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Integrating Thyroid Function with Body Composition: The BRITSH Ratio and Cardiovascular Risk – A Pilot Study

ABSTRACT

Background: Hypothyroidism is a known risk factor for cardiovascular diseases, affecting metabolic pathways such as dyslipidemia, insulin resistance, and visceral fat accumulation. This study aimed to investigate the value of the Body Roundness Index (BRI) and the newly defined BRI/TSH (thyroid-stimulating hormone) ratio (BRITSH) in predicting coronary artery disease (CAD) in patients with hypothyroidism.

Methods: This cross-sectional study included 152 hypothyroid patients, of whom 55 had CAD and 97 served as controls. Data collected included age, sex, body mass index (BMI), waist circumference, BRI, lipid profiles, and TSH levels. Diagnostic performance was assessed using receiver operating characteristic (ROC) curve analysis and logistic regression. A new ratio, BRITSH, was also evaluated.

Results: Patients with CAD had significantly higher BRI values ($P < .001$). The BRI/TSH ratio was significantly lower in the CAD group ($P = .005$). Non–high-density lipoprotein (non-HDL) cholesterol levels were also elevated in the CAD group ($P < .001$). Receiver operating characteristic analysis showed a strong predictive value for BRI (area under the curve [AUC] = 0.86). BRITSH ratio demonstrated a moderate predictive capacity (AUC = 0.67). In multiple logistic regression analysis, BRITSH, age, diabetes mellitus, high-sensitivity C-reactive protein, and non-HDL cholesterol remained independent predictors of CAD, whereas male sex, BMI, and smoking were not.

Conclusion: The new BRITSH ratio, combining body fat and thyroid function, was an independent predictor of CAD. The BRI also showed good ability to identify CAD risk in patients with hypothyroidism. These simple measures may help improve heart risk assessment and could be incorporated into routine care for patients with hypothyroidism.

Keywords: Body roundness index, BRITSH ratio, cardiovascular risk, coronary artery disease, hypothyroidism

ORIGINAL INVESTIGATION

INTRODUCTION

Hypothyroidism contributes significantly to cardiovascular disease (CVD) risk by disrupting metabolic homeostasis, leading to dyslipidemia, insulin resistance, and visceral adiposity, key drivers of atherosclerosis progression, particularly in subclinical hypothyroidism.[1] While traditional risk factors remain central to CVD assessment, emerging evidence supports the utility of novel anthropometric and biochemical indices in refining risk stratification. The Body Roundness Index (BRI) has been proposed as a more accurate measure for assessing central obesity and visceral fat distribution, outperforming conventional measures such as body mass index (BMI).[2] In this study, the BRITSH ratio (BRI/TSH), a novel index integrating adiposity and thyroid function, is also introduced to assess its potential role in cardiovascular risk stratification. This is the first study to examine the relationship between the BRI/TSH ratio and CAD, highlighting a novel anthropometric-endocrine marker for CAD risk. The aim was to evaluate the predictive value of BRI, BRITSH for coronary artery disease (CAD) in patients with hypothyroidism and highlight their potential clinical utility.

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METHODS

This pilot study included 152 consecutive patients with previously diagnosed hypothyroidism (subclinical or previously treated) who presented to the cardiology outpatient clinic. Patients in the CAD group had angiographically confirmed disease (>50% stenosis) or a documented history of revascularization, whereas controls were those without any evidence or history of coronary events. Indications for angiography included standard clinical reasons such as angina, ischemic electrocardiography (ECG) changes, or a positive stress test.

They were stratified into 2 main groups based on the presence or absence of CAD: 55 patients comprised the CAD group, and 97 served as controls. CAD was defined as the presence of greater than 50% stenosis in any coronary artery and/or documented history of coronary revascularization.

Patients with overt hypothyroidism, acute infection, malignancy, chronic renal, or hepatic failure were excluded. Only patients with a prior diagnosis of hypothyroidism (subclinical or previously treated) who were receiving levothyroxine replacement therapy at the time of enrollment were included. Detailed information regarding the initiation protocols, dosing strategies, and monitoring intervals of levothyroxine therapy was not available due to the retrospective design. However, all patients were on treatment at the time of enrollment.

Use of lipid-lowering therapies, statins, or statin-ezetimibe combinations was recorded as a single variable. The study adhered to the principles of the Declaration of Helsinki and was approved by the Trakya University Ethics Committee (approval no.: TUTF-GOBAEK 2025/73).

Biochemical Analyses and Anthropometric Measurements

Laboratory analyses included total cholesterol, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), non-HDL cholesterol (total cholesterol minus HDL-C), thyroid-stimulating hormone (TSH), HbA1c, fasting glucose, high-sensitivity C-reactive protein (hs-CRP), neutrophil, and lymphocyte counts.

Anthropometric parameters, including BMI, waist circumference (WC), height, and weight, were obtained from hospital records. Waist-to-height ratio (WHtR) was calculated as WC (cm) / height (cm), while BMI was calculated as weight (kg) / height^2 (m^2). BRI was calculated using the validated formula: $BRI = 364.2 - 365.5 \times \sqrt{[1 - (WC / 2\pi)^2 / (0.5 \times height^2)]}$.[3] A novel index, the BRITSH ratio, was derived by dividing BRI by TSH, hypothesizing a functional interaction between adiposity and thyroid activity.

Statistical Analysis

All statistical analyses were conducted using SPSS version 25.0 (SPSS, Chicago, IL, USA). The Shapiro–Wilk test assessed the normality of continuous variables. Normally distributed data were compared using the independent t-test, while nonparametric data were analyzed using the Mann–Whitney U test. Categorical variables were assessed using the Pearson chi-square test.

