyroidism would be associated with reduced aortic elasticity.

Methods

In this prospective cross-sectional study, 82 obese children (5–18 years) presenting to the Pediatric Endocrinology and Pediatric Cardiology clinics of Kütahya Health Sciences University City Hospital (March 2024–March 2025) were enrolled: 41 with mild subclinical hypothyroidism (thyroid-stimulating hormone 4.5–10 mIU/mL) and 41 euthyroid controls. Aortic strain, distensibility, stiffness index, and pressure–strain elastic modulus were calculated from M-mode echocardiography.

Results

Aortic elasticity parameters did not differ between the subclinical hypothyroidism and control groups (all $p > 0.05$). Aortic diastolic diameter, glucose, and aspartate aminotransferase were significantly higher in children with thyroid-stimulating hormone of 7 mIU/mL or higher ($p = 0.042$, 0.036 , and 0.026). In an exploratory, Bonferroni-corrected regression analysis, systolic blood pressure was the only independent predictor of aortic elasticity; thyroid-stimulating hormone showed no independent association with any parameter.

Conclusions

Subclinical hypothyroidism was not associated with measurable changes in aortic elasticity, refuting our hypothesis. A thyroid-stimulating hormone threshold of 7 mIU/mL or higher identified a subgroup with increased aortic diastolic diameter and metabolic perturbation, though this was not confirmed within the subclinical hypothyroidism group alone and did not survive Bonferroni correction. Systolic blood pressure, not thyroid-stimulating hormone, emerged as the independent correlate of aortic elasticity.

INTRODUCTION

Childhood obesity predisposes to early cardiovascular risk. Beyond its metabolic consequences, obesity initiates early vascular changes that may set the stage for adult cardiovascular disease; arterial

stiffness, an early, independent marker of cardiovascular risk, is detectable in obese children before overt disease develops [1, 2].

Echocardiographic aortic elasticity parameters — aortic strain (AS), aortic root distensibility (AD), aortic stiffness index (β), and pressure–strain elastic modulus (Ep) — provide non-invasive, reproducible measures of subclinical vascular damage obtainable during routine echocardiography [3, 4].

Subclinical hypothyroidism (SH) is defined by elevated TSH with normal free thyroxine (fT4); severe SH (TSH > 10 mIU/mL) generally warrants treatment, while mild SH (TSH 4.5–10 mIU/mL), the focus of this study, remains clinically debated and is typically asymptomatic [5, 6]. SH prevalence is 1.7–9.5% in the general pediatric population but rises to 10–23% among obese children [7, 8]. Thyroid hormones regulate heart rate, contractility, vascular resistance, and arterial wall compliance, so even subtle dysfunction may affect vascular structure [9].

In adults with obesity, SH is associated with increased arterial stiffness, endothelial dysfunction, dyslipidemia, and cardiovascular risk [10, 11], but pediatric evidence is considerably thinner. This study compared echocardiographic aortic elasticity parameters between obese children with and without SH.

MATERIAL AND METHODS

Study Design and Participants

This prospective cross-sectional study enrolled 82 obese children and adolescents aged 5–18 years, consecutively recruited at the Pediatric Endocrinology and Pediatric Cardiology outpatient clinics of Kütahya Health Sciences University Kütahya City Hospital between March 2024 and March 2025. Ethical approval was obtained from the Institutional Review Board of Kütahya Health Sciences University Faculty of Medicine (Decision No: 2024/05–41). Written informed consent was obtained from the parent/legal guardian of all participants, with assent obtained from participants where age-appropriate.

Forty-one patients with serum TSH 4.5–10 mIU/mL and normal fT4 constituted the SH group (Group 1); 41 with TSH within the normal reference range constituted the euthyroid control group (Group 2).

Exclusion criteria included syndromic or secondary (metabolic/endocrine) obesity (e.g., Cushing syndrome, growth hormone deficiency, hypothalamic obesity); known or previously diagnosed thyroid disease, positive thyroid autoantibodies, or risk factors for thyroid disease (e.g., prior neck radiation, family history, Down or Turner syndrome); known cardiovascular or congenital heart disease; and hypertension (blood pressure SDS > 2 on repeated measurement).

Anthropometric and Clinical Measurements

All measurements were taken with the patient in undergarments, without shoes. Height was measured with a calibrated Seca stadiometer (0.1 cm); weight with a calibrated Seca digital scale (0.1 kg). BMI was

calculated as weight (kg)/height² (m²); obesity was defined as age- and sex-specific BMI ≥ 95th percentile. BMI-SDS and blood pressure SDS were calculated using the Child Metrics web-based calculator [12].

