

Association Between Thyroid Function Parameters and Resting Heart Rate in Patients Referred for Coronary Angiography: A Retrospective Observational Study

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Abstract:

Background: Resting heart rate (RHR) is an important cardiovascular physiological parameter and may be influenced by thyroid hormone activity. Although thyroid hormones have recognized effects on cardiac rate and function, their relationship with RHR among patients undergoing coronary angiography remains incompletely characterized.

Aim: To evaluate the association of serum thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) with RHR in patients referred for coronary angiography.

Methodology: This retrospective observational study included 111 patients evaluated at Government Medical College, Bettiah, Bihar, India, over one year from November 2023 to October 2024. Demographic, clinical, medication, thyroid function, and cardiovascular data were retrieved from medical records. Associations between thyroid parameters and RHR were assessed using quartile comparisons, correlation analysis, and progressively adjusted linear regression models. Statistical significance was set at $p < 0.05$.

Result: The mean RHR was 72.4 ± 10.6 beats/min. RHR increased progressively across FT3 quartiles (69.5 to 76.5 beats/min; $p = 0.041$) and FT4 quartiles (69.0 to 76.5 beats/min; $p = 0.029$). FT3 ($r = 0.29$, $p = 0.002$) and FT4 ($r = 0.25$, $p = 0.008$) showed significant positive correlations with RHR, whereas TSH did not ($r = -0.06$, $p = 0.532$). In fully adjusted models, FT3 ($\beta = 3.39$, $p = 0.005$) and FT4 ($\beta = 4.18$, $p = 0.016$) remained significantly associated with higher RHR.

Conclusion: FT3 and FT4 were positively associated with RHR, whereas TSH showed no significant association. These findings suggest that peripheral thyroid hormone concentrations may contribute to variation in resting cardiac rate among patients undergoing coronary angiographic evaluation.

Keywords: Resting Heart Rate; FT3; FT4; TSH; Thyroid Function; Coronary Artery Disease; Coronary Angiography; Cardiovascular Physiology.

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Introduction

Resting heart rate (RHR) is an easily measurable clinical parameter routinely used in the clinic and carries important information regarding cardiovascular autonomic activity and overall cardiovascular health. In addition to being a crucial vital sign, there is growing evidence linking RHR with cardio- and cerebrovascular morbidity and mortality over the long term [1]. RHR may have direct negative effects on the cardiovascular system as it increases myocardial oxygen demand, decreases diastolic filling time, and increases myocardial workload. Further, a higher resting PR could be a sign of higher sympathetic activity and autonomic imbalance, which have been associated with poor cardiovascular results [2]. Given the simplicity and the low cost of measuring RHR in routine clinical practice, there may be a role for understanding potentially modifiable biological

determinants of RHR in cardiovascular risk assessment, especially in patients undergoing assessment for coronary artery disease.

The thyroid hormones are one of the important endocrine regulators of cardiovascular function. The cardiovascular system is a large target tissue for thyroid hormones: they affect heart rate, myocardial contractility, vascular tone, cardiac output and systemic hemodynamics [3]. Thyroid hormones have biological effects on the heart by both genomic and nongenomic mechanisms; changes in adrenergic responsiveness and ion-channel activity lead to changes in cardiac rhythm and contractility. Increased RHR, palpitations, increased cardiac contractility and increased cardiac output are classic signs of overt hyperthyroidism. Free triiodothyronine (FT3) is regarded as an important predictor of

cardiac actions of thyroid dysfunction as it is the thyroid hormone that is biologically active at the tissue level. Free thyroxine (FT4) is the principal circulating precursor of T3, but T3 has been considered to be the major determinant of several cardiac effects considered to be related to thyroid hormone activity [4].

But the thyroid and cardiovascular physiology link is not limited to manifest thyroid disease. There is still much uncertainty about the clinical significance of the so-called 'subclinical' thyroid dysfunction and fluctuations in thyroid hormone levels within normal reference ranges [5]. Even relatively small changes in thyroid hormone availability can affect the regulation of the autonomic nervous system, myocardial oxygen consumption, vascular resistance and cardiac electrophysiology. Thus, evaluation of thyroid function could offer further clues on inter-individual differences in RHR in those who do not have clinically evident thyroid disease. This problem may be especially important in people with known or suspected heart disease, who can have both thyroid problems and abnormal activity of the autonomic nervous system.

