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Thyroid Functions Are Associated with All-Cause Long-Term Mortality in Elderly Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Uygulanan ST Segmenti Yükselmeli Miyokard Enfarktüslü Yaşlı Hastalarda Tiroid Fonksiyonları Tüm Nedenlere Bağlı Uzun Dönem Mortalite ile İlişkilidir

ABSTRACT

Objective: Our aim in this study was to show the relationship between long-term all-cause mortality and thyroid functions in the elderly patient group that underwent primary percutaneous coronary intervention with the diagnosis of ST-segment elevation myocardial infarction.

Methods: Two-hundred seventy patients over 65 years of age who underwent primary percutaneous coronary intervention with the diagnosis of ST-segment elevation myocardial infarction were analyzed retrospectively. After applying the exclusion criteria, 198 patients were included in the study. The patients were divided into 2 groups according to their out-of-hospital mortality status. Angiographic, laboratory, echocardiographic, and electrocardiographic data were analyzed.

Results: The mean age of 198 patients in the study was 72.5 ± 6.6 years, and the median follow-up time was 101.7 months. Age was higher in the deceased group (70.4 ± 5.4 vs. 74.5 ± 6.9, $P < 0.001$). In multivariate analysis, age (odds ratio: 1.59, $P=0.003$), insulin (odds ratio: 2.561, $P=0.016$), angina balloon time (odds ratio: 1.134, $P=0.002$), number of serious stenoses (odds ratio: 1.702, $P=0.003$), creatinine (odds ratio: 3.043, $P < 0.001$), and fT4 (odds ratio: 2.026, $P=0.026$) were determined as independent predictors of mortality. The fT4 level was correlated with the uric acid level (R: 0.182, $P=0.02$) and the fT3 level was correlated with albumin (R: –0.253, $P=0.001$) and creatinine (R: –0.224, $P=0.003$) levels. A fT4 level cutoff value of 0.99 ng/mL had a sensitivity of 76%, a specificity of 54%, and an area under the curve of 0.675 in predicting mortality. In Kaplan–Meier analysis, fT4 elevation was strongly associated with mortality ($P=0.01$).

Conclusion: In our study, subclinical values in thyroid functions were found to be associated with increased mortality, apart from known factors in elderly patients who underwent primary PTCA with the diagnosis of ST-segment elevation myocardial infarction.

Keywords: Elderly, mortality, STEMI, thyroid

ÖZET

Amaç: Çalışmadaki amacımız STEMI tanısı ile primer perkütan koroner girişim yapılan ileri yaş hasta grubunda uzun dönem tüm nedenli mortalite ile tiroid fonksiyonları arasındaki ilişkiyi göstermektir.

Yöntem: STEMI tanısı ile primer PKG yapılan 65 yaş üzeri 270 hasta retrospektif olarak incelendi. Dışlanma kriterleri sonrası 198 hasta çalışmaya dahil edildi. Hastalar, hastane dışı mortalite durumuna göre 2 gruba ayrıldı. Anjiyografi, laboratuvar, ekokardiyografi ve elektrokardiyografi verileri analiz edildi.

Bulgular: Çalışmadaki 198 hastanın ortalama yaşı 72,5 ± 6,6 yıl, median takip süresi 1017 ay idi. Mortalite grubunda yaş yüksek saptandı (70,4 ± 5,4 vs. 74,5 ± 6,9, $P < 0,001$). Multivariate analizde yaş (OR: 1,59, $P=0,003$), insülin (OR: 2,561, $P=0,016$), Angina Balon zamanı (OR: 1,134, $P=0,002$), ciddi darlık sayısı (OR: 1,702, $P=0,003$), kreatinin (OR: 3,043, $P < 0,001$), sT4 (OR: 2,026, $P=0,026$) mortalitenin bağımsız prediktörleri olarak saptandı. Korelasyon analizinde sT4 düzeyi, ürik asit düzeyi ile (R: 0,182, $P=0,02$) sT3 ise albumin (R: –0,253, $P=0,001$) ve kreatinin (R: –0,224, $P=0,003$) düzeyleri ile korele bulundu. sT4 düzeyinin 0,99 ng/ml'nin

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üstünde olmasının mortaliteyi öngördürmedeki duyarlılığı %76, özgüllüğü %54, eğri altında kalan alan 0,675 olarak saptandı. Kaplan–Meier analizinde sT4 yüksekliğinin mortalite ile güçlü ilişki gösterdiği bulundu (P=0,01).