Blood pressure was measured with a Welch Allyn digital sphygmomanometer using an appropriately sized cuff; after ≥ 15 minutes of rest, three measurements were taken at 15-minute intervals in the seated position and averaged.

Biochemical Analysis

Venous blood was collected after a 12-hour fast into gel-separator tubes, centrifuged at 4000 rpm for 10 minutes, and analyzed at the Biochemistry Laboratory of Kütahya Health Sciences University. Fasting glucose, insulin, lipid profile, AST, ALT, HbA1c, TSH, and fT4 were measured using Roche Cobas c702 analyzers (electrochemiluminescence for TSH, fT4, insulin; colorimetric/enzymatic for others); HbA1c was measured by capillary electrophoresis (Capillarys Tera 3).

Echocardiographic Evaluation

All echocardiographic studies were performed by a single experienced pediatric cardiologist using a Philips Affinity 50C system with age-appropriate transducers. Patients were examined supine or in slight left lateral decubitus; absence of congenital or acquired valvular/structural heart disease was confirmed prior to aortic measurements.

Aortic diameters were measured 3 cm above the aortic valve in the parasternal long-axis view by two-dimensional guided M-mode echocardiography. Aortic systolic diameter (AOS) was measured at maximal valve opening; aortic diastolic diameter (AOD) at the peak of the QRS complex on simultaneous ECG. Aortic elasticity parameters were calculated as follows:

$$\text{Aortic Strain (AS, \%)} = 100 \times (\text{AOS} - \text{AOD}) / \text{AOD}$$

$$\text{Aortic Root Distensibility (AD, } \times 10^{-6} \text{ cm}^2/\text{dyn}) = 2 \times (\text{AOS} - \text{AOD}) / (\text{AOD} \times \text{PP}) \times 1333$$

$$\text{Aortic Stiffness Index } (\beta) = \ln(\text{SBP}/\text{DBP}) \times \text{AOD} / (\text{AOS} - \text{AOD})$$

$$\text{Aortic Pressure–Strain Elastic Modulus (Ep, mmHg)} = \text{PP} / [(\text{AOS} - \text{AOD}) / \text{AOD}]$$

PP denotes pulse pressure (SBP – DBP). AD values were converted from mmHg⁻¹ to ×10⁻⁶ cm²/dyn using the factor 1333 dyn/cm² per mmHg.

Statistical Analysis

Statistical analysis used SPSS version 26. Normality was assessed by Kolmogorov–Smirnov testing; normally distributed variables are presented as mean $\pm$ SD and compared by independent-samples t-test, non-normally distributed variables as median (IQR) and compared by Mann–Whitney U test, and categorical variables by chi-square or Fisher's exact test ($p < 0.05$ significant). A pre-specified secondary analysis compared TSH < 7 vs ≥ 7 mIU/mL subgroups; because this involved six aortic parameters and a small ($n = 9$) subgroup, Bonferroni correction was applied (corrected threshold $p < 0.008$). Linear regression with TSH as a continuous predictor (adjusted for age, height, BMI-SDS) tested whether categorical findings reflected a true dose–response relationship. In an exploratory analysis, univariate linear regression screened fifteen clinical/biochemical variables against the three continuous aortic elasticity parameters (stiffness index and distensibility log-transformed for non-normality); variables significant at $p < 0.10$ were entered into multivariate models with TSH (forced entry), with variance inflation factors checked for collinearity. Bonferroni correction was applied separately across the 45 univariate tests ($p < 0.0011$) and 16 multivariate coefficients ($p < 0.0031$).

RESULTS

Study Population

A total of 82 obese patients were enrolled: 41 in the SH group and 41 in the euthyroid control group, comprising 41 girls and 41 boys (50% each). Mean age was 11.62 ± 2.82 years; mean BMI 29.89 ± 4.87 kg/m² (median BMI-SDS 2.66, IQR 1.24, range 1.74–4.23).

Median fasting glucose was 88.90 mg/dL, insulin 24.84 μ U/mL, HbA1c 5.56%; mean TSH 4.36 ± 1.99 mIU/mL, fT4 1.06 ± 0.27 ng/dL; median SBP/DBP 106/66 mmHg.

Comparison between SH and Euthyroid Groups

Groups were well matched for age, weight, height, BMI, BMI-SDS, blood pressure, glucose, insulin, HbA1c, lipids, and liver enzymes (all $p > 0.05$). TSH was significantly higher in Group 1 (6.08 ± 1.09 vs. 2.65 ± 0.88 mIU/mL; $p < 0.001$); fT4 did not differ (1.05 ± 0.25 vs. 1.08 ± 0.29 ng/dL; $p = 0.66$).

