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Original article

Association of Thyroid Hormones Level with Coronary Lesion Complexity in Patients with Acute Coronary Syndrome

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Abstract

Aim: Our aim was to study the correlation between the thyroid hormones level and the coronary lesion complexity in patients with acute coronary syndrome (ACS). **Patients and Methods:** This is a prospective which included 100 patients with ACS who were admitted for percutaneous coronary intervention (PCI). The patients were divided according to thyroid functions into 3 groups: Euthyroid patients (90 patients), hyperthyroid patients (2 patients), and hypothyroid patients (8). **Results:** There was statistically significant correlation between 3 groups of thyroid hormone levels and BMI and myocardial infarction (MI). There was statistically non-significant differences between the 3 groups of thyroid functions(euthyroid, hyperthyroid and hypothyroidism) as regarded Age, Sex, Hypertension, DM, Coronary artery disease(CAD),Congestive heart failure (CHF), Blood diseases, PCI ,taking aspirin or warfarin, Ejection fraction, HbA1C, liver function tests, C-Reactive protein(CRP)level and Troponin marker. There was not a significant correlation between Syntax score and Age, International normalized ratio(INR), (Thyroid stimulating hormone) TSH level, Free Thyroxine (FT4), Ejection fraction and HbA1C.Syntax score was significantly inversely related to serum triiodothyronine (FT3) levels. In addition to its correlation with the syntax score, FT3 was shown to be a reliable predictor of CAD severity on its own. This suggests that FT3, rather than FT4 and TSH levels, may be utilized to predict the severity of CAD. **Conclusion:** FT3 levels below 2.65 nmol/L are a strong indicator of coronary artery lesion severity. A lower FT3 level is a continuous variable that may be utilized as a predictor of an increased risk for severe CAD.

Keywords: Acute Coronary Syndrome; Thyroid Functions; Percutaneous Coronary Intervention; Syntax Score; Coronary Artery Disease.

Introduction

Short-term and long-term mortality of individuals suffering from acute coronary syndrome (ACS) remains high despite advancements in medication and myocardial reperfusion methods [(1)].

The long-term prognosis for individuals with either ST-segment elevation myocardial infarction (STEMI) or non- NSTEMI is comparable, although the short-term prognosis is poorer for STEMI patients. The first Killip class clinical presentation and electrocardiogram (ECG) abnormalities are significantly predictive of early prognosis, in addition to clinical indications of risk such as advanced age, diabetes mellitus (DM), renal insufficiency, higher heart rate, and hypotension. In addition, biomarkers including high-sensitivity troponin, natriuretic peptides, and C-reactive protein (CRP) give added predictive value [(1)].

Thyroid hormones (THs) plasma concentrations have long been thought to fluctuate in response to sudden health crises [(2)].

There is a correlation between abnormal thyroid function tests and illness severity and death in people who are severely sick [(3)].

Patients without a history of intrinsic thyroid disease may have changes in plasma concentrations of THs, namely reduced triiodothyronine (T3) and/or free T3 (fT3), due to a wide range of acute and chronic diseases [(4)].

It is an independent predictor of both short-term and long-term death in these individuals.

Because THs have such profound impacts on the cardiovascular system, there is mounting evidence that THs change may have a predictive role in patients with ACS [(5)].

The purpose of this research was to examine the association between the level of thyroid hormones and the complexity of coronary lesions in patients with ACS by reviewing the relevant literature to better explain the function of THs variations during ACS and their possible predictive significance.

Patients and Methods:

This is a prospective study that included 100 consecutive patients with ACS who were admitted to the catheterization laboratory at Hospital of Benha University - for PCI from the period of November 2019 to May 2021.Patients with Age 30- 75 years old, both sexes were included, but Patients with impaired renal functions (serum creatinine more than 1.3mg/dl), refusal of participation to the study, diabetic Patients were excluded. The patients (100) were divided according to thyroid functions into 3 groups: Euthyroid patients (90 patients), hyperthyroid patients (2

patients), and hypothyroid patients (8 patients). All patients enrolled in the study were subjected to: Full history taking, clinical examination, and laboratory investigations such as Renal function tests (blood urea, serum creatinine, urine analysis, and eGFR), complete blood picture (CBC), Lipid profile (Total lipids, Serum total cholesterol, serum HDL cholesterol, total cholesterol/HDL cholesterol ratio, Serum triglycerides, LDL, VLDL, HDL), and cardiac enzymes (Troponin, CKMB, CK). Standard 12lead resting ECGs were recorded using a common ECG device (Hewlett Packard, Page-writer, USA) with a paper running speed of 25 mm/s.

Resting Transthoracic Echocardiography was done with special stress on RWMA and LVEF. Assessment of radial & femoral artery patency before and after the procedure (Clinical, pulse oximeter). PCI through radial or femoral approach.The evaluation of the presence of CIN and accesses, the clinical and procedural characteristics of the patients were compared between the two groups undergoing PCI through radial or femoral approach.