Sonuç: Çalışmamızda STEMI tanısı ile primer PTCA yapılan yaşlı hastalarda bilinen faktörlerin dışında tiroid fonksiyonlarındaki subklinik değerlerin mortalite artışı ile ilişkili olduğu saptanmıştır.

Anahtar Kelimeler: Yaşlı, mortalite, STEMI, tiroid

Although early diagnosis and interventional treatment provide significant improvements in prognosis of ST-segment elevation myocardial infarction (STEMI), studies show that mortality is still high in the advanced age group.[1]

Several changes occur in the endothelial layer through the various autocoids in advanced age, which has many functions such as vascular tone, angiogenesis, and inflammatory response. As a result of these changes, a decrease in coronary flow reserve occurs.[2] Because advanced age is an independent risk factor for morbidity and mortality, it was generally used as an exclusion criterion in studies investigating acute coronary syndrome and treatment strategies. For this reason, the number of studies that recommend treatment for elderly patients is limited. Treatment recommendations for this patient group are derived from studies with a lower mean age.[3,4]

Thyroid dysfunction can affect 10%-15% of the adult population. Subclinical hyper- and hypothyroidism conditions are both associated with a high risk of cardiovascular mortality and morbidity.[5] Even in people without significant thyroid disease, changes in thyroid hormone levels can accelerate the progression of cardiovascular disease (CVD) and increase mortality.[6] Thyroid hormones regulate many cardiovascular functions; these include blood lipid level, myocardial contractility, conduction system, blood pressure change, and endothelial function.[7] An underactive thyroid gland causes hyperlipidemia and ventricular arrhythmias, while overactive thyroid gland causes atrial arrhythmia; both conditions cause hypertension and heart failure. These cardiac abnormalities are usually reversible with the treatment of the underlying thyroid dysfunction.[8] However, the predictive effect of thyroid dysfunction in the setting of acute myocardial infarction remains unclear.[5]

Our aim in this study was to show the relationship between long-term all-cause mortality and thyroid functions in the elderly patients who underwent primary percutaneous coronary intervention (PCI) with the diagnosis of STEMI.

Materials and Methods

Patient Selection

This is a retrospective and registry based study. Patients who had STEMI between April 2011 and December 2014 and underwent primary PCI were included in the study consecutively. Patients aged 65 years and over with ischemia duration less than 12 hours were included in the study. Exclusion criteria were cardiogenic shock, coronary artery bypass surgery history, inhospital mortality, TIMI-2 and -3 flow grade on admission, and in-crossable lesion. Two-hundred seventy of 902 patients were 65 years old and over. We have included 198 patients meeting the eligibility criteria and have thyroid parameters. The study protocol was approved by the Kocaeli University Ethics Committee in accordance with the Declaration of Helsinki and good clinical practice (Approval Number: K. GOKAEK-2022/20.08, Date: 20.08.2022).

Echocardiographic and Electrocardiography Data

Wall motion score index was calculated via a 16-segment model described by the American Ultrasound Committee with a 4-points scale. Ejection fraction was calculated with the modified Simpson method. Mitral inflow parameters, *E*, *A* and mitral annulus velocity *E'* were measured for diastolic function assessment.

Angiographic Data

Coronary angiography was carried out with AXIOM-Artis 90806 (Siemens) TIMI flow was evaluated according to TIMI trial classifications[9] before and after the intervention. Corrected TIMI frame count was measured. The details about TIMI frame count calculation were described beforehand.[10]

Laboratory Data

Blood tests were evaluated from venous samples obtained within the first day of presentation. As routine tests in the cardiology clinic, complete blood count, fasting blood glucose, kidney function tests, lipid panel, C-reactive protein, thyroid-stimulating hormone (TSH), fT3, and fT4 were measured. The glomerular filtration rate was calculated with the Cockcroft–Gault formula.