Echocardiographic comparison showed no significant between-group differences in any aortic elasticity parameter (Table 1): AOS 2.29 ± 0.32 vs. 2.25 ± 0.28 cm ($p = 0.50$); AOD 1.98 ± 0.35 vs. 1.93 ± 0.29 cm ($p = 0.45$); AS 16.59 ± 7.80 vs. $17.14 \pm 7.10\%$ ($p = 0.74$); AD 6.48 ± 3.30 vs. $6.92 \pm 3.75 \times 10^{-6}$ cm²/dyn ($p = 0.58$); β 3.86 vs. 3.32 ($p = 0.98$); Ep 320.68 vs. 286.91 mmHg ($p = 0.94$). Parameters also did not differ by sex (all $p > 0.05$).

Table 1

Comparison of demographic, laboratory, and aortic parameters between the subclinical hypothyroidism (Group 1) and euthyroid control (Group 2) groups.

Parameter	Group 1 – SH (n = 41)	Group 2 – Control (n = 41)	p-value
Age (years)	12.03 ± 2.66	11.22 ± 2.95	0.19
Weight (kg)	73.00 (24.00)	73.00 (32.00)	0.67
Height (cm)	152.85 ± 14.84	149.20 ± 15.43	0.27
BMI (kg/m ²)	29.85 ± 4.72	29.94 ± 5.07	0.93
BMI-SDS	2.50 (0.77)	2.66 (0.73)	0.29
Glucose (mg/dL)	89.00 (12.00)	85.00 (9.00)	0.18
Insulin (μU/mL)	20.80 (12.65)	20.70 (17.40)	0.84
HbA1c (%)	5.60 (0.35)	5.60 (0.40)	0.75
TSH (mIU/mL)	6.08 ± 1.09	2.65 ± 0.88	< 0.001*
fT4 (ng/dL)	1.05 ± 0.25	1.08 ± 0.29	0.66
AST (U/L)	21.00 (8.60)	22.50 (7.00)	0.25
ALT (U/L)	18.60 (9.60)	22.00 (10.80)	0.13
Total Cholesterol (mg/dL)	155.00 (26.00)	152.00 (38.00)	0.93
Triglycerides (mg/dL)	116.00 (73.40)	109.00 (49.00)	0.30
HDL-C (mg/dL)	41.00 (7.00)	44.70 (14.00)	0.27
LDL-C (mg/dL)	89.66 ± 23.60	89.59 ± 29.14	0.99
SBP (mmHg)	110.00 (10.00)	110.00 (20.00)	0.93
DBP (mmHg)	70.00 (10.00)	70.00 (10.00)	0.63
SBP-SDS	0.20 (1.10)	0.33 (1.02)	0.50
DBP-SDS	0.58 (0.59)	0.58 (0.69)	0.68
AOS (cm)	2.29 ± 0.32	2.25 ± 0.28	0.50
AOD (cm)	1.98 ± 0.35	1.93 ± 0.29	0.45
Aortic Strain (%)	16.59 ± 7.80	17.14 ± 7.10	0.74
Aortic Distensibility (×10 ⁻⁶ cm ² /dyn)	6.48 ± 3.30	6.92 ± 3.75	0.58
Stiffness Index (β)	2.70 (2.68)	3.01 (1.68)	0.98

Parameter	Group 1 – SH (n = 41)	Group 2 – Control (n = 41)	p-value
Ep (mmHg)	320.68 (251.10)	286.91 (177.87)	0.94

Normally distributed values are mean $\pm$ SD; non-normally distributed values are median (IQR). Abbreviations as in List of Abbreviations.

Subgroup Analysis by TSH Threshold (≥ 7 mIU/mL)

Stratifying by TSH < 7 (n = 73) vs ≥ 7 mIU/mL (n = 9), the higher-TSH subgroup had greater AOD (2.16 ± 0.39 vs. 1.93 ± 0.30 cm; p = 0.042), though this did not survive Bonferroni correction (threshold p < 0.008). AOS, pulse pressure, strain, distensibility, β , and Ep did not differ (all p > 0.05). Glucose (p = 0.036) and AST (p = 0.026) were higher in the TSH ≥ 7 group; no other metabolic/lipid parameters differed (Table 2).

Table 2
Comparison of aortic and metabolic parameters between TSH < 7 mIU/mL and TSH ≥ 7 mIU/mL subgroups.

