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Original Article

Prognostic Implications of Subclinical Hypothyroidism in ST-Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Subclinical hypothyroidism (SCH), characterized by elevated thyroid-stimulating hormone with normal free thyroxine (FT4), is a potential cardiovascular risk factor. The effect of SCH on outcomes in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) has received limited investigation. We aimed to evaluate the association between SCH and anti–thyroid peroxidase antibody (anti-TPO) positivity with no-reflow and acute heart failure (HF) in patients with STEMI after PCI.

Methods: This prospective cohort study enrolled 303 patients with STEMI undergoing primary PCI at 2 tertiary centers. SCH was defined as thyroid-stimulating hormone levels greater than 4.5 mIU/L with normal FT4 (0.8–1.8 ng/dL). Outcomes included no-reflow (Thrombolysis in Myocardial Infarction [TIMI] flow ≤ 2 or corrected TIMI frame count > 27) and acute HF (Killip class > II). Multivariate logistic regression was used to assess SCH and anti-TPO positivity as predictors of no-reflow and acute HF, adjusting for age, sex, diabetes, hypertension, smoking, Gensini score, thrombus burden, preprocedural TIMI flow, ischemic time, and anti-TPO status.

Results: Patients with SCH (n = 37, 12.2%) were more likely to be female (51.4% vs 32.0% in euthyroid patients; *P* = .02) and anti-TPO positive (83.8% vs 6.4%; *P* < .001). SCH was associated with higher Gensini scores (*P* = .02), increased no-reflow, and acute HF with Killip class greater than II. SCH and left ventricular ejection fraction could predict the occurrence of acute HF (*P* = .04 and *P* < .001, respectively). SCH and anti-TPO positivity (*P* = .03 and *P* = .01, respectively) could be associated with increased no-reflow.

Conclusions: SCH and anti-TPO positivity could be associated with adverse outcomes in patients with STEMI post-PCI, suggesting a role for thyroid function screening in risk stratification. ***(Iranian Heart Journal 2026; 27(3): 49-59)***

KEYWORDS: hypothyroidism; no-reflow; acute heart failure

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Subclinical hypothyroidism (SCH), defined as an elevated thyroid-stimulating hormone (TSH) level with a normal free thyroxine (FT4) level, affects approximately 4% to 10% of adults and is increasingly recognized as a cardiovascular risk factor.[1] Predominantly affecting women and individuals older than 70 years, SCH incidence is also determined by autoimmune Hashimoto thyroiditis and increases with advancing age.[2]

The presence of anti–thyroid peroxidase antibody (anti-TPO) antibodies, suggesting autoimmune thyroid dysfunction, increases the risk of developing overt hypothyroidism and may increase the risk of cardiovascular complications.[3] While overt hypothyroidism is a well-established risk factor for coronary artery disease (CAD) and heart failure (HF), the role of SCH in acute cardiovascular events, such as ST-elevation myocardial infarction (STEMI), remains uncertain.[4, 5]

SCH is associated with small but significant cardiovascular abnormalities, including left ventricular diastolic dysfunction, increased systemic vascular resistance, and endothelial dysfunction.[1] Tissue Doppler echocardiography studies have shown prolonged isovolumetric relaxation times in participants with SCH, which can adversely affect exercise tolerance and contribute to systolic dysfunction.[7] In addition, SCH is associated with dyslipidemia, characterized by elevated low-density lipoprotein cholesterol and triglyceride levels in the context of moderate (grade 2) SCH, thereby increasing the risk of atherosclerosis.[8] These metabolic and vascular changes could be particularly hazardous in STEMI, in which ischemia already compromises myocardial function.[9]

T Thyroid hormones regulate critical cardiovascular parameters, including heart rate, cardiac output, and myocardial contractility.[10] Observational data suggest that SCH increases the risk of myocardial infarction and atherosclerosis, and levothyroxine treatment may reduce the risk of ischemic events.[11, 12] SCH in acute coronary syndromes (ACS) may exacerbate microvascular derangement and impair revascularization, leading to no-reflow or acute HF following primary percutaneous coronary intervention (PCI).[13]

The involvement of anti-TPO antibodies in these mechanisms remains unknown but may reflect autoimmune-mediated vascular inflammation.[14]

The present study investigated the prognostic impact of SCH and anti-TPO positivity on the procedural outcomes of participants with STEMI undergoing primary PCI, hypothesizing that SCH imposes an additional ischemic burden mediated by microvascular and autoimmune mechanisms.

