Thyroid hormone profile in patients diagnosed with acute myocardial infarction and its relation with mortality

Evren Dal1*, Hakan Topacoglu2

1 University of Health Sciences, Bursa Selur Training&Research Hospital, Dept. of Emergency Medicine, Bursa, TR
2 Okmeydani training and Research Hospital, Emergency Department, Istanbul, TR

* Corresponding Author: Evren Dal E-mail: evrendal2000@yahoo.com

ABSTRACT

Objective: Thyroid hormones have an important role in the cardiovascular system function. As maintaining cardiovascular homeostasis, even small fluctuations in thyroid hormone levels can increase cardiovascular-related mortality. This study aims to investigate the correlation between thyroid hormone disorders and mortality among patients admitted to the emergency department with chest pain and diagnosed with myocardial infarction.

Material and Methods: The primary objective of this retrospective study was to evaluate individuals who were admitted to the emergency department and diagnosed with acute myocardial infarction, focusing specifically on patients with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (non-STEMI). The study comprised a total of 70 patients who were enrolled as participants and various parameters including age, gender, medical history of chronic diseases, routine blood parameters, Low density lipoprotein (LDL) cholesterol, High density lipoprotein (HDL) cholesterol, triglyceride levels, as well as measurements of free Triiodothyronine (fT3), free Thyroxine (T4), and Thyroid Stimulation Hormone (TSH) were recorded. Additionally, diagnoses, discharge status, and in-hospital mortality were documented. The relationship between the mortality status of the patients and the observed changes in the current thyroid function tests was evaluated.

Results: The study encompassed a cohort of patients with a mean age of 64.46 ± 15.64 years (minimum: 29, maximum: 92), of which 22 individuals (31.4%) were female, and 48 (68.6%) were male. While no significant difference was found in the comparison of laboratory mean values of the patients included in the study by gender (p > 0.05), the difference between fT3, HtC and Hemoglobin values between the mortality group and the survival group was statistically significant (p < 0.05).

Conclusion: Thyroid hormone disorders pose risks related to coronary artery disease, encompassing hypertension, atherosclerosis, lipid metabolism, homocysteine production, and endothelial effects, which can amplify mortality rates among acute myocardial infarction patients. The "low T3 syndrome" denotes an imbalance of thyroid hormones that significantly impacts cardiovascular mechanisms. Aberrant thyroid hormone levels exhibit a higher prevalence within acute coronary syndromes.

Keywords: Acute Myocardial Infarction, fT3, fT4, TSHs

INTRODUCTION

Acute Coronary Syndrome (ACS) represents a significant public health concern due to its substantial hospitalization rates, detrimental impact on workforce productivity, increased morbidity, and elevated mortality rates. In addition to the substantial loss of life and health-related implications, acute coronary syndrome (ACS) imposes a significant economic load on national economies due to the expenses related to treatment and more than 2.5 million hospital admissions (1, 2). Based on data from 2020, coronary diseases persist as the foremost cause of mortality in the United States, with an annual occurrence of 605,000 new cases and 200,000 recurrent events. Furthermore, the annual mortality rates have exhibited a 0.9% increase (3).
Emergency physicians frequently evaluate patients presenting with angina and other possible symptoms suggestive of acute coronary syndrome, using electrocardiograms and biochemical diagnostic markers for differential diagnosis. Patients deemed to be at a heightened risk of experiencing acute myocardial infarction (AMI) following an initial assessment are either admitted to the hospital for reperfusion therapy in collaboration with a cardiologist or are closely monitored within the emergency department until a definitive diagnosis is established or ruled out. When patients are evaluated as low risk, they are discharged with a recommendation for cardiology outpatient clinic follow-up in the near term, and the situations that require emergency department admission are explained. It is not always easy to identify patients as low or high risk and clarify their eligibility for discharge. Studies show that between 2% and 8% of patients with AMI are sent home from the emergency department without a correct diagnosis (4, 5).