Parameter	TSH < 7 (n = 73)	TSH ≥ 7 (n = 9)	p-value
Age (years)	11.53 ± 2.85	12.38 ± 2.63	0.40
Weight (kg)	73.00 (31.00)	75.00 (22.40)	0.55
Height (cm)	150.37 ± 14.93	156.33 ± 16.85	0.27
BMI (kg/m ²)	29.86 ± 4.87	30.12 ± 5.15	0.89
BMI-SDS	2.60 (0.81)	2.33 (1.05)	0.34
Glucose (mg/dL)	86.00 (10.60)	93.00 (8.00)	0.036*
Insulin (μU/mL)	21.50 (14.72)	18.70 (12.30)	0.86
HbA1c (%)	5.60 (0.40)	5.50 (0.45)	0.92
TSH (mIU/mL)	3.94 ± 1.67	7.76 ± 0.62	< 0.001*
fT4 (ng/dL)	1.08 ± 0.27	0.95 ± 0.28	0.20
AST (U/L)	21.50 (8.00)	25.60 (6.00)	0.026*
ALT (U/L)	20.00 (10.00)	28.00 (17.20)	0.12
Total Cholesterol (mg/dL)	152.70 (30.30)	162.00 (14.00)	0.19
Triglycerides (mg/dL)	109.20 (64.00)	146.00 (85.70)	0.098
HDL-C (mg/dL)	44.00 (13.00)	39.00 (4.50)	0.12
LDL-C (mg/dL)	88.68 ± 26.91	97.22 ± 21.01	0.36
SBP (mmHg)	110.00 (10.00)	120.00 (20.00)	0.17
DBP (mmHg)	70.00 (10.00)	70.00 (0.00)	0.40
SBP-SDS	0.25 (1.24)	0.58 (1.12)	0.25
DBP-SDS	0.58 (0.69)	0.55 (0.22)	0.79
AOS (cm)	2.25 ± 0.30	2.42 ± 0.31	0.116
AOD (cm)	1.93 ± 0.30	2.16 ± 0.39	0.042*
Aortic Strain (%)	17.32 ± 7.36	13.20 ± 7.27	0.117
Aortic Distensibility (×10 ⁻⁶ cm ² /dyn)	6.83 ± 3.45	5.33 ± 3.92	0.226
Stiffness Index (β)	2.92 (1.77)	3.67 (4.96)	0.276
Ep (mmHg)	279.51 (171.97)	500.78 (632.54)	0.175

** $p < 0.05$. Normally distributed values are mean $\pm$ SD; non-normally distributed values are median (IQR).*

Abbreviations as in List of Abbreviations.

Within-Group Stratification of the Subclinical Hypothyroidism Group by TSH Magnitude

Restricting to the SH group alone (TSH ≥ 7 , $n = 9$, vs 4.5–6.9 mIU/mL, $n = 32$; euthyroid controls excluded), AOD no longer differed (2.16 ± 0.39 vs. 1.93 ± 0.32 cm; $p = 0.85$), nor did AOS or any other aortic elasticity parameter (all $p > 0.05$). AST ($25.60 [6.00]$ vs. $19.35 [7.50]$ U/L; $p = 0.008$) and ALT ($28.00 [17.20]$ vs. $17.00 [9.18]$ U/L; $p = 0.036$) remained significantly higher in the TSH ≥ 7 subgroup (Table 3).

Table 3

Comparison of demographic, laboratory, and aortic parameters within the subclinical hypothyroidism group, stratified by TSH ≥ 7 mIU/mL (n = 9) versus TSH 4.5–6.9 mIU/mL (n = 32).