METHODS

Study Design

This prospective cohort study comprised 303 consecutive participants undergoing primary PCI in the cardiology departments of Beni-Suef University and Tanta University, Egypt, from October 2024 through April 2025. ST-elevation myocardial infarction (STEMI) was diagnosed based on the Fourth Universal Definition of Myocardial Infarction, which requires ST-segment elevation (≥1 mm in contiguous leads or ≥ 2 mm in leads V_1–V_3) or elevated cardiac troponin levels with new left bundle branch block.[15] Participants who did not meet the inclusion and exclusion criteria were excluded.

Study Population

Participants were eligible for inclusion if they were adults older than 18 years with STEMI who were eligible for primary PCI within 12 hours of symptom onset. Participants were excluded if they were receiving thyroid replacement therapy; had

malignancy, bleeding or coagulation disorders, or end-stage renal disease requiring hemodialysis; refused to participate in the study; or had missing laboratory, demographic, or angiographic data. The enrolled participants with STEMI were divided into 2 groups according to TSH, free triiodothyronine (FT3), and FT4 levels: the SCH group and the euthyroid (ET) group. Blood samples were collected before coronary angiography to minimize the effect of iodinated contrast on thyroid function.

Ethics Approval and Consent to Participate

The current study was conducted in accordance with the principles of the Declaration of Helsinki and applicable guidelines. The study was approved by the ethics committees of Beni-Suef University (FMBSUREC/01092024/Amin, September 1, 2024) and Tanta University (36264PR822/8/24, August 21, 2024). All participants provided written informed consent.

Data Collection and Laboratory Assay

Baseline data—including demographics, cardiovascular risk factors (hypertension, diabetes, and smoking), and medical history—were collected by means of structured interviews and hospital records.

Thyroid hormone levels and antithyroid antibodies were measured using enzyme-linked immunosorbent assay (ELISA) methods according to the manufacturer's instructions. TSH levels were measured using the Human Thyroid Stimulating Hormone (TSH) ELISA Kit (catalog No. MBS705064; MyBioSource, Inc, USA). FT3 levels were determined using the Human Free Triiodothyronine (T3) ELISA Kit (catalog No. MBS495589; MyBioSource, Inc, USA). FT4 levels were assessed using the Free Thyroxine (T4) Human ELISA Kit (catalog No. ab108662; Abcam Inc, USA). Anti-TPO antibody levels were measured using the Human Thyroid Peroxidase IgG ELISA Kit (catalog No. MBS580088; MyBioSource, Inc, USA). SCH was defined as TSH greater than 4.5 mIU/L with normal FT4 (0.8–1.8 ng/dL) and no overt hypothyroid symptoms.[1] ET status was defined as TSH less than or equal to 4.5 mIU/L with normal FT4. Anti-TPO positivity was defined as a TPOAb level greater than 34 IU/mL.[16]

Participants were categorized into 2 groups: those with SCH (group I) and those with euthyroidism (group II).

Primary PCI and Angiographic Analysis

Primary PCI procedures were performed by experienced interventional cardiologists in accordance with the recommendations of the European Society of Cardiology,[17] with radial or femoral access and stent type at the operator's discretion. Coronary angiograms were analyzed offline by 2 interventional cardiologists. Coronary angiographic assessment included the Gensini score, Thrombolysis in Myocardial infarction (TIMI) flow grade, and thrombus burden. The Gensini score quantified the severity of coronary atherosclerosis by assigning scores of 1, 2, 4, 8, 16, and 32 for luminal narrowing of 25%, 50%, 75%, 90%, 99%, and 100%, respectively, multiplied by vessel-specific weighting factors.[18] TIMI flow grade was assessed before and after PCI (0 = no perfusion; 3 = complete perfusion). No-reflow was defined as a TIMI flow grade less than or equal to 2 or a corrected TIMI frame count greater than 27 after PCI despite a patent vessel.[19] Thrombus burden was graded after wire crossing or balloon restoration of flow (G0 = no thrombus; G5 = vessel occlusion).[20] Revascularization timing included the interval from symptom onset to STEMI

diagnosis, from diagnosis to wire crossing, and total ischemic time.