Coronary artery lesion complexity was evaluated by SYNTAX score I.[٦]

SYNTAX score I was calculated for all patients.

An informed consent was taken from each patient. The aim of the study was explained to the patients. No harm was caused to patients as blood samples were routinely collected from patients.

Official permission was obtained from the Faculty of Medicine, Benha University, and approval from the ethical committee in the faculty of medicine (Institutional Research Board IRB).

Statistical Analysis

IBM SPSS Statistics for Windows, Version 20.0 (developed by IBM) was used to conduct the statistical analysis. It was published by IBM in Armonk, New York. Quantitative and percentage descriptions were used for qualitative data. After ensuring normality using the Kolmogorov-Smirnov test, quantitative data was characterized with mean and standard deviation for parametric data. The acquired findings were considered significant at the 5% probability level.

Analysis of Data: The qualitative information: Test of independence using the chi-square distribution for comparing two or more groups. Evaluation of statistical significance using parametric tests for quantitative data between groups. Two groups were compared using the student t-test. The Mann-Whitney U-Test Is a Nonparametric Two groups were compared using the U test to determine statistical significance. To assess the strength and direction of a linear connection between

two non-normally distributed continuous and/or ordinal variables, researchers often turn to Spearman's rank-order correlation. None of the statistical analyses were one-sided. A p value of 0.05 or below was used to indicate statistical significance.(٧)

Results

There was significant correlation between both MI (P value=.012) and BMI (P value=.043) with groups of thyroid hormone levels.

No significant differences were reported between thyroid groups regarding Age (P value=.094), Sex (P value =.57), Smoking (P value =.49), hypertension (P value=.07), DM (P value = 1.0), CAD (P value =.64), congestive heart failure (P value =.58), blood diseases (P value =.96). Also, there was no correlation between thyroid hormone and performed PCI (P value =.89), no relationship between thyroid hormone levels and taking aspirin (P value =.78) nor taking warfarin (P value =.69) Hypothyroidism significantly higher regard BMI and MI sig associated with Euthyroid (Tab. 1)

Laboratory investigations and ECHO in the studied groups: No significant correlation was reported between our groups and HbA1C (P-Value=.53), Renal function test (P-Value=.32), CRP (P-Value=.27), Troponin (P-Value=.42), Ejection Fraction(P-Value=.074), INR(P-value=.491). (Tab. 2)

Correlation between Syntax score and other parameters (age, BMI, INR, TSH level, free T3, free T4, Ejection Fraction and HbA1C). There was statistically non-significant correlation between Syntax score and age (P = .075), BMI. (P =.061), INR (P value=.491), TSH level (P value=.936), free T4. (P =.307). (Tab. 3)

But there was statistically significant negative correlation between Syntax score and free T3 (P=.031), Syntax score was significantly negative correlated with T3. (Tab. 3)

AUC, CUTOFF and validity of FT3 regarding SYNTAX score: Significant area under curve with cut-off <2.65 with sensitivity 62.5% and specificity 58.3%. (Tab. 4) (Fig. 1)

Table 1: Relation between thyroid status and basic demographic and clinical data

			Group			F/X^2	P
			Euthyroid	**Hyperthyroidism**	**Hypothyroidism**		
Age	**Mean ±SD**		**57.36±7.99**	**45.5±2.12**	**59.0±7.05**	**2.42**	**0.094**
BMI	**Mean ±SD**		**23.81±2.13**	**22.50±0.70**	**25.75±3.19**	**3.24**	**0.043***
Sex	**Female**	**N**	26	0	3		
		%	28.9%	0.0%	37.5%		
	Male	**N**	64	2	5	1.09	0.57
		%	71.1%	100.0%	62.5%		
Smoking	**No**	**N**	32	0	2		
		%	35.6%	0.0%	25.0%		
	Yes	**N**	58	2	6	1.41	0.49
		%	64.4%	100.0%	75.0%		
HTN	**No**	**N**	28	2	4		
		%	31.1%	100.0%	50.0%		
	Yes	**N**	62	0	4	5.13	0.07
		%	68.9%	0.0%	50.0%		
DM	**No**	**N**	90	2	8		
		%	100.0%	100.0%	100.0%		
	Yes	**N**	0	0	0	0.0	1.0
		%	0.0%	0.0%	0.0%		
CAD	**No**	**N**	24	0	0		
		%	26.6%	0.0%	0.0%		
	Yes	**N**	66	2	8	2.85	0.46
		%	73.3%	100.0%	100.0%		
MI	**No**	**N**	57	2	6		
		%	63.3%	100.0%	75.0%	12.91	0.012*
	Yes	**N**	33	0	2		
		%	36.7%	0.0%	25.0%		
CHF	**No**	**N**	66	2	4		
		%	73.3%	100.0%	50.0%		
	Yes	**N**	24	0	4	2.86	0.58
		%	26.7%	0.0%	50.0%		
Blood disease	**No**	**N**	86	2	8		
		%	95.6%	100.0%	100.0%		
	Yes	**N**	4	0	0	0.28	0.96
		%	4.4%	0.0%	0.0%		
Coronary angiography	**yes**	**N**	2	0	0		
		%	2.2%	0.0%	0.0%		
	Yes	**N**	88	2	8	0.22	0.89
		%	97.8%	100.0%	100.0%		
Aspirin	**No**	**N**	40	0	3		
		%	44.4%	0.0%	37.5%	1.75	0.78
	Yes	**N**	50	2	5		
		%	55.6%	100.0%	62.5%		
warfarin	**No**	**N**	61	2	7		
		%	67.8%	100.0%	87.5%		
	Yes	**N**	29	0	1	2.25	0.69
		%	32.2%	0.0%	12.5%		
Total		**N**	90	2	8		
		%	100.0%	100.0%	100.0%		