Thyroid hormones are substances that impact all cells in the body, stimulating the production of structural proteins, enzyme proteins, and carrier proteins within cells. It has long been known that the plasma concentrations of thyroid hormones are altered in acute disease states (6). Thyroid hormones have inotropic, chronotropic and lusitropic effects on the heart and vascular system by increasing cardiac output and reducing vascular resistance. Even a small change in thyroid hormone levels can affect heart function, heart rate and cause dysrhythmia. This effect on the heart has a negative effect on mortality that may develop in the presence of coronary artery disease. (7-9). Its effects on the cardiovascular system are primarily related to activating the sympathetic nervous system. Under normal physiological circumstances, thyroid hormones enhance the heart's conduction rate, augment the myocardium's contractile strength, and raise the heart's stroke volume through the elevation of isometric tension. Additionally, these hormones induce peripheral vessel dilation, leading to heightened systolic pressure and reduced diastolic pressure (10, 11).

Cardiovascular morbidity in hypothyroid patients has been associated with elevated low density lipoprotein (LDL) level and diastolic hypertension. While there was a significant correlation between hyperhomocysteinemia and endothelial dysfunction in cases with significant hypothyroidism and in some cases of subclinical hypothyroidism, this was evaluated as an important risk factor for atherosclerosis. (12).

The primary objective of our study was to examine the association between thyroid hormone disorders at the time of presentation and mortality in patients who presented to the emergency department with chest pain and received a diagnosis of acute myocardial infarction. In the context of acute myocardial infarction, undiagnosed thyroid dysfunction can notably impact mortality, particularly among individuals deemed at high risk. By promptly identifying thyroid hormone disorders and achieving euthyroidism through suitable treatment interventions, it may be possible to mitigate the risk of acute myocardial infarction and the subsequent elevated mortality rates associated with the condition.

**MATERIAL and METHODS**

The study included patients admitted to the Emergency Service of Okmeydanı Training and Research Hospital over one year, diagnosed with acute myocardial infarction, and subsequently admitted to the coronary intensive care unit. The evaluation of thyroid function tests during the follow-up period served as the inclusion criterion for these patients. Retrospective review of patient records was conducted utilizing the hospital automation system and patient files. Individuals who were not subjected to thyroid dysfunction assessment during their follow-up period and those for whom data accessibility was not achievable were excluded from the study. Prior authorization for data usage was obtained from the hospital management.

Age, gender, chronic disease history, current diagnoses, Electrocardiography (ECG) findings and cardiac evaluation results of the patients were recorded. fT3, fT4, TSH, blood glucose level, blood urea nitrogen, creatinine, alanine serum transaminase, aspartate transaminase, sodium, potassium, lactate dehydrogenase, CK-MB, troponin I, LDL, HDL cholesterol and triglyceride levels were recorded. A total of 70 patients were included in the study.

The difference between the chronic disease history and laboratory test results between the patients who developed mortality during their follow-up and the living group was evaluated.

Data analysis was conducted using the SPSS 19.0 software package. Descriptive statistics were used to summarise the data, including mean, standard deviation, frequency, and ratio. The distribution of variables was assessed using the Kolmogorov-Smirnov test. Non-parametric data were analyzed using the Mann-Whitney U test, while the t-test was utilized for parametric data analysis. Proportional data were examined using the chi-square test, and Fisher's exact test was employed when the conditions for chi-square test were not met. All tests were conducted at a 95% confidence interval, and p-values below 0.05 were considered statistically significant.

**RESULTS**

The study population had a mean age of 64.46 ± 15.64 years, ranging from 29 to 92 years. Among the patients, 22 (31.4%) were female, while 48 (68.6%) were male. Hypertension was the most prevalent medical history, reported in 41 (58.7%) patients, followed by ischemic heart disease in 30 (42.8%) patients. Only 2 (2.9%) patients had a history of drug usage for hypothyroidism, while the remaining 68 (97.1%) patients had no diagnosed thyroid disease in their medical history and had not received any treatment.

In the study, 48.6% of the patients were diagnosed with NSTEMI, followed by 22.9% with anterior MI and 22.9% with inferior MI, respectively. Among the patients, 18.6% underwent primary percutaneous intervention, and a mortality rate of 5.7% was observed during the follow-up period. Figure 1 provides a summary of the patients' demographic attributes, diagnoses, and mortality status.
The mean age of patients in the mortality group was 87.3 ± 4.6 years, whereas the mean age of the survivors was 63.1 ± 15.0 years. The detected age disparity between these two groups was found to be statistically significant (p < 0.05).