Clinical Outcomes

Acute HF was assessed during hospitalization using the Killip classification: Class I (no HF), Class II (S3 gallop or bibasilar rales), Class III (pulmonary edema), and Class IV (cardiogenic shock).[21]

Statistical Analysis

Continuous data were presented as mean (SD) or median (interquartile range [IQR]), according to their distribution, as assessed with the Shapiro-Wilk test. Categorical data were presented as counts and percentages. Baseline characteristics between the SCH and ET groups were compared using the independent *t* test or the Mann-Whitney *U* test for continuous variables and the χ^2 test or Fisher exact test for categorical variables. Multivariable logistic regression was performed to assess the independent predictors of no-reflow and acute HF, adjusting for potential confounders, including age, sex, diabetes, hypertension, smoking, Gensini score, thrombus burden, preprocedural TIMI flow grade, ischemic time, and anti-TPO status. Anti-TPO positivity was tested as an interaction term. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported, and only statistically significant predictors were reported. The sample size (n = 303) was calculated using the G*Power software (Franz Faul, University of Kiel, Germany; version 3.1.9.4) with 80% power (α = .05), and an effect size of 0.25. Statistical analyses were performed using SPSS, version 27.0 (IBM Corp), with a *P* value below .05 considered statistically significant.

RESULTS

Of the 303 participants with STEMI treated with primary PCI, 37 (12.2%) had SCH (SCH group), and 266 (87.8%) were ET (ET group). Baseline characteristics of the 2 groups are summarized in Table 1.

Demographic and Baseline Characteristics

Participants with SCH were more likely to be women (51.4% vs 32.0%; *P* = .022) but were similar in age (mean [SD], 56.70 [7.21] vs 58.14 [7.02] years; *P* = .245). They had a higher prevalence of diabetes, dyslipidemia, hypertension, and higher body mass index (BMI), although these differences were not statistically significant.

Participants with SCH had higher TSH levels (mean [SD], 7.97 [1.27] vs 3.19 [0.75] mIU/L; *P* < .001), lower FT4 and FT3 levels (FT4: mean [SD], 1.09 [0.22] vs 1.16 [0.15] ng/dL; *P* = .023; FT3: mean [SD], 2.79 [0.48] vs 3.07 [0.42] pg/mL; *P* < .001), and a higher prevalence of anti-TPO positivity (31 [83.8%] vs 17 [6.4%]; *P* < .001).

No statistically significant differences were observed in troponin, hemoglobin, creatinine, platelet count, or left ventricular ejection fraction (LVEF) (mean [SD], 45.27 [6.56]% vs 46.83 [5.56]%; *P* = .118). Participants with SCH were more likely to present with Killip class greater than II (9 [24.3%] vs 6 [2.3%]; *P* < .001).

Angiographic and Procedural Outcomes

Angiographic findings are presented in Table 2. Participants with SCH had higher Gensini scores (*P* = .018), with 18.9% having scores greater than 52 compared with 8.6% of participants with ET (*P* = .048). No differences were observed in the culprit lesion, stent length, stent diameter, initial thrombus burden, or pre-PCI TIMI flow. Participants with SCH had a higher incidence of no-reflow, with failure to achieve TIMI flow grade III (29.7% vs 11.7%, *P* = .003), and required more bailout glycoprotein IIb/IIIa inhibitors (29.7% vs 16.2%; *P* = .043). The incidence of contrast-induced nephropathy was similar between the groups (*P* = .90).

Table 1. Comparison of Demographic, Clinical, and Laboratory Characteristics of the SCH and ET Groups