Statistical Analysis

Data were analyzed with a Statistical Package for the Social Sciences (SPSS) software package (version 23.0, SPSS, Inc., Chicago, Ill, USA). A 2-tailed P-value of <0.05 was identified as statistically significant. Normality assumptions were assessed visually (histograms and probability plots) and by analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk's test). Levene's test was used to evaluate the homogeneity of variances. Continuous variables are reported as mean ± SD, and categorical variables are reported as value and percentage. A chi-square or Fisher's exact test was employed to compare groups of categorical variables. A 2-tailed Student's *t*-test was applied to normally distributed parameters, and a Mann–Whitney *U*-test was applied to non-normally distributed, continuous variables. A univariate regression analysis was performed to assess the variables related to mortality. Variables with a P value were considered as confounding factors and included in a Cox backward multivariable

ABBREVIATIONS

CVD	Cardiovascular disease
DM	Diabetes mellitus
PCI	Percutaneous coronary intervention
STEMI	ST-segment elevation
TSH	Thyroid-stimulating hormone

regression analysis to evaluate independent predictors of mortality. Kaplan–Meier analysis was used to demonstrate the effect of fT4 on long-term mortality.

Results

The mean age of the 198 patients included in the study was 72.5 ± 6.6 years, and the median follow-up time was 101.7 months. Age was found to be higher in the deceased group (70.4 ± 5.4 vs. 74.5 ± 6.9, $P < 0.001$). In the deceased group, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use was lower (96.8% vs. 87.5%, $P=0.014$), and insulin use was higher (1.1% vs. 11.5%, $P=0.002$) in the discharge treatment. There was no difference between the groups in other characteristics (Table 1).

Table 1. Characteristics of Study Patients According to Mortality

Variable	Mortality (–) (n=94)	Mortality (+) (n=104)	*P*
	Demographic characteristics		
Age (years)	70.4 ± 5.4	74.5 ± 6.9	<0.001
Gender (male), n (%)	70 (74.5)	70 (67.3)	0.269
Hypertension, n (%)	58 (61.7)	71 (68.3)	0.206
Hyperlipidemia, n (%)	33 (35.1)	40 (38.5)	0.367
Diabetes mellitus, n (%)	25 (26.6)	35 (33.7)	0.178
Prior CVE, n (%)	5 (5.4)	11 (10.6)	0.142
Prior MI, n (%)	4 (4.3)	1 (1)	0.154
Preangina, n (%)	30 (31.9)	43 (41.3)	0.110
BMI, kg/m^2	27.5 ± 3.6	27.5 ± 4.4	0.994
Ejection fraction (%)	39.6 ± 10.7	37.1 ± 10.1	0.146
Wall motion index	1.7 ± 0.34	1.7 ± 0.37	0.967
Systolic BP (mmHg)	132.5 ± 23.1	130.1 ± 23.6	0.533
Diastolic BP (mmHg)	81.4 ± 11.6	82.3 ± 13.5	0.602
Heart rate, bp/min	75.6 ± 15.2	77.8 ± 18.1	0.362
Smoking, n (%)	22 (23.4)	16 (15.4)	0.106
Killip ≥2, n (%)	8 (8.5)	16 (15.4)	0.103
Anterior MI	48 (51.1)	47 (45.2)	0.247
	Discharge medical treatment		
Acetyl salicylic acid, n (%)	94 (100)	103 (99)	0.525
Clopidogrel, n (%)	93 (99)	104 (100)	0.998
ACEI/ARB, n (%)	91 (96.8)	91 (87.5)	0.014
Beta blocker, n (%)	87 (92.6)	99 (95.2)	0.316
CCB, n (%)	12 (12.8)	18 (17.3)	0.245
OAD/insulin, n (%)	7 (7.4)	7 (6.7)	0.531
Insulin, n (%)	1 (1.1)	12 (11.5)	0.002
Spironolactone, n (%)	18 (19.1)	26 (25)	0.222
Statins, n (%)	92 (97.8)	102 (98.1)	0.650

ACEİ, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; CCB, calcium channel blocker; CVE, cerebrovascular event; MI, myocardial infarction; OAD, oral antidiabetic.