BMI: Body Mass Index, HTN: Hypertension, DM: Diabetes Mellitus, CAD: Coronary artery disease, MI: Myocardial infarction, CHF: Congestive heart failure.

Table 2: Laboratory investigations and ECHO in the studied group

			Euthyroid Patients	Hyperthyroid Patients	Hypothyroid Patients	F/ Kruskal–Wallis	P
EF			57.66±7.71	69.50±0.70	54.62±6.69	3.05	0.074
HbA1C			5.83±0.49	5.45±0.21	5.87±0.50	0.62	0.53
RFT	**Normal**	**N**	73	2	8		
		%	81.1%	100.0%	100.0%		
	Abnormal	**N**	17	0	0	2.27	0.32
		%	18.9%	0.0%	0.0%		
CRP	**Negative**	**N**	75	2	5		
		%	83.3%	100.0%	62.5%		
	Positive	**N**	15	0	3	2.60	0.27
		%	16.7%	0.0%	37.5%		
Troponin	**Negative**	**N**	41	0	4		
		%	45.6%	0.0%	50.0%		
	Positive	**N**	49	2	4	1.72	0.42
		%	54.4%	100.0%	50.0%		
Total		**N**	90	2	8		
		%	100.0%	100.0%	100.0%		

EF: Ejection Fraction, LFT: Liver Function Test, CRP: C-reactive Protein, HbA1C: hemoglobin A1C.

Table 3: Relation between thyroid status and other parameters

		Syntax score
Age	**r**	-.179-
	P	.075
BMI	**r**	.188
	P	.061
INR	**r**	-.070-
	P	.491
TSH	**r**	.008
	P	.936
T3	**r**	-.216-*
	P	.031
T4	**r**	-.103-
	P	.307
EF	**r**	.135
	P	.179
HbA1C	**r**	-.054-
	P	.596

BMI=Body Mass Index, INR=International Normalized Ratio, TSH = thyroid stimulating hormone, T3 = triiodothyrodine, T4 = Thyroxin, EF = Ejection Fraction

Table 4: AUC, CUT-OFF and validity of FT3 regarding SYNTAX score

			95% Confidence Interval			
Area	Cutoff	P	Lower Bound	Upper Bound	Sensitivity	Specificity
0.641	**<2.65 nmol/L**	**0.052**	**0.496**	**0.747**	**62.5%**	**58.3%**