Parameter	TSH ≥ 7 (n = 9)	TSH 4.5–6.9 (n = 32)	p-value
Age (years)	12.38 $\pm$ 2.63	11.93 $\pm$ 2.70	0.65
Weight (kg)	75.00 (22.40)	73.00 (31.75)	0.67
Height (cm)	156.33 $\pm$ 16.85	152.87 $\pm$ 14.36	0.43
BMI (kg/m ²)	30.12 $\pm$ 5.15	29.77 $\pm$ 4.68	0.85
BMI-SDS	2.33 (1.05)	2.50 (0.77)	0.50
Glucose (mg/dL)	93.00 (8.00)	88.50 (10.65)	0.08
Insulin (μ U/mL)	18.70 (12.30)	21.60 (11.90)	0.74
HbA1c (%)	5.50 (0.45)	5.60 (0.33)	0.98
TSH (mIU/mL)	7.76 $\pm$ 0.62	5.15 $\pm$ 0.62	< 0.01*
fT4 (ng/dL)	0.95 $\pm$ 0.28	1.08 $\pm$ 0.25	0.20
Total Cholesterol (mg/dL)	162.00 (14.00)	153.30 (25.33)	0.13
Triglycerides (mg/dL)	146.00 (85.70)	111.85 (75.95)	0.20
HDL-C (mg/dL)	39.00 (4.50)	43.00 (11.25)	0.19
LDL-C (mg/dL)	97.22 $\pm$ 21.01	87.29 $\pm$ 28.34	0.28
AST (U/L)	25.60 (6.00)	19.35 (7.50)	0.008*
ALT (U/L)	28.00 (17.20)	17.00 (9.18)	0.036*
SBP (mmHg)	120.00 (20.00)	110.00 (10.00)	0.13
DBP (mmHg)	70.00 (0.00)	70.00 (10.00)	0.45
SBP-SDS	0.58 (1.12)	0.07 (0.94)	0.12
DBP-SDS	0.55 (0.22)	0.59 (0.67)	0.92
AOS (cm)	2.42 $\pm$ 0.31	2.26 $\pm$ 0.32	0.85
AOD (cm)	2.16 $\pm$ 0.39	1.93 $\pm$ 0.32	0.82
Aortic Strain (%)	13.20 $\pm$ 7.27	17.55 $\pm$ 7.78	0.14
Aortic Distensibility ($\times 10^{-6}$ cm ² /dyn)	5.34 $\pm$ 3.92	6.80 $\pm$ 3.10	0.24
Stiffness Index (β)	3.67 (4.96)	2.69 (1.93)	0.25
Ep (mmHg)	500.78 (632.54)	270.03 (162.04)	0.16

** $p < 0.05$. Normally distributed values are mean $\pm$ SD; non-normally distributed values are median (IQR). Euthyroid controls ($n = 41$) excluded. Abbreviations as in List of Abbreviations.*

Univariate and Multivariate Predictors of Aortic Elasticity Parameters

Because only aortic strain, stiffness index, and distensibility were available as continuous echocardiographic outcomes, univariate linear regression screened fifteen candidate variables (age, sex, BMI-SDS, TSH, glucose, insulin, HbA1c, AST, ALT, total cholesterol, triglycerides, HDL-C, LDL-C, SBP, DBP) against each outcome, with Bonferroni correction across 45 tests (threshold $p < 0.0011$; Table 4). After correction, DBP remained associated with strain, and SBP and age with both stiffness index and distensibility (all $p\text{-adj} < 0.03$); DBP was additionally significant for distensibility ($p\text{-adj} = 0.002$). No other variable, including HDL-C and total cholesterol, remained significant. TSH showed no association with any parameter, before or after correction (all $p\text{-adj} = 1.000$).

Variables significant at $p < 0.10$ univariately were entered into multivariate models with TSH (forced entry); VIFs were < 2.2 throughout. Bonferroni correction was applied across 16 coefficients (threshold $p < 0.0031$; Table 5). SBP was the only independent predictor surviving correction: for stiffness index (2.5% relative increase per mmHg; $p\text{-adj} = 0.017$) and distensibility (2.9% relative decrease per mmHg; $p\text{-adj} = 0.001$). DBP showed a comparable association with strain ($B = -0.43$; $p = 0.004$) but did not survive correction ($p\text{-adj} = 0.068$; $R^2 = 0.34$). HDL-C, nominally associated with all three outcomes before correction, remained non-significant afterward (all $p\text{-adj} \geq 0.18$). TSH was not an independent predictor in any model, before or after correction (all $p\text{-adj} = 1.000$).

Table 4

Univariate linear regression analyses of clinical and biochemical predictors of aortic elasticity parameters (whole cohort, n = 82), corrected for multiple testing. Columns 2–3: Aortic Strain (%); columns 4–5: ln(Aortic Stiffness Index); columns 6–7: ln(Aortic Distensibility).