Angina balloon time (3.98 ± 2.6 hours vs. 5.1 ± 3.1 hours, $P=0.025$) and the number of severe stenosis (3.5 ± 0.45 vs. 3.3 ± 0.41, $P=0.007$) were higher in the deceased group. In the surviving group, the stent diameter was higher (3.5 ± 0.45 mm vs. 3.3 ± 0.41 mm, $P=0.007$) and the predilatation rate was low (48.4% vs. 63.5%, $P=0.023$). No difference was found between the groups in other angiography-related data (Table 2).

While serum creatinine (0.90 ± 0.27 mg/dl vs. 1.13 ± 0.70 mg/dl, $P=0.003$) and uric acid (5.75 ± 1.5 mg/dl vs. 6.3 ± 1.7 mg/dl) levels were higher in the deceased group, albumin (3.86 ± 0.33 mg/dl vs. 3.68 ± 0.35 mg/dl, $P < 0.001$) level was found to be lower. In addition, there was no difference in TSH levels between the groups ($P=0.464$). In the deceased group, fT3 was lower (2.7 ± 0.45 ng/ml vs. 2.49 ± 0.54 ng/ml, $P=0.008$) and fT4 was higher (1.1 ± 0.2 ng/ml vs. 1.15 ± 0.36 ng/ml, $P=0.001$). No difference was found between the groups in other laboratory data (Table 2).

Univariate and multivariate analyses were performed to identify independent predictors of mortality. In univariate logistic regression analysis, age ($P \leq 0.001$), insulin ($P=0.005$), angina balloon time ($P=0.008$), stent diameter ($P=0.014$), number of severe stenosis ($P < 0.001$), serum creatinine ($P < 0.001$), uric acid ($P=0.024$), albumin ($P < 0.001$), fT3 ($P=0.014$), and fT4 ($P < 0.001$) were found to be associated with mortality. Age [odds ratio (OR): 1.59, $P=0.003$], insulin (OR: 2.561, $P=0.016$), angina balloon time (OR: 1.134, $P=0.002$), number of severe stenosis (OR: 1.702, $P=0.003$), serum creatinine (OR: 3.043, $P < 0.001$), and fT4 (OR: 2.026, $P=0.026$) were determined as independent predictors of mortality in multivariate logistic regression analysis (Table 3). The fT4 level was correlated with uric acid level (R: 0.182, $P=0.02$) and the fT3 level was correlated with albumin (R: –0.253, $P=0.001$) and creatinine (R: –0.224, $P=0.003$) levels in the correlation analysis (Table 4). The fT4 level cutoff value of 0.99 had a sensitivity of 76%, a specificity of 54%, and an area under the curve of 0.675 in predicting mortality (Table 5). Kaplan–Meier analysis showed that the elevation of fT4 levels was strongly associated with mortality ($P=0.01$) (Figure 1).

Discussion

In our study, the fT4 level was found to be an independent predictor of all-cause mortality in elderly patients who underwent primary PCI with the diagnosis of STEMI.

There are many mechanisms by which thyroid hormones affect cardiovascular functions. Thyroid hormones bind to thyroid hormone receptor-α in cardiac myocytes to regulate gene expression. This binding includes upregulation of myosin heavy chain-α and downregulation of myosin heavy chain-β, regulation of the calcium cycle to influence the contractile apparatus. The adrenergic response is enhanced by the induction of SERCA2a and downregulation of phospholamban and upregulation of the β1-adrenergic receptor. Thyroid hormones stimulate vasodilation by increasing nitric oxide production in vascular smooth muscle and calcium reuptake in arterioles, resulting in decreased coronary vascular tone and decreased systemic vascular resistance.[8,11]