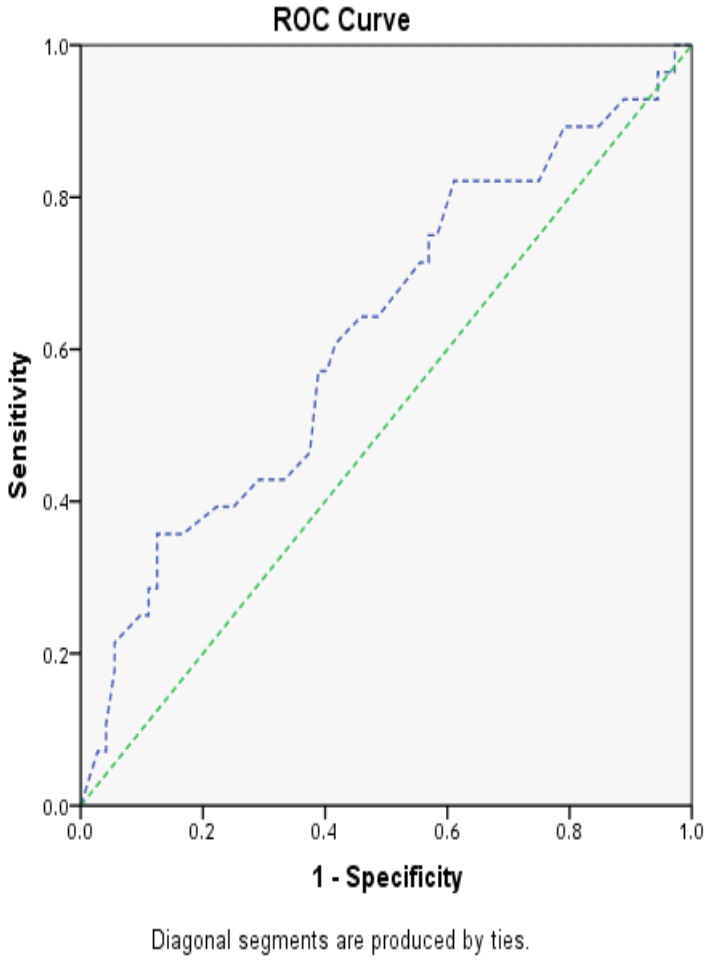

Figure 1: ROC curve for detection of suggested T3 cutoff regard high Syntax score.

Discussion

Short-term and long-term mortality of individuals suffering from acute coronary syndrome (ACS) remains high despite advancements in medication and myocardial reperfusion methods [(1)].

Thyroid hormones (THs) plasma concentrations have long been thought to fluctuate in response to sudden health crises [(2)]. Critically sick individuals who have abnormal thyroid function tests have a higher illness severity and fatality rate [(٨)].

With respect to HbA1C (P =.53) and Ejection fraction, there was no statistically significant association between the three thyroid function groups (euthyroid, hyperthyroid, and hypothyroidism).

To this end, a study [(٩)] observed no association between HbA1c and coronary atherosclerosis

severity in ACS, and their findings were corroborated by other researchers.

The association between syntactic score and TSH level was weak or non-existent in our research. (P =0.936)

This was in agreement with another study [10] who enrolled 100 patients with ACS and found a non-significant correlation between TSH (mean ±SD= 2.47+1.38) and severity of coronary artery disease estimated by Gensini score (P =.07).

In our study there was statistical non-significant correlation between Syntax score and T4 (P =.936).

This was in line with the result of the study done by another study. [11] on 100 patients with ACS and revealed non-significant correlation between T4 and severity of coronary artery disease evaluated by Gensini score.

There were statistically non-significant differences between the 3 groups of thyroid functions (euthyroid, hyperthyroid, and hypothyroid) as regard Ejection fraction. (P =.074), HbA1 C. (P=.53), liver function tests.(P =.32), CRP level.(P=.27), and troponin marker. (P =.42).

This was in disagreement with another study [9] which documented that LVEF was an independent predictor of Gensini score , this can be attributed to that we used SYNTAX score.

Neither the syntactic score nor the liver function tests were statistically linked in our investigation. (P=.32)

Although we employed other liver biomarkers, we could not find an association between bilirubin and SYNTAX score, which may predict future cardiovascular events in individuals with stable coronary artery disease, as did in other study. [12].

We found no evidence of a link between syntactic score and CRP in our investigation. (P=.27).

This was in agreement with another study. [13] which enrolled 2554 patient which shows low correlation coefficient with P = .08.

This was in acceptance with another study. [14] Who revealed that hsCRP level showed no significant association with CAD severity.

This agreed with another study. [15] who found no significant association between mean hs-CRP levels and the severity of CAD as evaluated by the Gensini score.

Although a study. [16] showed that low serum FT4 and high TSH were linked to advanced coronary atherosclerosis, they did not use the Gensini scoring method in their analysis.

In a study of 192 patients, a study. [11] demonstrated that high blood FT4 levels, even within normal range, may be a risk factor for

CAD. Despite this, they could not discover any link between FT4 and CAD.

Our findings were also consistent with those of a study. [17], who concluded that TSH levels beyond the standard range were not a significant predictor of CHD.

We found a statistically significant inverse relationship (P =.031) between Syntax score and free T3.

Results were consistent with those of a study. [10], who included 100 patients with free T3 (Mean SD= 2.84+0.49) and observed a strong inverse connection between FT3 and the severity of coronary artery disease as measured by the Gensini score.

Limitations to this research were minor. Because it was cross-sectional research, there was no way to determine causation. - Therefore, any findings from this research should be seen more as associational hypotheses than as proof of hypotheses. There was also a lack of homogeneity in the cohort and a rather small sample size. Thirdly, since it is a luminogram, coronary angiography is not the best method for quantifying atherosclerosis.

Conclusion

We found that FT3 levels below 2.65 nmol/L were a significant predictor of coronary artery lesion severity. Unfortunately, no correlation between TSH and FT4 levels and CAD prevalence or severity could be established. Therefore, a lower FT3 level is a continuous variable that may be utilized as an indication of increased risk for severe CAD.

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