No statistically significant difference was observed between the patients who experienced mortality and those who survived, with a history of hypertension, DM, thyroid disease, presence of chronic kidney failure, chronic cardiac and thyroid-related drug use. (p > 0.05), (p > 0.05) (p > 0.05) (p > 0.05) (p > 0.05) (p > 0.05))

Upon analyzing the discrepancies in laboratory test results between genders, a statistically significant distinction was observed solely in hemoglobin, hematocrit, and free T3 values between male and female patients (p < 0.05) (Table 1).

In the comparison of laboratory mean values between the mortality and the living groups, there was no statistically significant difference between Glucose, BUN, Creatinine, Sodium, Potassium, alanine aminotransferase (ALT), aspartate minotransferase (AST), creatine phosphokinase (CKMB), Troponin I, lactate dehydrogenase (LDH), , ST4, TSH, LDL, HDL, Triglyceride and Cholesterol levels (p > 0.05). Statistically significant differences were identified exclusively in hemoglobin, hematocrit, and free T3 levels. Free T3 levels were found to be significantly lower in the...
### Table 1. Distribution of laboratory tests by gender

<table>
<thead>
<tr>
<th></th>
<th>Female Mean ± standard deviation</th>
<th>Male Mean ± standard deviation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>124.1 ± 54.6</td>
<td>118.6 ± 82.7</td>
<td>0.092</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>65.6 ± 40.4</td>
<td>60.9 ± 40.9</td>
<td>0.650</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.3 ± 0.5</td>
<td>1.9 ± 1.8</td>
<td>0.258</td>
</tr>
<tr>
<td>Sodium</td>
<td>139.8 ± 3.1</td>
<td>139.7 ± 4.2</td>
<td>0.933</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.0 ± 0.6</td>
<td>5.2 ± 7.2</td>
<td>0.178</td>
</tr>
<tr>
<td>AST</td>
<td>109.3 ± 134.7</td>
<td>68.3 ± 83.4</td>
<td>0.268</td>
</tr>
<tr>
<td>ALT</td>
<td>57.4 ± 104.9</td>
<td>31.0 ± 30.1</td>
<td>0.599</td>
</tr>
<tr>
<td>CKMB</td>
<td>58.1 ± 81.0</td>
<td>46.8 ± 58.9</td>
<td>0.494</td>
</tr>
<tr>
<td>Troponin</td>
<td>12.4 ± 17.5</td>
<td>7.4 ± 14.7</td>
<td>0.115</td>
</tr>
<tr>
<td>LDH</td>
<td>411.5 ± 233.4</td>
<td>337.8 ±212.1</td>
<td>0.318</td>
</tr>
</tbody>
</table>

Mann Whitney U test/t test 95% confidence interval  
BUN: Blood Urea Nitrogen  
AST: Aspartate minotransferase  
ALT: Alanine aminotransferase  
CKMB: Creatine Phosphokinase  
LDH: Lactate dehydrogenase  
fT3: Free triiodothyronine  
fT4: Free thyroxine  
TSH: Thyroid-stimulating hormone  
LDL: Low-density lipoprotein  
HDL: High-density lipoprotein  
TG: Triglyceride  
WBC: White blood cell  
Hct: Hematocrit  
Hgb: Hemoglobin