Variable	SCH (n = 37)	ET (n = 266)	Effect Estimate (95% CI)	$t/X^2/Z$	*P*
Age, y	56.70 (7.21)	58.14 (7.02)	-1.440 (-3.875 to 0.994)	-1.164	.245
BMI, kg/m²	30.24 (4.03)	29.65 (3.35)	0.593 (-0.594 to 1.781)	0.983	.326
Female, No. (%)	19 (51.4%)	85 (32%)	2.25 (1.12 to 4.50)	5.421	.022*
Smoking, No, (%)	18 (48.6%)	122 (45.9%)	1.12 (0.56 to 2.23)	0.101	.750
Family history of CAD, No. (%)	8 (21.6%)	49 (18.4%)	1.22 (0.53 to 2.83)	0.218	.641
DM, No, (%)	16 (43.2%)	79 (29.7%)	1.80 (0.89 to 3.64)	2.768	.096
Hypertension, No, (%)	13 (35.1%)	80 (30.1%)	1.26 (0.61 to 2.60)	0.391	.532
Dyslipidemia, No, (%)	24 (64.9%)	138 (51.9%)	1.71 (0.84 to 3.51)	2.201	.138
PVD, No, (%)	2 (5.4%)	18 (6.8%)	0.79 (0.18 to 3.53)	0.098	.755
Positive anti-TPO Ab, No, (%)	31 (83.8%)	17 (6.4%)	75.68 (27.76 to 206.28)	145.93	<.001*
SBP, mm Hg	130.16 (25.79)	129.32 (24.39)	0.846 (-7.633 to 9.326)	0.196	.844
DBP, mm Hg	80.10 (14.16)	78.02 (11.83)	2.086 (-2.103 to 6.274)	0.980	.328
HR, beats/min	79.49 (11.52)	82.48 (15.83)	-2.995 (-8.305 to 2.315)	-1.110	.268
TSH, mIU/L	7.97 (1.27)	3.19 (0.75)	4.784 (4.497 to 5.070)	32.822	<.001*
FT4, ng/dL	1.09 (0.22)	1.16 (0.15)	-0.064 (-0.120 to -0.009)	-2.284	.023*
FT3, pg/mL	2.79 (0.48)	3.07 (0.42)	-0.284 (-0.432 to -0.135)	-3.757	<.001*
LVEF, %	45.27 (6.56)	46.83 (5.56)	-1.564 (-3.529 to 0.401)	-1.566	.118
Baseline troponin, ng/mL	1.28 (0.71)	1.28 (0.67)	-0.005 (-0.238 to 0.229)	-0.039	.969
Baseline creatinine, mg/dL	0.91 (0.22)	0.93 (0.30)	-0.023 (-0.122 to 0.077)	-0.444	.658
48h creatinine, mg/dL	1.05 (0.32)	1.08 (0.48)	-0.745 (-3.494 to 2.004)	-0.534	.594
Hb, g/dL	13.38 (1.187)	13.40 (1.87)	-0.017 (-0.661 to 0.628)	-0.051	.959
Platelets, cells/µL	213.30 (45.91)	206.23 (40.59)	7.072 (-7.177 to 21.320)	0.977	.330
TLC, cells/µL	8.55 (3.85)	7.82 (3.32)	0.736 (-0.433 to 1.905)	1.239	.216
Time from symptom onset to diagnosis, min	140 (106.25)	120 (62.5)	--	-1.779	.075
Time from diagnosis to wire crossing, min	30 (15)	30 (15)	--	-0.373	.707
Time from symptoms to wire crossing, min	180 (120)	160 (60)	--	-1.173	.83
Killip Class at Presentation					
Class I	19 (51.4%)	217 (81.6%)	--	39.824	<.001*
Class II	9 (24.3%)	43 (16.2%)			
Class III	5 (13.5%)	5 (1.9%)			
Class IV	4 (10.8%)	1 (0.4%)			
Killip Class > II, No. (%)	9 (24.3%)	6 (2.3%)	13.929 (4.62 to 42.01)	33.620	<.001*

anti-TPO Ab: anti-thyroid peroxidase antibody; BMI: body mass index; CAD: coronary artery disease; CI: confidence interval; DBP: diastolic blood pressure; DM: diabetes mellitus; ET: [insert full term]; FT3: free triiodothyronine; FT4: free thyroxine; Hb: hemoglobin; HR: heart rate; LVEF: left ventricular ejection fraction; PVD: peripheral vascular disease; SCH: subclinical hypothyroidism ; SBP: systolic blood pressure; TLC: total leukocyte count; TSH: thyroid-stimulating hormone

Data are presented as mean (SD), median (IQR), or No. (%). Continuous variables with normal distribution were compared using the independent-samples *t* test and are presented with the mean difference (95% CI) and *t* statistic. Categorical variables were compared using the χ^2 test and are presented with ORs and 95% CIs. Non-normally distributed variables were compared using the Mann–Whitney *U* test and are presented with the Z statistic. Statistical significance was defined as a 2-sided *P* value < .05.