Descriptive statistics were reported as mean ± SD for continuous variables and frequencies (percentages) for categorical variables. Non-normally distributed variables were summarized using median and interquartile range (IQR). The diagnostic performance of BRI and BRITSH ratio was evaluated using receiver operating characteristic (ROC) curve analysis, with area under the curve (AUC) values and optimal cutoff points reported. Independent predictors of CAD were evaluated by both univariate and multiple regression analyses using known risk factors (age, sex, diabetes, smoking, hypertension). A two-tailed P-value < .05 was considered statistically significant. To minimize multiplicity and potential overfitting, exploratory variables not central to the study aim were excluded from the main analysis; relevant summaries are provided in the Supplementary Material.

RESULTS

A total of 152 hypothyroid patients were included, with 97 (63.80%) in the control group and 55 (36.20%) in the CAD group. The overall population was predominantly female (78.9%, $P = .025$) (Table 1). Patients with CAD were significantly older than controls (57 (40-64) vs. 45 (36-57) years, $P = .001$). Smoking (50.9% vs. 36.1%), diabetes mellitus (34.5% vs. 11.3%, $P < .001$), and hypertension (30.9% vs. 17.5%) were more prevalent in the CAD group, although the difference for hypertension did not reach statistical significance ($P = .072$).

Lipid analysis showed lower LDL-C and HDL-C levels in the CAD group, whereas non-HDL cholesterol was significantly elevated ($P < .001$) (Table 1). Total cholesterol and TG levels did not differ between the groups. The use of lipid-lowering therapy was more common in CAD patients. TSH levels at inclusion were significantly higher in the CAD group compared to the control group (5.98 ± 2.29 mIU/L vs. 3.91 ± 2.31 mIU/L, $P < .001$).

No significant difference was observed in BMI between groups ($P = .099$), while WC, WHtR, BRI were significantly higher in the CAD group ($P < .001$ for both). The distribution of BRI within the study population is illustrated in Figure 1A. The BRITSH ratio was significantly lower in CAD patients ($P = .005$).

Correlation analyses revealed a positive correlation between BRI and TSH ($r = 0.3798$, $P < .001$) (Figure 1B). BRI was also

HIGHLIGHTS

- Although body mass index (BMI) is a widely used measurement, it is limited in cardiovascular risk assessment as it does not adequately reflect visceral adiposity.
- The Body Roundness Index (BRI) reflects central adiposity better than BMI and shows strong discrimination for coronary artery disease in hypothyroid patients.
- The BRITSH ratio (BRI/TSH) ratio may serve as a novel parameter for improving cardiovascular risk stratification in hypothyroid populations by incorporating both adiposity and thyroid function.

Table 1. Clinical Characteristics of Patients of the Study Population

Variables	Control (n = 97)	CAD (n = 55)	*P*
Age (years)	48.87 ± 14.14	54.12 ± 16.03	.001
Sex, n (%)			.025
Male	15 (15.46)	17 (30.91)	
Female	82 (84.54)	38 (69.09)	
BMI, kg/m^2	26.67 (23.05-30.29)	27.89 (25.95-30.48)	.141
Waist (cm)	109.76 ± 5.54	116.18 ± 5.64	<.001
BRI/TSH ratio	1.83 (1.27-2.71)	1.3 (1.11-1.91)	.005
DM, n (%)	11 (11.34)	19 (34.54)	<.001
HT, n (%)	17 (17.53)	17 (30.90)	.072
Smoker, n (%)	35 (36.08)	28 (50.91)	.075
Anti-lipid medication	30 (30.92)	43 (78.18)	<.001
TSH, mIU/L	3.91 ± 2.31	5.98 ± 2.29	<.001
fT4, ng/dL	0.91 ± 0.59	0.89 ± 0.44	.957
fT3, pg/mL	2.65 ± 0.78	2.83 ± 0.81	.179
Blood glucose	97.12 ± 16.70	107.47 ± 24.75	.003
Neutrophile (×10^9/L)	3.30 ± 1.16	4.48 ± 1.26	<.001
Lymphocyte (×10^9/L)	2.22 ± 0.51	2.24 ± 0.50	.575
hs-CRP, mg/mL	2.95 ± 1.32	3.84 ± 1.68	<.001
Hba1C, %	6.1 (5.8-6.7)	6.9 (6.1-7.2)	.001
TG, mg/dL	181.32 ± 50.94	168.25 ± 40.56	.084
LDL-C, mg/dL	157 (121-188)	121 (104-142)	<.001
HDL-C, mg/dL	58 (52-62)	38 (34-50)	<.001
Non-HDL-C, mg/dL	116.04 ± 46.49	147.92 ± 47.56	<.001
Total cholesterol, mg/dL	168 (137-188)	171 (147-190)	.061

BMI, body mass index; BRI, Body Roundness Index; CAD, coronary artery disease; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high sensitive C-reactive protein; HT, hypertension; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; TSH, thyroid-stimulating hormone.

moderately correlated with WHtR ($r = 0.3112$, $P < .001$), HbA1c ($r = 0.2901$, $P < .001$), and non-HDL cholesterol ($r = 0.2775$, $P < .001$) (Figure 2). The BRITSH ratio showed a weak negative correlation with non-HDL cholesterol ($r = -0.2405$, $P = .003$) (Figure 3). Finally, WHtR was weak but significantly correlated with non-HDL-C ($r = 0.2697$, $P < .001$).

The cutoff values and predictive power of BRI and BRITSH ratio for CAD prediction are presented in Table 2. ROC curve analysis demonstrated strong predictive performance for BRI (AUC = 0.86, 95% CI: 0.80-0.91) and BRITSH (AUC = 0.67, 95% CI: 0.52-0.68). The ROC curves for BRI and BRITSH ratio are depicted in Figure 4.