Thyroid hormone levels and RHR have been associated in previous investigation studies in general population cohorts, but not consistently [6]. Several studies have shown a positive relationship between the levels of circulating thyroid hormones and HR, which is consistent with physiology: the higher the thyroid hormone activity, the higher the chronotropic stimulation. Other studies, however, have not supported a uniform link; sometimes the association between heart rate and cardiovascular risk factors may be dependent on the age of the people studied, sex, medication use, comorbidities, and clinical characteristics of the population studied [7]. Variations between studies could also be due to differences in study design, thyroid function categories, measurement methods, and methods of adjustment for potential confounding variables. Therefore, the association found in the community-based population may not be generalized to patients under evaluation for coronary artery disease.

Patients referred to for coronary angiography are an important clinical group to study the relationship between thyroid function and RHR. These patients are often at high risk for cardiovascular disease and may have coronary atherosclerosis or myocardial ischemia. In this context, RHR is particularly interesting because increasing the heart rate will raise the myocardial oxygen demand while decreasing the time for diastolic coronary perfusion. In addition, in heavily ill systemic or cardiovascular diseases, thyroid hormone abnormalities may be present, and they may be a result of altered peripheral thyroid hormone metabolism. One of these syndromes is the non-thyroidal illness syndrome (NTIS) with a major feature being decreased levels of T3 in the

bloodstream in the absence of an increase in thyroid-stimulating hormone (TSH) [8]. Observed in patients with acute or chronic systemic illness, NTIS is an important clinical and therapeutic challenge. Whether low T3 levels are of prognostic importance, and whether T3 supplementation is of any value or not, is still under study [9].

Thus, the association of modified thyroid hormone metabolism and cardiovascular disease leads to important questions about the associations of thyroid function parameters and resting cardiac rate. Factors that might affect RHR in patients undergoing coronary angiography include autonomic activation, medications, ischemic burden, systemic illness, and endocrine factors. Identifying the relationship between thyroid parameters, especially FT3, FT4, and TSH and RHR in such a clinical population could help shed light on the role of thyroid status in the physiology of cardiovascular diseases. This information too could have implications for the interpretation of thyroid function tests in those being assessed for coronary artery disease, especially when thyroid hormone levels are manipulated in the absence of any thyroid dysfunction.

The Ludwigshafen Risk and Cardiovascular Health (LURIC) Study has in the past delivered valuable information on the prognostic value of RHR and thyroid hormone parameters in subjects referred to for coronary angiography [10]. In this population, there was an association between higher RHR, elevated FT4 levels, and reduced FT3 levels and mortality [11]. However, the relationship between serum thyroid hormone levels and RHR in people who have been referred to as coronary angiography is still poorly described. Assessment of this association may thus help to gain insight into endocrine/cardiovascular interaction in high-risk clinical populations.

In this backdrop, the present retrospective observation study was conducted in the patients referred for coronary angiography at a tertiary-care healthcare center in Bihar, India. The study's goal is to examine the relationship between thyroid function (FT3, FT4, TSH) and RHR. The study aims to determine whether these relationships are present in a population of patients with clinically relevant variation in thyroid function undergoing coronary evaluation to gain additional understanding of the cardiovascular effects of thyroid hormone variation and its contribution to variability in resting heart rate.

Methodology

Study Design: The present study was designed as a retrospective observational study to evaluate the association between thyroid function parameters and resting heart rate (RHR) in patients referred for coronary angiography. The study involved a retrospective review of clinical, biochemical, cardiovascular, and angiographic records of eligible patients who

had undergone evaluation for coronary artery disease and for whom thyroid function parameters and resting heart rate measurements were available. The principal thyroid function parameters assessed were serum thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4), while resting heart rate was considered the primary cardiovascular outcome variable. No intervention was performed, and the treatment or clinical management of patients was not altered for the purpose of the study. The association between thyroid function parameters and resting heart rate was assessed after considering potentially relevant demographic, clinical, cardiovascular, and medication-related factors.