### Table 2. Relationship between laboratory test results and mortality

<table>
<thead>
<tr>
<th></th>
<th>Survival group Mean ± standard deviation</th>
<th>Mortality group Mean ± standard deviation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.1 ±15.0</td>
<td>87.3 ± 4.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Glucose</td>
<td>59.7 ± 39.6</td>
<td>106.5 ± 32.3</td>
<td>0.019</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.7 ± 1.5</td>
<td>1.8 ± 0.6</td>
<td>0.201</td>
</tr>
<tr>
<td>Sodium</td>
<td>139.6 ± 3.9</td>
<td>141.8 ± 4.6</td>
<td>0.286</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.9 ± 6.2</td>
<td>4.3 ± 0.8</td>
<td>0.806</td>
</tr>
<tr>
<td>AST</td>
<td>72.1 ± 83.9</td>
<td>231.0 ± 245.5</td>
<td>0.511</td>
</tr>
<tr>
<td>ALT</td>
<td>31.1 ± 29.0</td>
<td>174.5 ± 225.2</td>
<td>0.176</td>
</tr>
<tr>
<td>CKMB</td>
<td>50.9 ± 68.0</td>
<td>41.0 ± 25.0</td>
<td>0.411</td>
</tr>
<tr>
<td>Troponin</td>
<td>8.6 ± 15.4</td>
<td>16.4 ± 20.2</td>
<td>0.544</td>
</tr>
<tr>
<td>LDH</td>
<td>352.0 ± 212.4</td>
<td>569.8 ± 291.5</td>
<td>0.055</td>
</tr>
<tr>
<td>fT3</td>
<td>2.6 ± 0.5</td>
<td>2.0 ± 0.1</td>
<td>0.030</td>
</tr>
<tr>
<td>fT4</td>
<td>1.0 ± 0.4</td>
<td>1.2 ± 0.2</td>
<td>0.117</td>
</tr>
<tr>
<td>TSH</td>
<td>1.5 ± 1.2</td>
<td>2.8 ± 2.5</td>
<td>0.188</td>
</tr>
<tr>
<td>LDL</td>
<td>118.0 ± 35.5</td>
<td>91.0 ± 35.8</td>
<td>0.144</td>
</tr>
<tr>
<td>HLD</td>
<td>37.2 ± 9.6</td>
<td>33.3 ± 7.1</td>
<td>0.417</td>
</tr>
<tr>
<td>TG</td>
<td>189.6 ± 84.9</td>
<td>123.3 ± 17.9</td>
<td>0.125</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>193.7 ± 46.5</td>
<td>148.8 ± 36.1</td>
<td>0.063</td>
</tr>
<tr>
<td>WBC</td>
<td>9.8 ± 3.4</td>
<td>14.7 ± 6.7</td>
<td>0.011</td>
</tr>
<tr>
<td>Hct</td>
<td>38.2 ± 6.6</td>
<td>31.0 ± 5.5</td>
<td>0.036</td>
</tr>
<tr>
<td>Hgb</td>
<td>12.7 ±2.5</td>
<td>10.2 ± 1.6</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Mann Whitney U test/t test 95% güven aralığı  
BUN: Blood Urea Nitrogen  
AST: Aspartate minotransferase  
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Hgb: Hemoglobin
DISCUSSION

In the absence of pre-existing intrinsic thyroid disorders, alterations in thyroid hormone plasma levels during acute and chronic illnesses are described in the literature using diverse terminologies such as "euthyroid sick syndrome," "non-thyroidal illness syndrome," and "low T3 syndrome" in patients without documented intrinsic thyroid pathology.(12). It produces an adaptive response by reducing energy expenditure as an organ-specific response related to the time of inflammation development during disease.

Acute coronary syndromes are clinical conditions with high mortality risk based on coronary atherosclerotic plaque and acute myocardial ischemia. Coronary atherosclerotic formation and subsequent thrombus formation constitute the basic pathophysiological mechanism, while developing inflammation triggers thrombosis, sympathetic system activation and stress hormone release (12, 13).

Multiple studies have reported a reduction in total triiodothyronine (T3) and/or free T3 concentrations, along with an elevation in reverse T3 (rT3) levels following an acute coronary event (14-16). The precise prevalence of low T3 syndrome among patients diagnosed with ACS remains inadequately defined in the current literature. A wide proportional range of 5% to 35% has been reported in the literature due to wide distribution differences in the population included in the studies. (16-18). Thyroid hormone disorders affect many parameters in terms of coronary artery disease and pose a risk by direct and indirect mechanisms.

Within the scope of this study, it was observed that the levels of free triiodothyronine (fT3) were significantly lower in the mortality group. However, no statistically significant differences were found in thyroid-stimulating hormone (TSH) and free thyroxine (fT4) values. These findings highlight the significance of low T3 as a predictive factor for the severity of acute myocardial infarction and its potential as a predictor of mortality. These data we obtained support the idea that thyroid dysfunctions pose a serious risk for AMI in the literature.