Table 2. Comparison of Angiographic Findings and Procedure Outcomes

Variable	SCH (n = 37)	ET (n = 266)	Effect Estimate (95% CI)	t/X^2/Z	*P*
Gensini Score Category					
< 26	21 (56.8%)	120 (45.1%)	--	7.989	.018*
26 – 52	9 (24.3%)	123 (46.2%)			
> 52	7 (18.9%)	23 (8.6%)			
Gensini Score > 52	7 (18.9%)	23 (8.6%)	2.465 (0.975 to 6.231)	3.842	.048*
Culprit Lesion					
RCA	7 (18.9%)	62 (23.3%)	--	8.115	.230
OM	3 (8.1%)	38 (14.3%)			
LAD	22 (59.5%)	120 (45.1%)			
LM	2 (5.4%)	5 (1.9%)			
Venous graft	1 (2.7%)	3 (1.1%)			
Diagonal	1 (2.7%)	4 (1.5%)			
CX	1 (2.7%)	34 (12.8%)			
Culprit lesion stent diameter	3.11(0.36	3.11(0.31	0.004 (-0.105 to 0.114)	0.071	.943
Culprit lesion stent length	23.41(7.95	25.05(7.95	-1.639 (-4.280 to 1.001)	-1.222	.233
Initial Thrombus Burden					
Grade 0	1 (2.7%)	9 (3.4%)	--	2.533	.639
Grade I	1 (2.7%)	13 (4.9%)			
Grade II	2 (5.4%)	21 (7.9%)			
Grade III	8 (21.6%)	34 (12.8%)			
Grade IV	25 (67.6%)	189 (71.1%)			
Initial thrombus burden ≥ 3	35 (94.6%)	244 (91.7%)	1.578 (0.356 to 7.003)	0.366	.545
Post-Flow achievement Thrombus Burden					
Grade 0	0 (0%)	19 (7.1%)	--	8.729	.120
Grade I	9 (24.3%)	43 (16.2%)			
Grade II	2 (5.4%)	30 (11.3%)			
Grade III	11 (29.7%)	71 (26.7%)			
Grade IV	13 (35.1%)	100 (37.6%)			
Grade V	2 (5.4%)	3 (1.1%)			
Post-flow thrombus burden ≥ 3	26 (70.3)	174 (65.4%)	1.250 (0.591 to 2.643)	0.341	.559
Initial TIMI Flow Score					
Grade 0	26 (70.3%)	184 (69.2%)	--	0.840	.840
Grade I	8 (21.6%)	50 (18.8%)			
Grade II	2 (5.4%)	26 (9.8%)			
Grade III	1 (2.7%)	6 (2.3%)			
Initial TIMI flow score ≤ I	34 (91.9%)	234 (88%)	1.550 (0.450 to 5.339)	0.489	.484
Initial TIMI flow score ≤ II	36 (97.3%)	260 (97.7%)	0.831 (0.097 to 7.100)	0.029	.865
Final TIMI Flow Score					
Grade 0	2 (5.4%)	3 (1.1%)	--	9.927	.019*
Grade I	3 (8.1%)	10 (3.8%)			
Grade II	6 (16.2%)	18 (6.8%)			
Grade III	26 (70.3%)	235 (88.3%)			
Final TIMI flow score ≤ II	11 (29.73%)	31 (11.65%)	3.207 (1.444 to 7.125)	8.888	.003*
Contrast-induced nephropathy	4 (10.8%)	27 (10.2%)	1.073 (0.353 to 3.260)	0.015	.901
GP IIB/IIIA bailout use	11 (29.7%)	43 (16.2%)	2.194 (1.009 to 4.771)	4.081	.043*
Use of thrombus aspiration	3 (8.1%)	16 (6%)	1.379 (0.382 to 4.979)	0.242	.623

CX; circumflex; ET; euthyroid; GP IIb/IIIa; glycoprotein IIb/IIIa; LAD; left anterior descending; LM; left main; OM; obtuse marginal; RCA; right coronary artery; SCH; subclinical hypothyroidism; TIMI; Thrombolysis in Myocardial Infarction

Data are presented as mean (SD) or No. (%), as appropriate. Continuous variables with normal distribution were compared using the independent-samples *t* test and are presented with the mean difference (95% CI) and *t* statistic. Categorical variables were compared using the χ^2 test and are presented with ORs and corresponding 95% CIs. Statistical significance was defined as a 2-sided *P* value < .05.

Regression Analysis

Multivariable logistic regression (Table 3) identified SCH and LVEF as independent predictors of acute HF (Killip class > II), with ORs (95% CIs) of 0.298 (0.095 to 0.937) and 1.498 (1.262 to 1.780) and *P* values of .039 and less than .001, respectively. For no-reflow (Table 4), anti-TPO positivity and SCH were associated with postprocedural no-reflow (TIMI flow ≤ 2), with ORs (95% CIs) of 0.400 (0.188 to 0.852) and 0.312 (0.140 to 0.693) and *P* values of .012 and .031, respectively.