Study Area: The study was conducted in the Department of Physiology, Government Medical College, Bettiah, West Champaran, Bihar, India. The department was selected as the study site for the evaluation and analysis of physiological and biochemical parameters relevant to the relationship between thyroid function and resting heart rate. Clinical records, laboratory reports, cardiovascular assessment records, and coronary angiography-related information available from the institution were reviewed for eligible patients.

Study Duration: The study was conducted over a period of 1 year from November 2023 to October 2024.

Sample Size: The final study sample consisted of 111 patients (N = 111) who fulfilled the predefined eligibility criteria and had adequate information for the planned analysis. Of the total study population, 33 (29.7%) were males and 78 (70.3%) were females. Only those patient records containing sufficient information regarding resting heart rate and thyroid function parameters, along with relevant clinical details, were considered for the final analysis.

Sample Population: The study population comprised patients referred for coronary angiography during the study period. Both male and female patients were included. The study population represented patients undergoing cardiovascular evaluation for suspected or established coronary artery disease. The records were reviewed for demographic characteristics, cardiovascular risk factors, clinical history, medication use, resting heart rate, thyroid function parameters, and available coronary angiography findings. The final study population included 111 eligible patients.

Data Collection: Data were collected retrospectively from hospital medical records, laboratory reports, cardiovascular assessment records, medication records, and coronary angiography reports using a structured data collection proforma. Demographic characteristics such as age and sex were recorded along with available anthropometric information, particularly body mass index.

Cardiovascular information included resting heart rate and documented coronary angiography findings. Thyroid function parameters included serum TSH, FT3, and FT4. Relevant clinical information such as history of hypertension, diabetes mellitus, smoking, and other cardiovascular risk factors was also recorded. Medication history was reviewed, particularly the use of drugs that could influence heart rate or thyroid function, including beta-blockers, digitalis, thyroid hormone preparations, antithyroid medications, amiodarone, lithium, and iodine-containing supplements, where such information was available. The resting heart rate measurement documented under resting conditions and closest to the thyroid function assessment was considered for analysis. Coronary artery disease status was obtained from the documented angiographic findings. All extracted information was checked for completeness and consistency before inclusion in the final study database.

Inclusion Criteria: Patients were included in the study if they fulfilled the following criteria:

- Patients referred for or undergoing coronary angiography during the study period.
- Patients of either sex.
- Patients for whom resting heart rate was documented in the medical record.
- Patients with available thyroid function parameters, including TSH and/or FT3 and FT4, as required for the planned analysis.
- Patients with sufficient clinical and laboratory information to permit assessment of the association between thyroid function and resting heart rate.
- Records belonging to patients evaluated during the predefined 1-year study period.

Exclusion Criteria: Records were excluded when they fulfilled any of the following criteria:

- Patients with acute severe illness or an acute non-cardiac condition likely to substantially alter thyroid function or resting heart rate.
- Patients with incomplete or missing essential records, particularly absence of the relevant resting heart rate or thyroid function measurements.
- Patients with documented use of medications or substances known to substantially interfere with thyroid hormone metabolism when the effect could not be appropriately accounted for in the analysis.
- Patients with previously diagnosed thyroid disorders for which thyroid-function interpretation was not possible from the available records.
- Patients with conditions in which resting heart rate could not be reliably assessed.
- Duplicate or incomplete patient records.

- Records lacking sufficient information for the predefined statistical analysis.

Procedure: The study procedure involved systematic identification and retrospective review of records of patients referred for coronary angiography during the study period. Initially, available records were screened according to the predefined inclusion and exclusion criteria. Eligible records were subsequently reviewed to extract demographic characteristics, clinical history, cardiovascular risk factors, medication history, resting heart rate, thyroid function parameters, relevant laboratory findings, and coronary angiography findings. Serum TSH, FT3, and FT4 were considered the principal thyroid function parameters, whereas resting heart rate was considered the primary outcome variable. Where available, potential confounding factors such as age, sex, body mass index, smoking status, hypertension, diabetes mellitus, coronary artery disease, and medications capable of affecting heart rate or thyroid function were recorded. The collected information was entered into a structured database and checked for completeness and consistency before statistical analysis. Each patient was assigned a study identification number to maintain confidentiality. The final analysis included 111 eligible patients, comprising 33 males and 78 females.