In the univariate analysis, older age, male sex, diabetes mellitus, BRI, BRITSH, hs-CRP, and non-HDL cholesterol were significantly associated with CAD, whereas BMI and smoking were not. In the multiple binary logistic regression analyses, age (OR = 1.041, $P = .008$, 95% CI: 1.01-1.07), diabetes mellitus (OR = 5.31, $P = .001$, 95% CI: 1.94-14.51), BRITSH (OR = 0.64, $P = .024$, 95% CI: 0.43-0.94), hs-CRP (OR = 1.58, $P = .003$, 95% CI: 1.17-2.13), and non-HDL cholesterol (OR = 1.018, $P < .001$, 95% CI: 1.01-1.03) remained independent predictors of CAD, whereas male sex, BMI, and smoking were not (Table 3).

DISCUSSION

Main findings of this study are as follows: 1) BRI demonstrated a strong predictive value for CAD, with a threshold of 7.61, yielding 70% sensitivity and 90% specificity; 2) BRITISH ratio was identified as an independent predictor of CAD, with significantly high odds ratios (BRITISH: OR = 0.64, $P = .024$); 3) TSH levels showed a positive correlation with both BRI, suggesting a potential link between thyroid function and body fat distribution (adiposity) (Figure 1); 4) The BRITSH ratio demonstrated significant diagnostic performance for CAD, with a cutoff value of 1.34 (AUC = 0.67, $P \leq .001$); and 5) The non-HDL-cholesterol levels were significantly higher in the CAD group and identified as an independent predictor. As expected, CAD patients receiving statin therapy had lower LDL-C levels compared to the control group. Moreover, non-HDL-cholesterol was positively correlated with BRI, indicating that individuals with greater adiposity and altered fat distribution exhibit a more atherogenic lipid profile**.** Additionally, a significant negative association was observed between non-HDL cholesterol and the BRITSH index, suggesting that higher BRITSH values may coincide with a less atherogenic lipid profile."

Elevated TSH levels are known to increase ApoB-containing lipoproteins. Mechanistically, TSH exerts regulatory effects on lipid metabolism through its receptors on adipocytes and hepatocytes. Triiodothyronine (T3) stimulates cholesterol synthesis by upregulating hepatic HMG-CoA reductase and may enhance intestinal cholesterol absorption via the Niemann-Pick C1-like 1 (NPC1L1) transporter.[4] T3 also upregulates hepatic LDL receptors, promoting LDL clearance, a mechanism impaired in hypothyroidism. Moreover, reduced activity of lipoprotein lipase and hepatic lipase in hypothyroid states impairs TG-rich lipoprotein catabolism.[5] Thyroid hormones downregulate proprotein convertase subtilisin/kexin type 9 (PCSK9), a key regulator of LDL receptor degradation; thus, elevated PCSK9 levels in hypothyroidism exacerbate LDL-C accumulation. T3 also stimulates cholesterol 7 alpha-hydroxylase (CYP7A1), promoting bile acid synthesis from cholesterol—another pathway attenuated in thyroid hormone deficiency.[6] These effects are mediated through nuclear thyroid hormone receptors, THR-α and THR-β, with THR-α primarily regulating cardiac and adipose tissue function, while THR-β modulates hepatic lipid metabolism and TSH secretion. Consequently, thyroid hormones regulate lipid regulation in a tissue-specific manner, influencing fatty acid oxidation, lipogenesis, and systemic lipid homeostasis.[7] Although all the patients had a prior diagnosis of hypothyroidism and were on levothyroxine therapy, TSH levels at inclusion (CAD group: 5.98 ± 2.29 mIU/L; Control group: 3.91 ± 2.31 mIU/L) may suggest incomplete hormonal control,