Table 2. Angiographic and Laboratory Data

Variable	Mortality (–) (n=94)	Mortality (+) (n=104)	*P*
	Angiographic data		
Angina balloon time (hours)	3.98 ± 2.6	5.1 ± 3.1	0.025
Collateral, n (%)	7 (7.4)	15 (14.4)	0.090
Thrombectomy, n (%)	29 (30.9)	33 (31.7)	0.508
Stent length (mm)	16.4 ± 7.2	17.4 ± 6.9	0.346
Number of stents	0.94 ± 0.45	0.98 ± 0.5	0.621
Stent diameter (mm)	3.5 ± 0.45	3.3 ± 0.41	0.007
Pre-dilatation, n (%)	45 (48.4)	66 (63.5)	0.023
Post-dilatation, n (%)	12 (12.9)	23 (22.1)	0.066
Dilatation pressure (mmHg)	13.3 ± 2.5	13.9 ± 3.4	0.201
Number of serious stenosis	1.67 ± 0.79	2.02 ± 0.81	0.003
PCI time (minutes)	34.3 ± 20.6	34.1 ± 18.9	0.864
Culprit artery LAD, n (%)	48 (51.1)	47 (45.2)	0.247
Post cTFC	31.08 ± 21.7	31.7 ± 14.6	0.805
GBPIIa-IIIb inhibitor	23 (25)	29 (27.9)	0.385
Post TIMI 3 flow	81 (87.1)	82 (79.6)	0.184
High thrombus burden	75 (80.6)	88 (85.4)	0.241
	Laboratory data		
Glucose (mg/dL)	144.5 ± 56	150.8 ± 68.2	0.506
Creatinine (mg/dL)	0.90 ± 0.27	1.13 ± 0.70	0.003
WBC (10^3/μL)	10.2 ± 2.4	10.8 ± 3.6	0.169
Uric acid (mg/dl)	5.75 ± 1.5	6.3 ± 17	0.026
Neutrophil/lymphocyte ratio	6.7 ± 4.3	7.4 ± 5.2	0.275
Total protein (mg/dl)	6.78 ± 0.58	6.66 ± 0.68	0.194
Albumin (mg/dl)	3.86 ± 0.33	3.68 ± 0.35	<0.001
TSH (IU/l)	0.89 (0.48-1.59)	0.91 (0.52-1.66)	0.464
fT3 (ng/>ml)	2.7 ± 0.45	2.49 ± 0.54	0.008
fT4 (ng/ml)	1.1 ± 0.2	1.15 ± 0.36	0.001
Hgb (g/dL)	13.7 ± 2.8	13.1 ± 1.6	0.083
CRP (mg/dL)	0.78 (0.30-2.44)	1.03 (0.41-3.75)	0.206
Total cholesterol (mg/dL)	175.4 ± 46	168.3 ± 40.7	0.272
Triglyceride (mg/dL)	119.5 ± 66	113.5 ± 58	0.526
HDL (mg/dL)	38.5 ± 10.5	38.5 ± 13.5	0.992
LDL (mg/dL)	111.8 ± 41.5	107.8 ± 37.1	0.435

CRP, C-reactive protein; cTFC, corrected TIMI frame count; GBP, glycoprotein; HDL, high-density lipoprotein; Hgb, hemoglobin; LAD, left anterior descending; LDL, low-density lipoprotein; PCI, percutaneous coronary intervention; TSH, thyroid-stimulating hormone; WBC, white blood cell.

In a study conducted by Yeap et al,[12] high fT4 was found to be associated with long-term all-cause mortality in euthyroid elderly men, while the TSH level did not have any effect. In the study of Van den Beld et al,[13] the fT4 level was found to be associated with all-cause mortality in the elderly patient group, while TSH and fT3 levels were not found to be related. Merke et al[14] also found that high fT4 and low fT3 levels were associated with all-cause long-term mortality in patients who underwent angiography. Ataoğlu et al[15] showed that both low fT3 and high fT4 levels are independent mortality risk indicators in chronic patients hospitalized for non-thyroid disease. In the study of He et al,[16] in which the fT3/fT4 ratio was evaluated as a separate parameter, unlike other studies, the patients were divided into 3 groups according to the fT3/fT4 ratio in acute myocardial infarction patients with type 2 diabetes mellitus (DM). Low fT3/fT4 ratio after acute myocardial infarction was found to be an independent risk factor for poor prognosis. In general, although there are conflicting results about fT3 and TSH in the literature, the view that high fT4 is associated with all-cause and cardiovascular mortality is dominant. In our study, a strong correlation was found between high fT4 level and mortality ($P=0.001$). Although low fT3 level was more frequent in the group with mortality ($P=0.008$), and was significant in univariate analysis ($P=0.014$), but no correlation was found in multivariate analysis. No significant relation were found for the TSH. Unlike fT3 a high fT4 levels showed a stronger correlation in univariate analysis ($P < 0.001$). In addition, its significance continued in multivariate analysis ($P=0.026$). A high fT4 level with a cutoff value of 0.99 mg/ml, showed a sensitivity of 76% and a specificity of 54%, with a strong correlation of high fT4 in Kaplan–Meier analysis.