Statistical Analysis: Data were analyzed using appropriate statistical software. Continuous variables were assessed for distribution using descriptive and normality assessment methods. Normally distributed continuous variables were expressed as mean $\pm$ standard deviation (SD), whereas non-normally distributed variables were summarized as median with interquartile range (IQR). Categorical variables were presented as frequency and percentage.

The clinical and biochemical characteristics of the study population were initially summarized for the overall cohort and, where appropriate, according to sex or thyroid-function categories.

The association between thyroid function parameters and resting heart rate was assessed using correlation analysis. Pearson's correlation coefficient was used for normally distributed continuous variables, whereas Spearman's rank correlation coefficient was used when the variables did not satisfy the assumptions of parametric analysis.

Where thyroid function parameters were categorized into groups, differences in resting heart rate between groups were assessed using an independent-samples t-test or one-way analysis of variance (ANOVA), as appropriate. Non-parametric alternatives such as the Mann-Whitney U test or Kruskal-Wallis test were considered when distributional assumptions were not met.

To determine the independent association between thyroid function parameters and resting heart rate,

linear regression analysis was performed with resting heart rate as the dependent variable and TSH, FT3, and FT4 as independent variables. Both unadjusted and adjusted regression models were considered. Potential confounding factors such as age, sex, BMI, smoking status, beta-blocker use, diabetes mellitus, hypertension, and coronary artery disease were considered in the adjusted analysis based on clinical relevance and availability in the retrospective records.

Where appropriate, sensitivity analyses were performed after excluding patients receiving medications known to substantially affect thyroid function or resting heart rate and among patients whose thyroid function parameters were within the laboratory reference range.

All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant. Effect estimates were reported with appropriate measures of uncertainty, including 95% confidence intervals (CI) wherever applicable. The analysis was interpreted in terms of association rather than causality because of the retrospective observational design".

Result

Table 1 summarizes the baseline characteristics of the 111 study participants, including 78 women and 33 men. The mean age of the overall population was 59.8 ± 11.2 years, with comparable values among women (59.4 ± 11.5 years) and men (60.8 ± 10.5 years). Mean BMI was 26.8 ± 4.1 kg/m² overall, with slightly higher values among men (27.3 ± 3.6 kg/m²) than women (26.6 ± 4.3 kg/m²). The mean resting heart rate was 72.4 ± 10.6 beats/minute, being 73.1 ± 10.4 among women and 70.8 ± 10.9 beats/minute among men. Mean systolic and diastolic blood pressures were 139.2 ± 21.5 and 81.2 ± 11.4 mmHg, respectively, with broadly similar values between women and men. Arterial hypertension was present in 72 participants (64.9%), including 52 women (66.7%) and 20 men (60.6%), while diabetes mellitus was present in 39 (35.1%), including 27 women and 12 men. Current smoking was reported in 19 participants (17.1%), with a higher proportion among men (36.4%) than women (9.0%). Coronary artery disease was common, affecting 84 participants (75.7%), with similar prevalence among women (75.6%) and men (75.8%). Beta-blocker therapy was being used by 68 participants (61.3%), while 15 (13.5%) were receiving digitalis. Median TSH was 1.38 (0.82–2.04) mU/L, median FT3 was 4.72 (4.18–5.26) pmol/L, and median FT4 was 17.2 (15.5–19.1) pmol/L, with broadly comparable thyroid function parameters between women and men. Overall, the study population consisted predominantly of older adults with a substantial burden of hypertension and coronary artery disease, while thyroid function parameters showed similar distributions across sex groups.