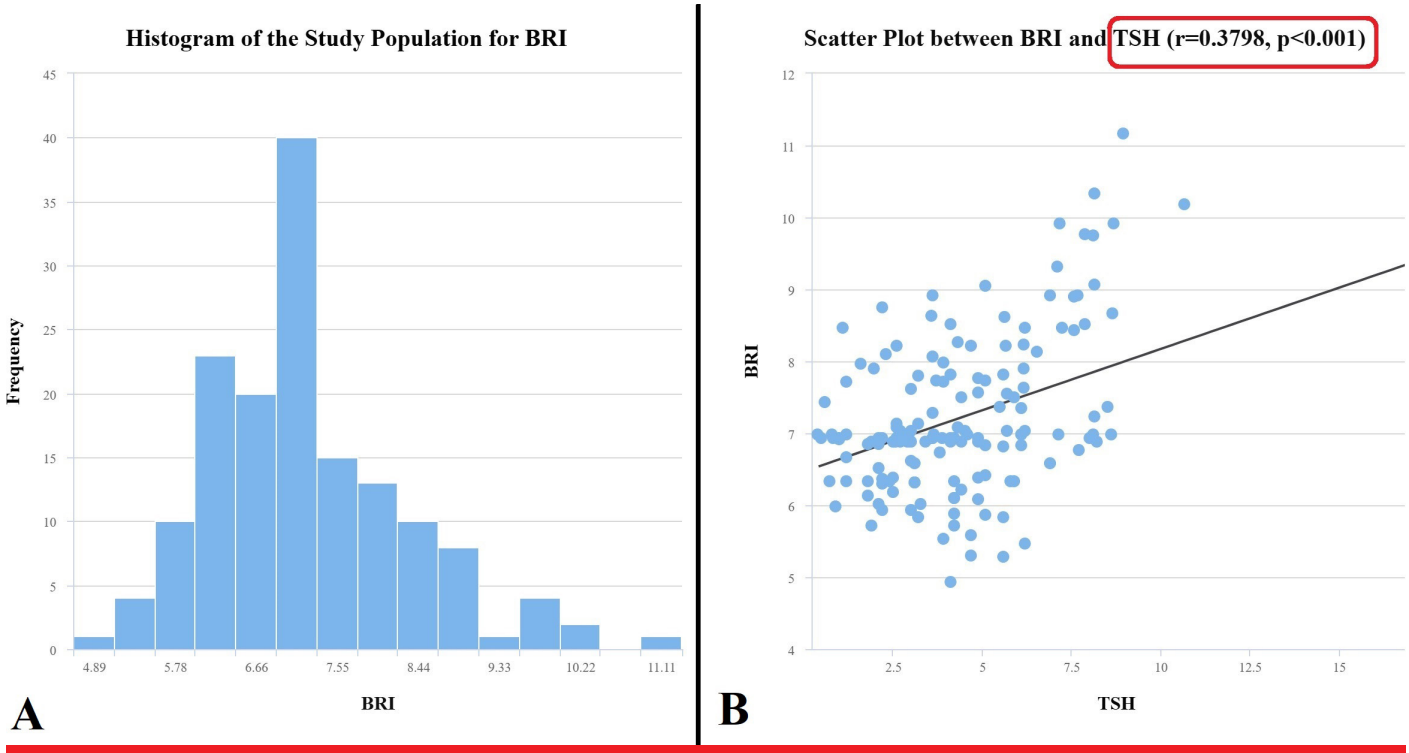

Figure 1. Histogram of the study population for the Body Roundness Index and scatter plot between BRI and thyroid-stimulating hormone.

which may have contributed to the observed metabolic abnormalities. This finding may be explained by real-world factors such as cautious low-dose initiation of levothyroxine in cardiac patients, variable adherence, concomitant medications affecting absorption (e.g., calcium or iron), and the possibility that residual TSH elevation itself reflects cardiovascular risk. Importantly, in daily practice patients with CAD are typically started on lower levothyroxine doses (25-50 µg/day) with gradual titration, in line with international guideline recommendations, to avoid ischemic complications. This conservative approach may result in transiently higher TSH values. Additionally, medication interactions and adherence issues may contribute to suboptimal biochemical control. Finally, it is also plausible that higher TSH represents not only treatment variability but also an intrinsic marker of cardiovascular risk, consistent with prior studies linking subclinical hypothyroidism to adverse outcomes.

This study underscores the clinical relevance of BRI in predicting CAD among patients with hypothyroidism. BRI, a

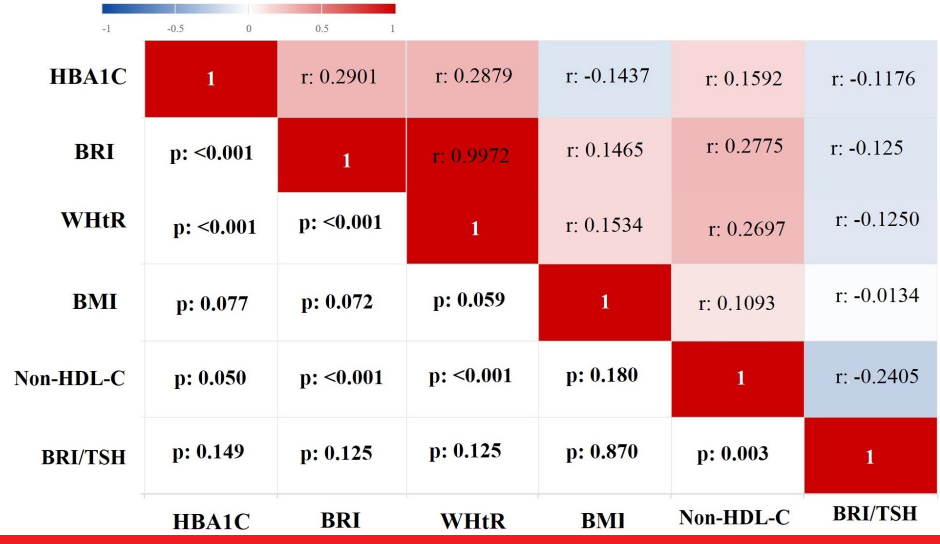

Figure 2. Correlogram with some indexes and parameters.

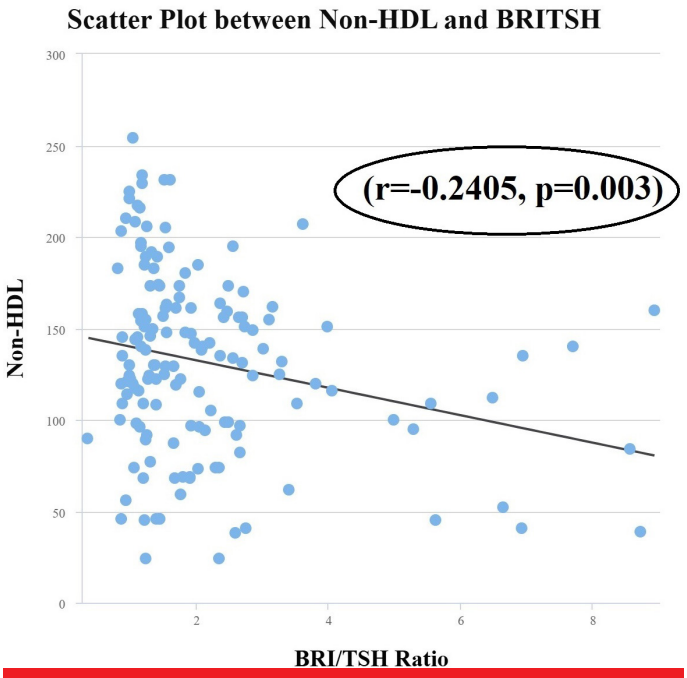

Figure 3. Scatter plot between non–high-density lipoprotein and BRITSH.