There is increasing evidence that decreased activity of the deionidase enzyme in the kidney can cause high fT4 and low fT3 levels, and increased fT4 and suppressed fT3 levels are associated with inflammation and cardiovascular damage.[14] In the study conducted by Ahmed et al,[17] which included 486 patients, patients were divided into 4 groups according to creatinine level, and their thyroid hormone levels were compared. As the renal insufficiency level increased, a significant decrease was found in the ST3 level ($P=0.005$). When the groups with normal renal function and those with severe renal failure were compared, an increase in ST4 level was observed ($P=0.028$). No change was observed in TSH levels as renal functions deteriorated. The fact that creatinine and ST4 values were high and ST3 levels were low in the deceased group and that there was no difference in TSH levels between the groups demonstrates that our study reveals the relationship between renal function and thyroid hormones in line with the literature. In our correlation analysis, creatinine value was associated with low fT3 ($P=0.003$) but not with high fT4 level ($P=0.270$). Nevertheless in our study, high fT4 was found to be associated with increased mortality regardless of the serum creatinine value. It is especially important that the creatinine value continues to be significant in univariate analysis (OR: 1.750, $P < 0.001$) and continues to show a significant correlation with mortality in multivariate analysis (OR: 3.043, $P < 0.001$).

Hyperuricemia causes endothelial dysfunction, and is associated with chronic kidney disease and CVDs.[18] However, the relationship between uric acid level and all-cause and CVD mortality is controversial. Results of the association between uric acid level and mortality are inconsistent.[19] The general view on the relationship between mortality and uric acid is in the form of a J-curve.[20] There is conflicting information about the relationship between thyroid hormones and uric acid level. Chao et al[21] found

Table 3. Independent Predictors of Mortality Cox Regression

	Univariate			Multivariate		
Variable	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age (years)	1.060	1.031-1.090	<0.001	1.059	1.019-1.101	0.003
Insulin	2.369	1.293-4.342	0.005	2.561	1.195-5.489	0.016
Angina balloon time	1.002	1.025-1.182	0.008	1.134	1.048-1.227	0.002
Stent diameter	0.551	0.343-0.885	0.014			
Pre-dilatation	1.341	0.898-2.001	0.152			
Number of serious stenosis	1.495	1.183-1.890	<0.001	1.702	1.199-2.415	0.003
Creatinine	1.750	1.309-22.340	<0.001	3.043	1.849-5.007	<0.001
Uric acid	1.144	1.108-1.278	0.024			
Albumin	0.412	0.259-0.657	<0.001			
fT3	0.606	0.406-0.904	0.014			
fT4	2.505	1.495-4.196	<0.001	2.026	1.086-3.779	0.026

OR, odds ratio.

Table 4. Correlation Analysis of Thyroid Hormones and Albumin, Uric Acid, and Creatinine

	Albumin		Uric Acid		Creatinine	
	R	***P***	***R***	***P***	***R***	***P***
fT3	0.253	0.001	–0.139	0.077	–0.224	0.003
fT4	–0.068	0.359	0.182	0.020	0.083	0.270

Table 5. Sensitivity and Specificity

Variable	Sensitivity	Specificity
fT4 > 0.99	76%	54%
fT4 > 0.95	80%	44%
fT4 > 1	59%	67%