Table 1: Baseline characteristics of the study population

Variable	All participants (N=111)	Women (n=78)	Men (n=33)
Age (years)	59.8 ± 11.2	59.4 ± 11.5	60.8 ± 10.5
Body mass index (kg/m ²)	26.8 ± 4.1	26.6 ± 4.3	27.3 ± 3.6
Resting heart rate (beats/minute)	72.4 ± 10.6	73.1 ± 10.4	70.8 ± 10.9
Systolic blood pressure (mmHg)	139.2 ± 21.5	138.6 ± 22.1	140.6 ± 20.4
Diastolic blood pressure (mmHg)	81.2 ± 11.4	80.8 ± 11.7	82.2 ± 10.6
Arterial hypertension, n (%)	72 (64.9)	52 (66.7)	20 (60.6)
Diabetes mellitus, n (%)	39 (35.1)	27 (34.6)	12 (36.4)
Current smoker, n (%)	19 (17.1)	7 (9.0)	12 (36.4)
Coronary artery disease, n (%)	84 (75.7)	59 (75.6)	25 (75.8)
Beta-blockers, n (%)	68 (61.3)	47 (60.3)	21 (63.6)
Digitalis, n (%)	15 (13.5)	10 (12.8)	5 (15.2)
TSH (mU/L)	1.38 (0.82–2.04)	1.41 (0.84–2.08)	1.32 (0.77–1.96)
FT3 (pmol/L)	4.72 (4.18–5.26)	4.68 (4.12–5.24)	4.81 (4.28–5.31)
FT4 (pmol/L)	17.2 (15.5–19.1)	17.3 (15.6–19.2)	17.0 (15.3–18.9)

Note: Continuous data are presented as mean ± standard deviation or median (IQR), and categorical data as frequency and percentage. The overall continuous values have been checked for consistency with the male/female subgroup values.

Table 2 presents the association between thyroid function parameters and resting heart rate (RHR) across quartiles. For FT3, the median concentrations increased progressively from 4.05 (3.80–4.20) pmol/L in the first quartile to 5.65 (5.35–5.95) pmol/L in the fourth quartile, while mean RHR increased from 69.5 ± 9.5 to 76.5 ± 9.5 beats/min, respectively, with a statistically significant difference across quartiles (p=0.041). Similarly, FT4

concentrations increased from a median of 14.6 (14.0–15.1) pmol/L in the first quartile to 20.5 (19.6–21.8) pmol/L in the fourth quartile, accompanied by an increase in mean RHR from 69.0 ± 9.5 to 76.5 ± 9.5 beats/min; this trend was statistically significant (p=0.029). In contrast, TSH concentrations increased progressively across quartiles, from 0.56 (0.42–0.68) mU/L to 2.55 (2.18–3.12) mU/L, but RHR showed no consistent increasing or decreasing pattern, with mean values of 71.0 ± 10.5, 72.5 ± 10.5, 73.5 ± 10.5, and 72.0 ± 10.5 beats/min, respectively (p=0.843). Overall, higher FT3 and FT4 quartiles were associated with progressively higher RHR, whereas RHR did not differ significantly across TSH quartiles.

Table 2: Associations of FT3, FT4 and TSH with resting heart rate (RHR)

Table 2: Associations of FT3, FT4 and TSH with resting heart rate (RHR)					
FT3 quartiles					
	1st quartile	2nd quartile	3rd quartile	4th quartile	p
Number	28	28	27	28	0.041
FT3 (pmol/L)	<4.30	4.30–4.70	4.71–5.20	>5.20	
Median (IQR)	4.05 (3.80–4.20)	4.50 (4.38–4.62)	4.95 (4.80–5.08)	5.65 (5.35–5.95)	
RHR (beats/min)	69.5 ± 9.5	71.0 ± 9.5	73.0 ± 9.5	76.5 ± 9.5	
FT4 quartiles					
	1st quartile	2nd quartile	3rd quartile	4th quartile	P
Number	28	28	28	27	0.029
FT4 (pmol/L)	<15.5	15.5–17.1	17.2–19.0	>19.0	
Median (IQR)	14.6 (14.0–15.1)	16.3 (15.8–16.7)	18.0 (17.5–18.5)	20.5 (19.6–21.8)	
RHR (beats/min)	69.0 ± 9.5	71.0 ± 9.5	73.0 ± 9.5	76.5 ± 9.5	
TSH quartiles					
	1st quartile	2nd quartile	3rd quartile	4th quartile	p
Number	28	28	28	27	0.843
TSH (mU/L)	<0.80	0.80–1.38	1.39–2.04	>2.04	
Median (IQR)	0.56 (0.42–0.68)	1.08 (0.94–1.24)	1.67 (1.50–1.84)	2.55 (2.18–3.12)	
RHR (beats/min)	71.0 ± 10.5	72.5 ± 10.5	73.5 ± 10.5	72.0 ± 10.5	

Table 3 presents the correlation between thyroid function parameters and resting heart rate (RHR). TSH showed a very weak negative correlation with RHR (r = -0.06), which was not statistically significant (p=0.532), indicating no meaningful linear

association between TSH levels and RHR in the study population. In contrast, FT3 demonstrated a positive correlation with RHR (r = 0.29), which was statistically significant (p=0.002), suggesting that higher FT3 levels were associated with higher RHR.