Parameter	B (95% CI)	p / p-adj	B (95% CI)	p / p-adj	B (95% CI)	p / p-adj
Age	-0.901 (-1.450, -0.352)	0.002 / 0.072	0.071 (0.032, 0.110)	< 0.001 / 0.024*	-0.090 (-0.131, -0.049)	< 0.001 / 0.002*
Sex	0.643 (-2.636, 3.922)	0.697 / 1.000	-0.051 (-0.287, 0.185)	0.666 / 1.000	0.043 (-0.214, 0.299)	0.741 / 1.000
BMI-SDS	-0.118 (-3.124, 2.888)	0.938 / 1.000	0.062 (-0.154, 0.278)	0.568 / 1.000	-0.091 (-0.325, 0.143)	0.440 / 1.000
TSH	-0.514 (-1.336, 0.307)	0.216 / 1.000	0.038 (-0.021, 0.097)	0.207 / 1.000	-0.040 (-0.105, 0.024)	0.214 / 1.000
Fasting glucose	-0.062 (-0.262, 0.137)	0.534 / 1.000	0.008 (-0.007, 0.022)	0.285 / 1.000	-0.011 (-0.026, 0.005)	0.169 / 1.000
Insulin	0.022 (-0.076, 0.120)	0.659 / 1.000	-0.002 (-0.009, 0.005)	0.537 / 1.000	0.001 (-0.007, 0.009)	0.794 / 1.000
HbA1c	-1.201 (-6.641, 4.240)	0.662 / 1.000	0.064 (-0.328, 0.456)	0.745 / 1.000	-0.079 (-0.504, 0.346)	0.712 / 1.000
AST	-0.067 (-0.229, 0.096)	0.415 / 1.000	0.001 (-0.011, 0.013)	0.873 / 1.000	-0.001 (-0.014, 0.012)	0.857 / 1.000
ALT	-0.054 (-0.135, 0.027)	0.191 / 1.000	0.002 (-0.004, 0.008)	0.569 / 1.000	-0.002 (-0.009, 0.004)	0.445 / 1.000
Total cholesterol	-0.046 (-0.095, 0.003)	0.067 / 1.000	0.003 (-0.001, 0.006)	0.158 / 1.000	-0.003 (-0.007, 0.001)	0.138 / 1.000
Triglycerides	-0.019 (-0.046, 0.009)	0.188 / 1.000	0.001 (-0.001, 0.003)	0.325 / 1.000	-0.001 (-0.004, 0.001)	0.196 / 1.000
HDL-C	-0.262 (-0.439, -0.085)	0.004 / 0.190	0.014 (0.001, 0.027)	0.033 / 1.000	-0.015 (-0.029, -0.000)	0.043 / 1.000
LDL-C	-0.035 (-0.097, 0.027)	0.270 / 1.000	0.002 (-0.002, 0.007)	0.308 / 1.000	-0.002 (-0.007, 0.002)	0.322 / 1.000

Parameter	B (95% CI)	p / p-adj	B (95% CI)	p / p-adj	B (95% CI)	p / p-adj
SBP	-0.251 (-0.401, -0.101)	0.001 / 0.060	0.024 (0.014, 0.035)	< 0.001 / <0.001*	-0.032 (-0.043, -0.022)	< 0.001 / <0.001*
DBP	-0.589 (-0.815, -0.363)	< 0.001 / <0.001*	0.027 (0.010, 0.045)	0.003 / 0.137	-0.040 (-0.058, -0.021)	< 0.001 / 0.002*

*B, unstandardized regression coefficient; CI, confidence interval. p / p-adj: raw / Bonferroni-corrected p-value across the 45 univariate tests (threshold $p < 0.0011$); *p-adj < 0.05. Stiffness index and distensibility were log-transformed for non-normality; strain was untransformed. Other abbreviations as in List of Abbreviations.*

Table 5

Multivariate linear regression models for independent predictors of aortic elasticity parameters, adjusted for TSH (forced entry) and covariates significant at $p < 0.10$ in univariate analysis, corrected for multiple testing.

Parameter	Aortic Strain (%) B (95% CI)	p / p-adj	ln(Stiffness Index) B (95% CI)	p / p-adj	ln(Distensibility) B (95% CI)	p / p-adj
Age	-0.162 (-0.816, 0.492)	0.624 / 1.000	0.012 (-0.035, 0.058)	0.620 / 1.000	-0.011 (-0.058, 0.035)	0.635 / 1.000
SBP	-0.074 (-0.274, 0.127)	0.467 / 1.000	0.024 (0.010, 0.039)	0.001 / 0.017*	-0.030 (-0.044, -0.015)	< 0.001 / 0.001*
DBP	-0.426 (-0.714, -0.139)	0.004 / 0.068	-0.003 (-0.024, 0.018)	0.760 / 1.000	-0.004 (-0.025, 0.017)	0.695 / 1.000
HDL-C	-0.204 (-0.391, -0.016)	0.034 / 0.539	0.016 (0.004, 0.028)	0.011 / 0.182	-0.016 (-0.028, -0.004)	0.011 / 0.173
Total cholesterol	-0.007 (-0.056, 0.042)	0.781 / 1.000	—	—	—	—
TSH	-0.367 (-1.079, 0.344)	0.307 / 1.000	0.035 (-0.016, 0.087)	0.179 / 1.000	-0.036 (-0.087, 0.016)	0.173 / 1.000
R ² (adj.)	0.335 (0.282)		0.310 (0.265)		0.416 (0.377)	