geometry-based anthropometric measure, more accurately reflects visceral fat distribution than traditional indices such as WC or BMI.[8] Prior research has demonstrated BRI's utility in identifying cardiovascular-kidney-metabolic (CKM) syndrome (formerly metabolic syndrome) and in predicting cardiovascular events.[9] Given that CKM syndrome components including abdominal adiposity and insulin resistance are frequently present in hypothyroid individuals, particularly those with elevated TSH levels, increased BRI may serve as an early indicator of cardiometabolic risk.[10] Hypothyroidism facilitates fat accumulation by reducing basal metabolic rate and altering lipid metabolism, thereby enhancing cardiovascular vulnerability. As a marker of central obesity, BRI has been associated with metabolic dysfunction, systemic inflammation, vascular dysfunction, and oxidative stress, all of which contribute to atherogenesis.[11] Emerging evidence suggests that BRI outperforms BMI and WC in identifying CKM syndrome and insulin resistance, supporting its use in cardiovascular risk stratification in hypothyroid individuals.[12]

BMI is a convenient measure of overall body size but lacks sensitivity to body fat distribution, limiting its utility in cardiovascular risk assessment. Unlike visceral adiposity indices, it does not distinguish fat from lean mass. Evidence shows that abdominal obesity measures, such as WC and waist-to-height ratio, better predict CVD mortality than BMI.[13] In line with these findings, BMI was not significantly different between groups in this study, underscoring its limited value in CAD risk assessment. These findings agree with growing evidence that body-shape measures like BRI show heart disease risk better than BMI. For patients with hypothyroidism, BRI could be an easy, non-invasive method of identifying those at a higher risk of CAD during routine care. However, this requires confirmation in future studies. Yamashita et al[14] reported that BMI alone was not a reliable prognostic marker in patients undergoing transcatheter aortic valve replacement (TAVR), as the obesity paradox was not confirmed and obesity was associated with worse outcomes in the presence of comorbidities. These findings highlight the limitations of BMI and support the use of novel anthropometric-endocrine indices such as BRI, and the BRITSH ratio for improved cardiovascular risk prediction.

This study population consisted of treated hypothyroid patients on levothyroxine therapy, among whom serum TSH levels showed interindividual variability, reflecting differences in treatment duration, adherence, or dose titration. Elevated TSH levels, even within the high-normal range, have been associated with increased cardiovascular mortality.[15] Gönülalan et al[16] reported higher BRI values in hypothyroid patients compared to euthyroid controls yet found no significant correlation between BRI and TSH. This discrepancy may stem from demographic and clinical differences; this cohort had a higher mean age, a confirmed hypothyroidism diagnosis under treatment, and greater comorbidity burden. In contrast, this study demonstrated a positive correlation between BRI and TSH levels, suggesting that monitoring TSH levels in individuals with thyroid dysfunction may aid in cardiovascular risk management.

Non-HDL cholesterol has emerged as a strong predictor of atherosclerotic risk and is closely associated with CKM syndrome, obesity, and diabetes.[17,18] It has been suggested that non-HDL cholesterol may be a better risk indicator than LDL-C, especially in those with cardiometabolic disturbances and insulin resistance. Notably, its predictive capacity persists even when LDL-C levels are within normal limits.[19] In this study, non-HDL cholesterol was significantly higher in the CAD group, despite lower LDL-C levels, likely reflecting statin use. These findings emphasize the utility of non-HDL cholesterol in assessing residual risk, particularly in hypothyroid populations where lipid-lowering response may be attenuated.

The BRITSH ratio was developed to reflect how body fat and thyroid function work together to affect heart health. BRI

Table 2. Diagnostic Performance of the Body Roundness Index and BRI/TSH Ratio in the Group of Coronary Artery Disease

Diagnostic Performance of BRI and BRI/TSH Ratio					
	Cutoff	AUC (95% CI)	Sensitivity	Specificity	*P*
BRI	7.61	0.86 (0.80-0.91)	0.70 (0.57-0.81)	0.90 (0.85-0.96)	<.001
BRITSH	1.34	0.67 (0.52-0.68)	0.56(0.43-0.68)	0.73 (0.63-0.81)	<.001

AUC, area under the curve; BRI, Body Roundness Index; BRISTH, BRI/TSH ratio; TSH, thyroid-stimulating hormone.

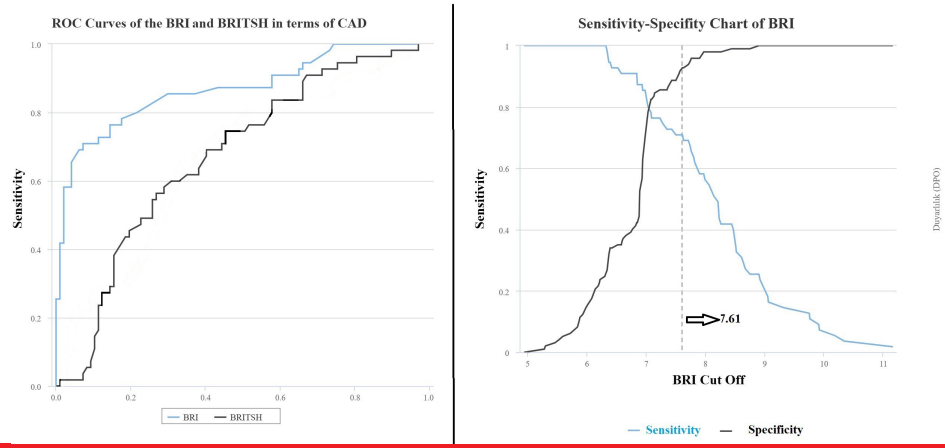

Figure 4. Receiver operating characteristic curves of the Body Roundness Index (BRI) and BRI/TSH ratio in terms of coronary artery disease and sensitivity–specificity chart of BRI.