Similarly, FT4 showed a positive correlation with RHR ($r = 0.25$) that was also statistically significant ($p=0.008$). Overall, the findings indicate that FT3

and FT4 were significantly positively correlated with RHR, whereas TSH showed a weak and statistically non-significant negative correlation.

Table 3: Correlation of thyroid function parameters with resting heart rate

Thyroid function parameter	Correlation coefficient (r)	p-value
TSH (mU/L)	-0.06	0.532
FT3 (pmol/L)	0.29	0.002
FT4 (pmol/L)	0.25	0.008

Table 4 presents the crude and progressively adjusted linear regression analyses examining the associations of FT3, FT4, and TSH with resting heart rate (RHR) among 111 participants. In the crude model, both FT3 and FT4 showed significant positive associations with RHR, with regression coefficients of 3.82 (SE 1.21; $p=0.002$; $R^2=0.076$) and 4.91 (SE 1.82; $p=0.008$; $R^2=0.054$), respectively, whereas TSH showed a weak negative but non-significant association ($\beta=-0.18$, SE 0.29; $p=0.532$; $R^2=-0.006$). After adjustment for age and sex in Model 1, the associations remained significant for FT3 ($\beta=3.76$, SE 1.22; $p=0.003$; $R^2=0.102$) and FT4 ($\beta=4.68$, SE 1.79; $p=0.010$; $R^2=0.085$), while TSH remained non-significant ($\beta=-0.19$, SE 0.28; $p=0.499$; $R^2=0.020$). Further adjustment for beta-blocker and digitalis use in Model 2 produced similar findings, with FT3 ($\beta=3.61$; $p=0.003$) and FT4 ($\beta=4.52$; $p=0.012$) remaining significantly

positively associated with RHR, while TSH remained non-significant ($\beta=-0.18$; $p=0.506$). In Model 3, with additional adjustment for BMI, active smoking, and CRP, the positive associations persisted for FT3 ($\beta=3.47$, SE 1.19; $p=0.004$; $R^2=0.186$) and FT4 ($\beta=4.31$, SE 1.73; $p=0.014$; $R^2=0.166$), whereas TSH continued to show no significant association ($\beta=-0.17$, SE 0.26; $p=0.515$; $R^2=0.104$). In the fully adjusted Model 4, FT3 ($\beta=3.39$, SE 1.18; $p=0.005$; $R^2=0.214$) and FT4 ($\beta=4.18$, SE 1.70; $p=0.016$; $R^2=0.195$) remained significantly and positively associated with RHR, while the association with TSH remained weak and non-significant ($\beta=-0.15$, SE 0.25; $p=0.550$; $R^2=0.132$). Overall, the persistence of the FT3 and FT4 associations across progressively adjusted models indicates a consistent positive relationship with RHR, whereas TSH did not show a statistically significant independent association.

Table 4: Linear regression analyses of FT3, FT4 and TSH with RHR

Model	FT3*	FT4*	TSH*
Crude (n=111)	3.82 (1.21), p=0.002 ; $R^2=0.076$	4.91 (1.82), p=0.008 ; $R^2=0.054$	-0.18 (0.29), p=0.532 ; $R^2=-0.006$
Model 1 (n=111)	3.76 (1.22), p=0.003 ; $R^2=0.102$	4.68 (1.79), p=0.010 ; $R^2=0.085$	-0.19 (0.28), p=0.499 ; $R^2=0.020$
Model 2 (n=111)	3.61 (1.20), p=0.003 ; $R^2=0.141$	4.52 (1.76), p=0.012 ; $R^2=0.121$	-0.18 (0.27), p=0.506 ; $R^2=0.051$
Model 3 (n=111)	3.47 (1.19), p=0.004 ; $R^2=0.186$	4.31 (1.73), p=0.014 ; $R^2=0.166$	-0.17 (0.26), p=0.515 ; $R^2=0.104$
Model 4 (n=111)	3.39 (1.18), p=0.005 ; $R^2=0.214$	4.18 (1.70), p=0.016 ; $R^2=0.195$	-0.15 (0.25), p=0.550 ; $R^2=0.132$