*Each column pair reports the adjusted coefficient (95% CI) and raw/Bonferroni-corrected p-value across the 16 coefficients tested (threshold $p < 0.0031$); *p-adj < 0.05. Aortic Strain model additionally adjusted for total*

cholesterol (TC), not included in the other two models (did not meet $p < 0.10$ screening). VIFs were < 2.2 throughout, indicating no problematic multicollinearity. Other abbreviations as in List of Abbreviations.

DISCUSSION

The principal finding is that obese children with SH, compared as a group to euthyroid obese controls, showed no significant differences in aortic elasticity parameters. However, a pre-specified TSH ≥ 7 mIU/mL subgroup analysis revealed a larger AOD along with higher glucose and AST, though these findings require cautious interpretation given the small subgroup and did not remain significant after Bonferroni correction. When restricted to the SH group alone (TSH ≥ 7 vs. 4.5–6.9 mIU/mL, excluding controls), the AOD difference was no longer significant, likely reflecting the narrower comparison; however, AST and ALT remained significantly elevated in the higher-TSH subgroup, reinforcing a possible link between higher TSH burden and early hepatic/metabolic perturbation independent of comparison group (Table 3).

Our exploratory regression analysis (Tables 4 and 5), with Bonferroni correction, supports this: TSH was not an independent predictor of any aortic elasticity parameter, before or after correction (all $p\text{-adj} = 1.000$). Systolic blood pressure alone remained independent after correction, for stiffness index and distensibility — physiologically expected, since arterial pressure directly loads the aortic wall. Diastolic blood pressure and HDL-cholesterol showed nominal associations that did not survive correction ($p\text{-adj} = 0.068$ and ≥ 0.18) and should be regarded as hypothesis-generating, explaining why the isolated AOD finding in the TSH ≥ 7 subgroup (Table 2) also did not persist.

Our results are consistent with existing pediatric literature. Brienza et al. [13] found no significant differences in BMI-SDS, blood pressure, lipids, or insulin resistance between 34 obese children with SH and 60 euthyroid obese controls. Cerbone et al. [14] found no differences in blood pressure, BMI, or homocysteine between 49 children with idiopathic SH and 49 controls, though the SH group showed mildly pro-atherogenic lipid abnormalities. Sert et al. [15] similarly found no association between SH and cardiovascular risk factors in obese adolescents, with obesity itself the dominant risk modifier. To our knowledge, this is the first study in the literature to evaluate aortic elasticity parameters in obese children with and without SH, demonstrating that these parameters do not differ between the two groups; we believe this represents a novel contribution to the existing literature.

The contrast between the robust adult evidence base and our neutral pediatric findings is biologically plausible. Adult arteries accumulate decades of insults — elastin degradation, collagen deposition, glycation cross-linking, intimal thickening — that alter mechanical properties, whereas pediatric arteries have a high elastin-to-collagen ratio, an intact intima, and strong endothelial regenerative capacity [16]. This may explain why group-level stiffness differences were undetectable in our cohort despite significantly elevated TSH in one group. TSH elevation in children more often reflects a transient, functional state than persistent, structural hypothyroidism, and may not exert a chronic enough influence to damage the vascular wall.

Nevertheless, the increased AOD in the TSH ≥ 7 mIU/mL subgroup warrants attention. Aortic diastolic diameter reflects resting aortic caliber and may increase in early reduced-compliance states, as the vessel cannot efficiently recoil during diastole. Its increase without a concomitant AOS change could reflect an early, isolated impairment in diastolic recoil – a possible precursor to more pronounced stiffness changes. This aligns with adult data showing subtle arterial stiffness changes even within the upper-normal TSH range, detectable by pulse-wave analysis [17, 21].

The higher glucose and AST in the TSH ≥ 7 group are also noteworthy: elevated glucose may reflect early hepatic insulin resistance, consistent with elevated AST (a marker of hepatic inflammation/early fatty liver disease); if sustained, these could raise long-term risk of diabetes and steatohepatitis, both linked to accelerated vascular aging [18, 19]. However, hepatic steatosis and glucose tolerance were not formally assessed.