shows the amount of central or abdominal fat, while TSH indicates how well the thyroid regulates metabolism and cholesterol balance. Because both excess fat and low thyroid activity can cause inflammation, abnormal lipids, and damage to blood vessels, combining them in 1 measure may give a clearer view of heart disease risk in people with hypothyroidism. In this way, the BRITSH ratio may offer a simple and practical way to connect both hormonal and metabolic factors related to CAD.

Additionally, the BRITSH ratio, which integrates visceral adiposity and thyroid function, may serve as a complementary metric to albumin-based nutritional indices such as prognostic nutritional index (PNI) and controlling nutritional status (CONUT). Given that serum albumin reflects systemic inflammation, oxidative stress, and vascular dysfunction in acute coronary syndrome (ACS), as highlighted by Hayıroğlu and Altay,[20] combining BRITSH with albumin-centered scores may provide a more comprehensive cardiometabolic risk assessment in hypothyroid patients.

Inflammatory burden, as reflected by hs-CRP in this model, remained independently associated with CAD, aligning with the inflammatory component of hypothyroidism-related cardiometabolic risk. In the literature, Christ-Crain et al[21] reported that CRP rises with worsening thyroid failure, potentially serving as "an additional risk factor for the development of coronary heart disease in hypothyroid patients.

The BRITSH ratio, by integrating visceral adiposity with the thyroid axis, may complement traditional lipid-lowering strategies in high-risk patients such as those with ACS. In the context of Özdoğan et al's[22] country-specific algorithm for ACS management in Türkiye, incorporating novel indices like BRITSH could enhance the precision of cardiometabolic risk stratification, moving beyond LDL-centric models to include cardiometabolic interplay.

A novel index, the BRITSH ratio (BRI/TSH), was introduced to assess the interplay between thyroid function and body composition in relation to cardiovascular risk. This ratio differed significantly between groups and emerged as an independent predictor of CAD in regression analysis. These findings suggest that integrating TSH into adiposity-based indices may improve cardiovascular risk stratification in hypothyroid patients. Further validation in prospective cohorts is warranted to establish its clinical applicability.

Limitations and Strengths of the Study

Strengths of this study include its focus on a specific and clinically relevant patient population with hypothyroidism, who

Table 3. Univariate and Multiple Binary Logistic Regression Analysis for the Coronary Artery Disease

	Univariate Model			Multiple Model		
	OR	95% CI	*P*	OR	95% CI	*P*
Age (years)	1.031	1.01-1.06	.002	1.041	1.01-1.07	.008
Sex (Male)	2.460	1.10-5.40	.027	1.72	0.62-4.76	.292
DM	4.121	1.78-9.54	<.001	5.31	1.94-14.51	.001
Smoking	1.834	0.93-3.62	.079	1.68	0.70-3.99	.238
BMI kg/m^2	1.071	0.98-1.16	.120	1.04	0.93-1.15	.476
BRITSH	0.633	0.44-0.89	.010	0.64	0.43-0.94	.024
hs-CRP mg/mL	1.49	1.18-1.89	<.001	1.58	1.17-2.13	.003
Non-HDL-c	1.022	1.012-1.029	<.001	1.018	1.01-1.03	<.001

BMI, body mass index; BRISTH, BRI/TSH ratio; CAD, coronary artery disease; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high sensitive C-reactive protein; OR, odds ratio.

are often underrepresented in cardiovascular risk research. The investigation of novel indices such as BRI, and the BRITSH ratio provides new insights into the interplay between thyroid function, adiposity, and cardiovascular risk. The use of comprehensive anthropometric, biochemical, and statistical analyses, including ROC curve and multiple regression, strengthens the robustness of the findings.

However, several limitations should be acknowledged. First, the cross-sectional design precludes causal inference. Second, the relatively small sample size and single-center setting limit the generalizability of the results. Because this was a cardiology outpatient-based cohort, patients who underwent angiography did so for standard clinical indications (such as angina or ischemic ECG findings) rather than population screening, which may limit the generalizability of the results. Third, the predominance of female participants may have influenced sex-specific associations, potentially overestimating the odds ratio for male sex. Fourth, residual confounding from unmeasured variables such as dietary habits, physical activity, genetic predisposition, or medication adherence cannot be excluded. Moreover, detailed data on levothyroxine dosing history, titration intervals, or treatment adherence were not available, which may partly explain the higher TSH levels observed in the CAD group. Finally, the absence of long-term follow-up prevents assessment of the prognostic utility of the proposed indices over time.

CONCLUSION

The BRITSH ratio, introduced in this study, demonstrated significant potential as an independent predictor of CAD risk in hypothyroid patients. By integrating thyroid function and adiposity into a single metric, it may offer a more precise assessment of cardiovascular risk, potentially enhancing risk stratification and personalized management in clinical practice.

The current findings also highlight the utility of BRI as an easily obtainable anthropometric index and underscore the independent association of the BRITSH ratio with CAD in hypothyroid patients. Incorporating BRITSH alongside established clinical and biochemical markers (e.g., non-HDL cholesterol and hs-CRP) may refine cardiovascular risk stratification in this population.