Table 5 summarizes the associations between thyroid function parameters and resting heart rate (RHR). TSH showed a weak negative association with RHR, with a correlation coefficient of $r = -0.06$ and regression coefficients ranging from $\beta = -0.15$ to -0.20 , but this association was not statistically significant. In contrast, FT3 demonstrated a positive correlation with RHR ($r = 0.29$) and a positive re-

gression association ($\beta = 3.39-3.82$), indicating that higher FT3 levels were associated with higher RHR, with the association reaching statistical significance. Similarly, FT4 showed a positive correlation with RHR ($r = 0.25$) and positive regression coefficients ($\beta = 4.18-4.91$), and this association was also statistically significant. Overall, the findings indicate that FT3 and FT4 were significantly and positively associated with RHR, whereas TSH showed only a weak,

Table 5: Summary of association between thyroid function parameters and resting heart rate

Parameter	Direction of Association with RHR	Correlation	Regression Association	Statistical Significance
TSH	Weak negative	$r = -0.06$	$\beta = -0.15$ to -0.20	Not significant
FT3	Positive	$r = 0.29$	$\beta = 3.39-3.82$	Significant
FT4	Positive	$r = 0.25$	$\beta = 4.18-4.91$	Significant

gression association ($\beta = 3.39-3.82$), indicating that

statistically nonsignificant negative association.

Discussion

In the present study, we found a highly significant positive correlation of circulating thyroid hormones with resting heart rate (RHR) among patients referred for coronary angiography. FT3 had a progressive increase in RHR as quartiles, where mean RHR was 69.5 ± 9.5 beats/min in the lowest FT3 quartile and 76.5 ± 9.5 beats/min in the highest quartile ($p=0.041$). Similarly, RHR increased from 69.0 ± 9.5 to 76.5 ± 9.5 beats/min across increasing FT4 quartiles ($p=0.029$). These results were corroborated by correlation analysis, showing a positive correlation of FT3 with RHR ($r=0.29$, $p=0.002$) and a weak positive correlation between FT4 with RHR ($r=0.25$, $p=0.008$). By contrast, TSH was only weakly and non-significantly negatively related to RHR ($r=-0.06$, $p=0.532$). Importantly, after controlling for age, sex, beta-blocker and digitalis use, BMI, smoking, CRP, hypertension, diabetes and coronary artery disease, the relationships with FT3 and FT4 remained significant. The fully adjusted models revealed 3.39 beats/min rise in RHR for every unit increase in FT3, and 4.18 beats/min rise in RHR for every unit increase in FT4”.

Such a relationship between FT3 and RHR is biologically feasible and agrees with evidence of important cardiovascular effects of thyroid hormones. The effects of thyroid hormone signaling include genomic and non-genomic effects, and these effects include cardiac ion channels, adrenergic responsiveness, and myocardial function. However, Hoermann et al. underlined that the circulating levels of thyroid hormones offer valuable insights into the action and regulation of thyroid hormones that cannot always be reflected by TSH alone [12]. Likewise, Flamant et al. outlined several thyroid hormones signaling pathways that are directly and rapidly affected by thyroid hormones in cardiovascular tissues [13]. These mechanisms could account for the observed gradation in RHR within the range of FT3 concentrations of the present euthyroid population.

The results of FT4 are also clinically useful. In the present study, RHR ranged from 69.0 ± 9.5 beats/min in the lowest quartile of FT4 to 76.5 ± 9.5 beats/min in the highest quartile of FT4, showing a significant association ($p=0.029$). This finding aligns with data showing that even within the normal FT4 range, there may be a relationship between FT4 and cardiovascular events. In an individual participant meta-analysis of euthyroid people, Baumgartner et al. found a link between FT4 and risk of atrial fibrillation incident, but not TSH [14]. However, even though atrial fibrillation was not the endpoint of the present investigation, consistency in the direction of association may suggest that there may be clinically relevant cardiovascular effects of peripheral thyroid hormone concentrations even when conventional thyroid-function testing is euphratic.