Table 3. Univariable and Multivariable Logistic Regression Analysis of Predictors of Killip Class > II

	Univariable		Multivariable	
Variable	*P*	OR (95% CI)	*P*	OR (95% CI)
SCH	<.001	0.072 (0.024 to 0.217)	.039*	0.298 (0.095 to 0.937)
TSH	<.001	0.630 (0.512 to 0.775)	.329	1.140 (0.708 to 2.808)
FT4, ng/dL	.001	15.534 (3.128 to 77.137)	.074	5.663 (0.845 to 37.953)
Positive anti-TPO Ab	<.001	0.104 (0.035 to 0.310)	.144	0.170 (0.016 to 1.830)
LVEF	<.001	1.366 (1.218 to 1.533)	<.001*	1.498 (1.262 to 1.780)

FT4; free thyroxine; LVEF; left ventricular ejection fraction; SCH; subclinical hypothyroidism; TPO; thyroid peroxidase; TSH; thyroid-stimulating hormone

Table 4. Univariable and Multivariable Logistic Regression Analysis of Predictors of Final TIMI Flow Score ≤ 2

	Univariate		Multivariate	
Variable	*P*	OR (95% CI)	*P*	OR (95% CI)
SCH	.004	0.312 (0.140 to 0.693)	.031*	0.102 (0.013 to 0.807)
Positive anti-TPO Ab	.018	0.400 (0.188 to 0.852)	.012*	0.380 (0.175 to 0.775)
TSH	.04	0.853 (0.728 to 0.998)	.164	1.319 (0.893 to 1.947)
Time from symptom onset to diagnosis	.011	0.997 (0.995 to 0.999)	.213	0.992 (0.979 to 1.005)
Time from symptom onset to wire crossing	.019	0.997 (0.995 to 0.999)	.484	1.005 (0.992 to 1.018)

SCH; subclinical hypothyroidism; TIMI; Thrombolysis in Myocardial Infarction; TPO; thyroid peroxidase; TSH; thyroid-stimulating hormone.

DISCUSSION

Our research sought to investigate the association between SCH and short-term clinical outcomes in patients with STEMI and ACS necessitating PCI. The results indicate that SCH has a significant influence on the clinical characteristics and short-term prognosis of these patients.

There were minimal variations in baseline patient characteristics between the SCH and ET groups, which legitimized them for comparison. A significant sex imbalance was observed, with a higher proportion of females in the SCH group (51.4%) compared with the ET group (32.0%) (*P* = .02). This finding is consistent with prior research that noted an increased incidence of SCH in women with ACS who underwent primary PCI. [22]

The prevalence of SCH in our study was 12.2%, which is similar to the findings of Arambam et al, [23] who reported a prevalence of SCH of 11% among patients with acute coronary syndrome.

The SCH group also showed a markedly higher prevalence of positive anti-TPO antibodies (83.8%) compared with the ET group (6.4%) (*P* < .001), corroborating findings from previous studies, such as those of Han C et al [22] and Jabbar A et al. [24] This finding suggests that autoimmune mechanisms may play a significant role in the pathogenesis of SCH in these patients.[25] These baseline differences are attributed to the disease itself, not to selection bias.

Albeit not yet statistically significant, the SCH group exhibited a higher prevalence of diabetes mellitus (43.2% vs 29.7%; *P* = .096) and dyslipidemia (64.9% vs 51.9%; *P* = .138). Our results align with prior research suggesting an association between SCH and increased cardiovascular risk.[26]

Although LVEF was marginally lower in the SCH group, this difference did not reach statistical significance (mean [SD], 45.27 [6.56] vs 46.83 [5.56]; *P* = .118); patients in the SCH group experienced more severe clinical symptoms of HF with a statistically significant proportion of patients having Killip class greater than II (24.3% vs 2.3%; *P* < .001).

Our results corroborate prior studies indicating that SCH may lead to mild but significant alterations in cardiac performance.[27, 28] Multiple pathways could account for these observations. SCH is linked to metabolic syndrome, which elevates systemic vascular resistance and promotes endothelial dysfunction through diminished nitric oxide levels.[11]

Previous studies have found that individuals with subclinical hypothyroidism have diastolic dysfunction.[1] Restoring the ET state improves these abnormalities, with a decrease in isovolumic relaxation time, a decrease in pre-ejection period–ejection time ratio, and an increase in the early diastolic–late diastolic mitral flow velocity ratio.[11]

The Gensini score, used to determine the severity and distribution of coronary artery atherosclerosis, revealed a higher percentage of scores above 52 in the SCH group compared with the ET group (18.9% vs 8.6%; *P* = .048).