Thyroid hormones regulate vascular smooth muscle tone, endothelial nitric oxide bioavailability, and elastin–collagen balance in the arterial wall; even subclinical deficiency may impair endothelial-dependent vasodilation and increase peripheral resistance, with effects accumulating over years [9]. A 2022 meta-analysis of 1239 SH patients, 81 overt hypothyroid patients, 338 thyrotoxicosis patients, and 12,715 controls across 11 adult observational studies found both overt and subclinical hypothyroidism significantly associated with increased aortic stiffness [20]. Our study does not provide sufficient evidence that SH causes clinically meaningful cardiac effects in childhood.

There is ongoing debate about the threshold for initiating levothyroxine in children with SH; guidelines generally recommend treatment above TSH 10 mIU/mL [5, 6]. Our finding at TSH ≥ 7 mIU/mL should be interpreted cautiously, since the AOD difference was not confirmed within the SH group alone (Table 3). Yadav et al. [22] similarly found adverse cardiovascular risk profiles above TSH 7.5 mIU/mL; nonetheless, our data are insufficient to establish clinically meaningful cardiac effects of SH in childhood, and we continue to regard TSH > 10 mIU/mL as the more appropriate treatment threshold, including in obese children, for whom the same targets apply as normal-weight peers [23].

Study Limitations

This study has several limitations. The TSH ≥ 7 mIU/mL subgroup ($n = 9$) is small and limits power; Bonferroni correction was applied, after which the AOD difference lost significance. The cross-sectional design precludes causal inference despite prospective enrollment; longitudinal follow-up is needed. We did not measure pulse wave velocity or carotid intima-media thickness, which might have captured additional dimensions of vascular stiffness. The study was single-center. Pubertal stage (Tanner staging) was not assessed despite its likely influence on TSH, lipids, and vascular parameters across this 5–18-year cohort. Finally, echocardiography was performed by a single cardiologist without formal intra-/inter-observer reproducibility assessment.

CONCLUSIONS

Subclinical hypothyroidism, as a categorical diagnosis in obese children, was not independently associated with measurable changes in aortic elasticity compared to euthyroid controls, corroborated by multivariate regression with Bonferroni correction, in which TSH was not an independent predictor in any model ($p\text{-adj} = 1.000$). Systolic blood pressure was the only variable that remained an independent, Bonferroni-corrected predictor of aortic elasticity. A TSH ≥ 7 mIU/mL threshold identified a subgroup with increased aortic diastolic diameter and elevated glucose and AST in the whole-cohort comparison, though the AOD difference was not confirmed within the SH group alone (Table 3). Overall, our study does not provide sufficient evidence that SH is associated with clinically meaningful cardiac effects in children with obesity. We continue to regard TSH > 10 mIU/mL, per current guidelines, as the more appropriate treatment threshold, including in obese children, for whom the same targets apply as in normal-weight peers. Multi-center longitudinal studies with larger samples are needed to clarify whether SH in childhood carries long-term vascular consequences.

Abbreviations

SH

subclinical hypothyroidism

TSH

thyroid-stimulating hormone (thyrotropin)

fT4

free thyroxine

BMI

body mass index

SDS

standard deviation score

SBP

systolic blood pressure

DBP

diastolic blood pressure

HbA1c

glycated hemoglobin

AST

aspartate aminotransferase

ALT

alanine aminotransferase

HDL-C

high-density lipoprotein cholesterol

LDL-C

low-density lipoprotein cholesterol

TG

triglycerides
AOS
aortic systolic diameter
AOD
aortic diastolic diameter
AS
aortic strain
AD
aortic root distensibility
 β
aortic stiffness index
Ep
aortic pressure–strain elastic modulus
PP
pulse pressure
IQR
interquartile range
SD
standard deviation.

Declarations

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Competing interests: The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval: This study was approved by the Institutional Review Board of Kütahya Health Sciences University Faculty of Medicine (Decision No: 2024/05-41) and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Consent to participate: Written informed consent was obtained from the parent/legal guardian of all participants, with assent obtained from participants where age-appropriate.

Consent to publish: Not applicable.

Data availability: The datasets generated and analysed during the current study are not publicly available due to patient privacy and the terms of the institutional ethics approval under which they were collected, but are available from the corresponding author upon reasonable request.

Author contributions: İH conceived and designed the study and performed the statistical analysis. TGE performed the data collection. İH and TGE drafted the manuscript. AS performed the echocardiographic

examinations and critically reviewed the manuscript. VNB contributed to data analysis, critically reviewed the manuscript, and contributed intellectual content. All authors read and approved the final manuscript.

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