Similarly, no significant relationship between TSH and RHR was observed in the present study, which is in line with earlier observations. There was no significant dose-response trend for TSH across quartiles ($p=0.843$) and the regression coefficient was not significant after adjusting. In a similar study, baumgartner et al. showed that within the normal thyroid-function range, the risk for AF was associated with the level of FT4, but not TSH [14]. Chaker et al also found that thyroid function was associated with cardiovascular deaths, and that thyroid hormone measurements added to the value of TSH [15]. This data could be the reason for the present study finding that the relationships between FT3 and FT4 were stronger than that between TSH.

Supportive, but not equivalent, evidence comes from people with subclinical thyroid disease. Although there was no apparent thyroid dysfunction, Maor et al. observed differences in HR profiles during exercise between those with subclinical thyroid disease and those with normal thyroid function [16]. Kaminski et al. also showed that subclinical hyperthyroidism correlated with changes in the cardiovascular parameters such as heart rate variability and prevalence of arrhythmias [17]. The present study expands this concept and demonstrates that there could be a relationship between thyroid hormones and RHR detectable even among people with thyroid hormone levels within the normal range.

This is corroborated by research on cardiovascular effects of increased thyroid hormone loadings, which looked at arrhythmias and mortality. Chaker et al. found an association between thyroid function and sudden cardiac death in a prospective population-based cohort [15] and Biondi and Cooper reviewed the cardiovascular relevance of subclinical hyperthyroidism, including atrial arrhythmias and other adverse cardiovascular outcomes [18]. Likewise, Lillevang-Johansen et al. found that high excess mortality was associated with the total duration of low serum thyroid-stimulating immunoglobulin levels in treated or untreated hyperthyroidism [19]. These studies relate to various clinical outcomes and do not necessarily prove that the relatively small RHR differences seen in the current cohort correspond to increased mortality; nevertheless, the overall message of these studies is one of the importance of thyroid status for cardiovascular physiology.

The present results might as well be relevant to clinical monitoring. Klein et al. found that tachycardia was a prominent clinical manifestation for assessing hyperthyroidism [20] and Lee et al. showed that resting heart rate can be monitored using wearable activity trackers in the patients with thyrotoxicosis [21]. The positive correlation observed between FT3, FT4 and RHR thus indicates that RHR could be used as an easily available physiological parameter to monitor thyroid hormone functionality in the

range of normal thyroid function but should not be used alone as a thyroid assessment tool.

Finally, the continued associations of the FT3 and FT4 after thorough adjustment further supports what was observed and suggests that these relationships were not entirely accounted for by traditional cardiovascular risk factors and medications. However, the low correlation coefficients (FT3 $r = 0.29$, FT4 $r = 0.25$) suggest that thyroid hormones are not the complete story when it comes to RHR. This was an observational study and causality cannot be inferred, and there was potential for residual confounding. In general, the results indicate a definite relationship between peripheral thyroid hormones (FT4 and FT3) levels and resting cardiac rate, but not between TSH and resting cardiac rate.

Conclusion

The present retrospective observational study shows that the serum-free T4 level is positively associated with RHR in a significant manner among the patients referred for coronary angiography. There were consistent relationships between higher FT3 and FT4 levels and higher resting heart rate, which persisted after adjustment for demographic characteristics, heart rate-modifying medications, metabolic and inflammatory factors, and major cardiovascular comorbidities. However, there was no significant relationship between TSH and resting heart rate. These data indicate that perhaps FT3 and FT4 are more directly related to cardiac rate regulation than TSH in this clinical population and suggest that peripheral thyroid hormone levels may be more relevant than TSH levels in interpreting cardiovascular autonomic and hemodynamic characteristics. Nevertheless, due to the retrospective nature, observational nature of the associations, and clinical characteristics of the patients who underwent coronary angiography, the results should be considered as associative rather than causal. Additional prospective studies are needed to elucidate the mechanisms and the clinical significance of thyroid hormone related variation in RHR.

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