Together, these parameters provide a more nuanced understanding of cardiometabolic risk, reinforcing the interrelationship between adiposity, thyroid dysfunction, and dyslipidemia. These results underscore the need to incorporate assessments of thyroid function and lipid metabolism into cardiovascular risk models, particularly in patients with increased central adiposity. Future large-scale, prospective studies are warranted to validate these indices and determine their long-term clinical applicability.

Ethics Committee Approval: The Trakya University Ethics Committee approved this study (approval no.: TUTF-GOBAEK 2025/73, Date: 03.03.2025).

Informed Consent: Individual patient consent was waived due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Ç.K., S.A., M.K.; Design – Ç.K., S.A., M.K.; Supervision – Ç.K., S.A., M.K.; Fundings – Ç.K., S.A., M.K.; Materials – Ç.K., S.A., M.K.; Data collection and/or processing – Ç.K., S.A., M.K.; Analysis and/or interpretation – Ç.K., S.A., M.K.; Literature review – Ç.K., S.A., M.K.; Writing – Ç.K., S.A., M.K.; Critical review – Ç.K., S.A., M.K.

Declaration of Interests: Ç.K. reports honoraria (for lectures or consultancy) from Humanis, Novartis, and NovoNordisk. Research funding from NovoNordisk and Lilly for the past 3 years.

S.A. serves as the Editor-in-Chief of the Balkan Medical Journal. S.A. reports honoraria (for lectures or consultancy) from Novartis, Abdi Ibrahim, Novo Nordisk, and Pfizer, and research funding from NovoNordisk and Lilly for the past 3 years.

M.K. serves as an Associate Editor for the Archives of the Turkish Society of Cardiology. M.K. reports honoraria (for lectures or consultancy) from Abbott, Abdi Ibrahim, Amgen, LIB Therapeutics, MSD, Novartis, Novo Nordisk, Pfizer, Recordati, and Ultragenix and research funding from Amgen, Ionis, LIB Therapeutics, Lilly, MSD, and Novartis for the past 3 years.

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SUPPLEMENTARY FILE

Supplementary Introduction

In our study, we compiled additional analyses, tables, and figures for parameters that, although not included in the main regression models due to potential multicollinearity, were considered valuable for exploratory assessment. The supplementary indices and their formulas are presented below:

- **Plasma Atherogenicity Index (PAI):** calculated as log (TG / HDL-C), representing the relationship between lipid profile and cardiovascular risk.
- **Lipid Accumulation Product (LAP):** calculated as (WC – 65) × TG (mmol/L) for men and (WC – 58) × TG (mmol/L) for women.
- **Neutrophil-to-Lymphocyte Ratio (NLR):** calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Supplementary Discussion

PAI, calculated as log (TG/HDL-C), is a well-recognized indicator of atherogenic dyslipidemia and endothelial dysfunction, particularly in thyroid disorders. In hypothyroidism, reduced thyroid hormone activity elevates TGs, lowers HDL-C, and increases PAI. Its utility in risk stratification has been demonstrated across various conditions, including liver disease, stroke, and thyroid dysfunction. A recent meta-analysis by Assempoor et al. confirmed elevated PAI in CAD patients. Consistently, our study found significantly higher PAI levels in the CAD group, supporting the relevance of this finding in hypothyroid populations.[1] Although PAI showed a strong association, the wide confidence interval suggests some statistical uncertainty, likely due to the sample size and the scale of the index. This finding should therefore be interpreted with caution and validated in larger cohorts.

The strong correlation between PAI and LAP ($r = 0.7162$, $p < 0.001$) highlights the link between visceral adiposity and atherogenic lipid profiles. The moderate correlation between BRI and LAP ($r = 0.4711$, $p < 0.001$) further supports the role of central fat accumulation in CAD risk. These findings align with prior studies associating elevated BRI and LAP with CKM syndrome and cardiovascular events, emphasizing their utility in cardiometabolic risk assessment.[2]

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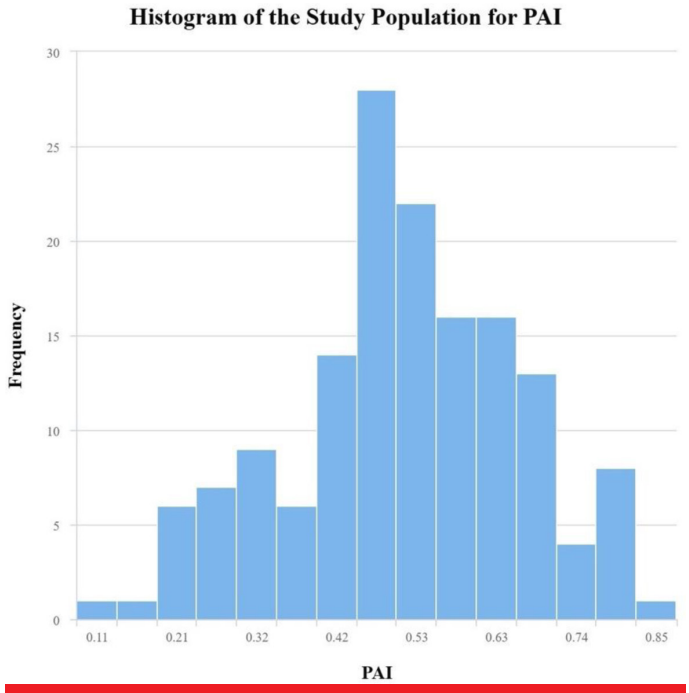
Supplementary Table 1. Other Parameters of the study population