The exact time of occurrence of thyroid hormone level changes after ACS has not been clearly determined. Pawlov et al. investigated the frequency of euthyroid sick syndrome in 114 patients (72 male, 42 female), 95 of whom were with AMI and 19 with USAP. In the first five days of the disease, significant low TT3 and high RT3 levels were detected in all patients, while ST3 and ST4 did not change. High RT3 and low TT3 levels were found to be more prominent in patients with complicated infarction compared to those with uncomplicated infarction, and TSH, T4, TBG and Albumin were found to be significantly lower only in patients with complicated infarction (19).

Hypertension, diabetes mellitus, hyperlipidemia, ischemic heart disease, smoking, and sedentary lifestyle have been widely recognized as prominent risk factors for AMI.(20, 21). In our study, according to the literature, hypertension was the most prevalent medical history among the patient population, observed in 58.6% of individuals, followed by ischemic heart disease (42.9%) and diabetes mellitus (31.4%). ACS presentation may be similar between men and women; In more than 80% of both, the presenting symptom is chest pain. However, more women report additional symptoms without chest pain (22). Unlike in our study, 48 (68.6%) of our patients were men. In accordance with existing literature data, the approximate parity of women-to-men ratio is linked to the attenuation of premenopausal protective factors among women during the postmenopausal phase. However, while discussing the effect of gender difference on the diagnosis of AMI, it is understood that these figures may be different in studies with sufficient sample size (22, 23).

Gaining insights into the distinct pathophysiological mechanisms and management approaches for NSTEMI segment elevation, collectively referred to as acute coronary syndrome, is crucial for effectively evaluating patients and implementing appropriate treatment strategies. Over the past decade, there has been a notable decline in the number of patients presenting STEMI, whereas there has been a modest increase in the incidence of NSTEMI. This may also be due to the increased diagnostics of NSTEMI patients. In particular, the incidence rates of ST-elevation myocardial infarction (STEMI) experienced a minor decline from 121 to 77 per 100,000 between 1997 and 2005, while for non-ST-elevation myocardial infarction (NSTEMI), there was a slight increase from 126 to 132 per 100,000 (24, 25).

Over the past two decades, the massive development and use of high-sensitivity troponin tests has made NSTEMI easier to diagnose. In our study, 48.6% of our patients were found to have NSTEMI. This proportional difference can be explained by the fact that the patients for whom primary percutaneous intervention was preferred as the reperfusion strategy were mostly from the STEMI group. Significant changes in public health policies are expected, focusing on primary prevention strategies to efficiently prevent and manage coronary artery disease. Alongside this, heightened awareness regarding risk factors associated with coronary artery disease is projected to contribute to an overall decline in the incidence of STEMI.

CONCLUSION

Thyroid function test alterations are frequently observed in individuals with acute coronary syndrome (ACS), particularly those diagnosed with ST-segment elevation myocardial infarction (STEMI). The occurrence of low triiodothyronine (T3) syndrome indicates an inherent hormonal imbalance that can profoundly impact pathophysiological mechanisms and cardiovascular hemodynamics. Given the substantial influence of thyroid hormones (THs) on the cardiovascular system, a mounting body of evidence suggests a potential prognostic significance of TH fluctuations in ACS patients. If thyroid hormone disorders are identified and adequately managed, leading to the attainment of euthyroidism, the associated risk of coronary artery disease may cease to pose a grave concern.

Limitations

The first limitation of our study is that it is retrospective and single-centered. The second limitation is that some of the patients evaluated for acute coronary syndrome in our hospital were referred to external centers for percutaneous intervention and intensive care due to hospital occupancy. Our patient number and follow-up may have been delayed at this point.

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Author Contributions: ED, HT contributed to the conception of the work, execution of the study, revision of the draft, approval of the final manuscript version, and concur with all aspects of the work. ED: Revisions. All authors have reviewed the manuscript and confirm that they meet the criteria for authorship set by the International Committee of Medical Journal Editors (ICMJE).

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions.

REFERENCES