This conclusion further underscores the association between SCH and higher cardiovascular risk, increased burden, and atherosclerosis. This finding is consistent with the study by Han et al[22] in patients with non–STEMI.[22]

Studies have shown that hypothyroidism and autoimmune thyroiditis are associated with a higher cardiovascular risk, as also noted in the meta-analysis by Moon et al.[29] Moreover, the final TIMI flow score, measuring coronary flow after revascularization, was also significantly reduced in the SCH group (*P* = .019), with prognostic implications of worse outcomes after revascularization.

The increased use of glycoprotein IIb/IIIa inhibitors in the SCH group (29.7% vs 16.2%; *P* = .043) may reflect a higher thrombotic burden and the need for more aggressive antithrombotic therapy in these patients, consistent with other studies that found poorer revascularization outcomes in patients with SCH and ACS.[13, 30]

The association between SCH and more aggressive atherosclerosis, as well as poor angiographic outcome after primary PCI, can be explained by several mechanisms. SCH is usually associated with metabolic syndrome and increased insulin resistance,[31] which are established risk factors for atherosclerosis. Further, SCH is associated with hypercoagulable and hypofibrinolytic states, which may lead to overactivity of plasminogen activator inhibitor-1 and factor VII and an increased risk of thrombosis.[32]

Additionally, some studies have found that elevated mean fibrinogen levels are observed in patients with ET Hashimoto thyroiditis compared with ET controls.[33] This may explain our finding that the presence of autoantibodies is an independent predictor of poor TIMI flow after primary PCI.

Furthermore, Mavai et al[25] found in their study that the presence of autoantibodies, specifically in patients with SCH, was associated with autonomic imbalance. They concluded that anti-TPO antibody–positive patients exhibited modifications in heart rate variability characterized by decreased parasympathetic modulation, which is

suggestive of increased risk of autonomic dysfunction. This autonomic imbalance may play a role in the development of HF and no-reflow by affecting peripheral vascular resistance.

On the other hand, there is some evidence suggesting a strong involvement of systemic vascular inflammation, which may also impact the remodeling process.[34] Zhang et al[35] found TSH levels to be positively correlated with C-reactive protein, interleukin-6, and erythrocyte sedimentation rate in patients with SCH, and these markers were significantly higher in the SCH group.

The increased systemic inflammatory markers may play a role in explaining the significant effect of SCH and the presence of autoantibodies on cardiac function and outcome after primary PCI, resulting in a higher incidence of HF and no-reflow. These results support routine thyroid function testing in patients with STEMI to identify those at risk for adverse outcomes.

Limitations of the Study

The observational design of our study precludes establishing causality. Although the sample size was acceptable for primary endpoints, it may limit detailed subgroup evaluations. Latent selection bias may have been introduced by excluding patients who refused participation, which could affect generalizability. Long-term outcomes and the effects of levothyroxine therapy were not evaluated. Some baseline differences, possible residual confounding, and variability in definitions may affect the results.

CONCLUSIONS

Patients with STEMI and SCH may have higher rates of no-reflow and acute HF after primary PCI. Anti-TPO positivity could be used as a predictor of more severe no-reflow, suggesting an autoimmune component. Thyroid function screening may enhance risk stratification and inform targeted therapies in patients with STEMI.

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Author Contributions:

OA: conceptualization, coronary intervention, data collection, writing; HS: data collection, review; HK: laboratory tests, writing, and manuscript editing; AH: statistical analysis, writing, and manuscript editing; AA: supervision, coronary intervention, writing, review. All authors contributed to the drafting of the manuscript and approved the final version.

Ethics Approval and Consent to Participate: The present study was conducted in adherence to the Declaration of Helsinki and in accordance with applicable guidelines. The study was approved by the Institutional Review Board of Beni-Suef University (FMBSUREC/01092024/Amin, September 1, 2024) and Tanta University (36264PR822/8/24, August 21, 2024). Written informed consent was obtained from all participants.

Data Availability: Datasets are available from the corresponding author upon reasonable request.

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