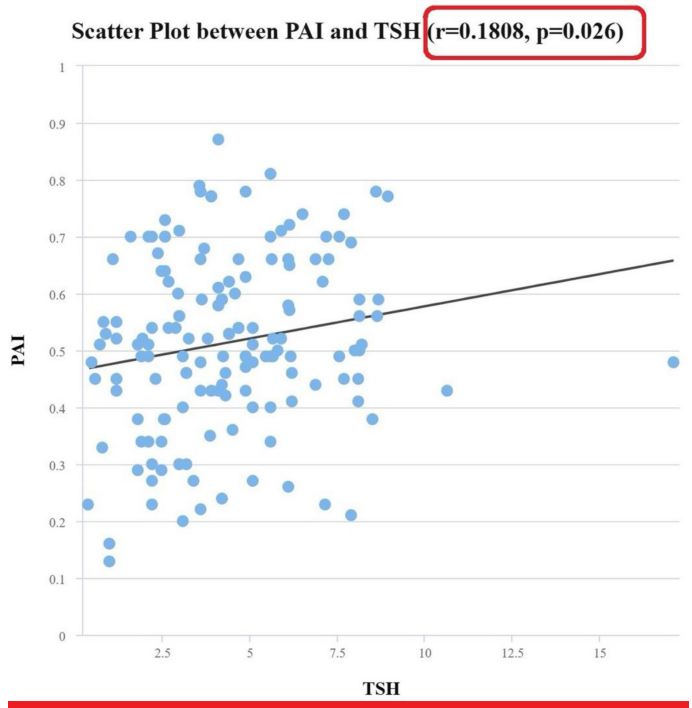
Variables	Control (n=97)	CAD (n=55)	*P*
LAP cm × mmol/L	474.39±133.20	567.63±183.09	<0.001
PAI	0.46±0.12	0.60±0.15	<0.001
NLR	1.54±0.65	2.10±0.76	<0.001

Supplementary Table 2. Diagnostic Performance of PAI in ROC Analyses

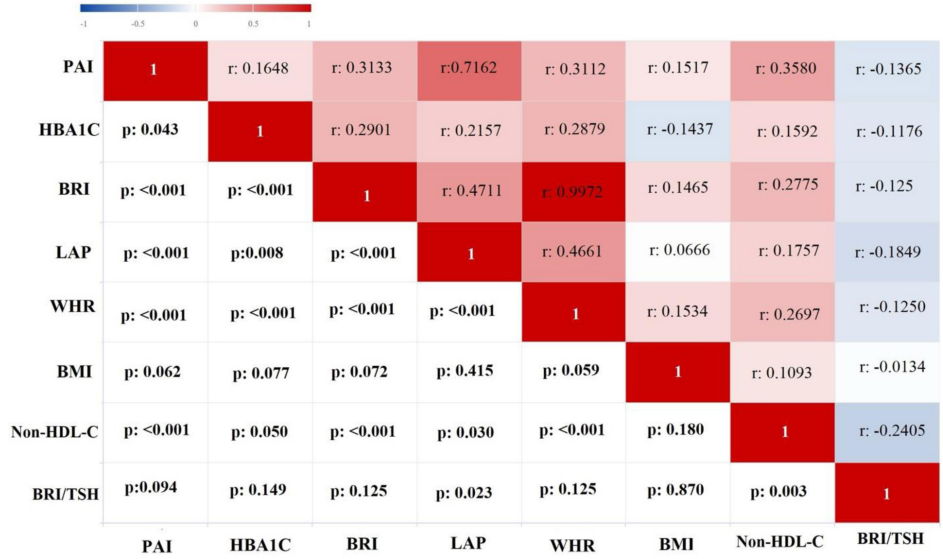
	Diagnostic Performance of BRI, and BRI/TSH ratio				
	Cut off	**AUC (95% CI)**	**Sensitivity**	**Specificity**	***P***
PAI	0.61	0.76 (0.69-0.83)	0.60 (0.46-0.71)	0.90 (0.83-0.95)	<0.001



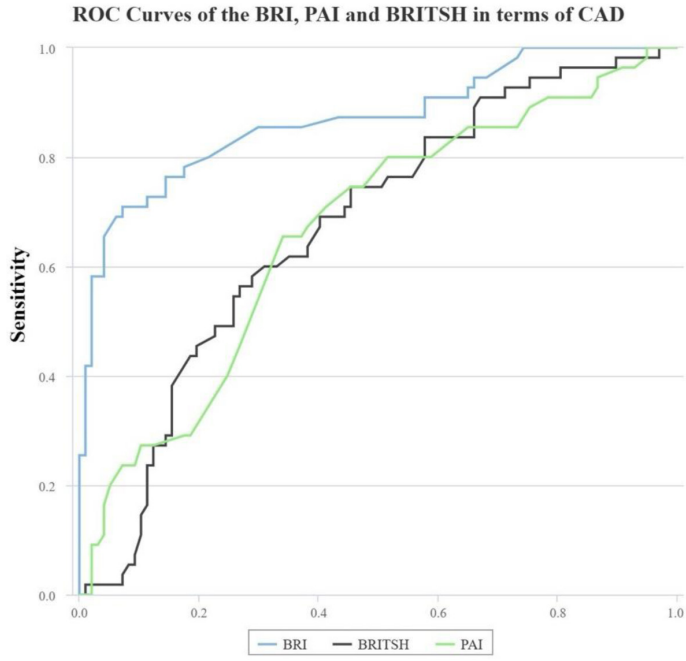
Supplementary Figure 1. Histogram of PAI.



Supplementary Figure 2. Supp: Scatter plot between PAI and TSH.



Supplementary Figure 3. Supp: Correlogram of all indices and parameters with PAI and LAP



Supplementary Figure 4. Supp: ROC Curves of the BRI, PAI and BRITSH in terms of CAD