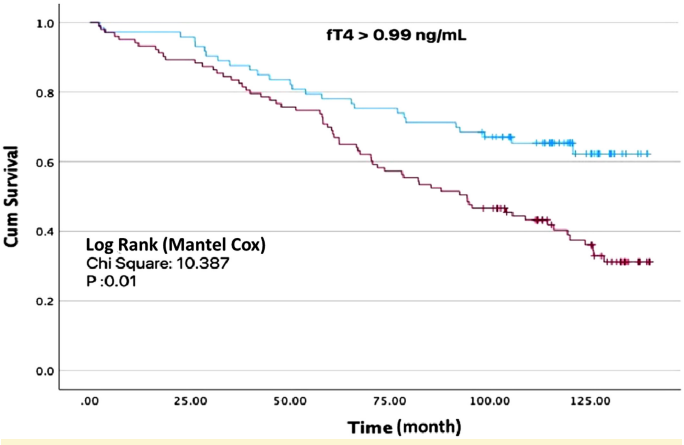

Figure 1. Kaplan–Meier survival analysis. The Kaplan–Meier curve shows the survival curves according to cutoff fT4 >0.99 ng/ml.

that serum uric acid levels were positively correlated with ST3 and ST4 levels in their study with healthy people. In an another study, hyperthyroidism was found to be associated with high serum uric acid levels.[22] Xing et al[23] conducted a large-scale systematic study with data from 4 databases to find the relationship between subclinical thyroid dysfunction and uric acid. High uric acid levels were found to be associated with subclinical hypothyroidism but not with subclinical hyperthyroidism and normal control group. However, it was found that uric acid levels decreased after the treatment of patients with subclinical hypothyroidism. In our study, despite the fT4 levels correlating with high uric acid levels, the correlation with low fT3 levels tended to be significant ($P=0.003$, $P=0.077$). Therefore, it should not be forgotten that there are different underlying pathologies in the treatment of hyperuricemia.

It has been well recognized that hypoalbuminemia is a strong prognostic marker in the general population and in many pathological conditions. Regardless of traditional risk factors, there is increasing evidence that low serum albumin levels are associated with various CVDs, such as ischemic heart disease, heart failure, atrial fibrillation, stroke, and venous thromboembolism.[24] In a prospective study, 734 patients with stable coronary artery disease were followed for 18 months, and hypoalbuminemia was found to predict overall ($P=0.048$) and cardiovascular ($P=0.037$) mortality independent of other factors.[25] In the observational study of Wada et al,[26] 2860 patients with albumin levels who underwent the first PCI were followed for an average of 7.4 years. In the Kaplan–Meier analysis performed by dividing the patients into 3 groups, low albumin was found to be strongly associated with all-cause mortality ($P < 0.0001$) and major cardiovascular events ($P < 0.0001$). In our study, in parallel with the literature, albumin was found to be low in the deceased group ($P < 0.001$). Studies examining the relationship between thyroid hormones and albumin levels are limited. In the study of Tsuji et al,[27] ST3, ST4, and TSH levels were evaluated in 338 rheumatoid arthritis patients. Although a low ST3 level was correlated with anemia and hypoalbuminemia, no correlation was found with ST4 and TSH. Low ST3 has been associated with the inflammatory process, and increased interleukin-6 and tumor necrosis factor-α in this process cause hypoalbuminemia by suppressing albumin production from the liver.[28] In our study, although low

albumin levels, low ST3 levels, and high ST4 levels were detected in the deceased group, only hypoalbuminemia and low fT3 levels were correlated ($P=0.001$). It should be noted that hypoalbuminemia, which is associated with many CVDs, may be a part of thyroid dysfunction or an inflammatory process, and it is important to approach the underlying pathology in this manner.

In our study, the insulin usage level was associated with high mortality. Although there was no difference in terms of DM presence between the groups, the high usage of insulin in the deceased group suggests that DM is more important in this group ($P=0.002$). In addition, the most dangerous side effect of insulin in diabetic patients is hypoglycemia. Especially in elderly diabetic patients, hypoglycemia can be seen more frequently and can have a fatal course. In the study conducted by Geller et al,[29] hospital admissions and hospitalizations due to insulin-related hypoglycemia were found to be 5 times higher in the elderly patient group compared to the younger patient group. In the light of this data, we suggest that elderly, diabetic, and insulin-using patients who underwent primary PCI with the diagnosis of STEMI should be closely followed in terms of both possible complications of DM and risk of hypoglycemia.

In our study, angina balloon time was found to be associated with mortality regardless of all causes. Angina balloon time is important in the context of time-myocardium concept in STEMI. The longer angina balloon time durations in the deceased group in our study may be explained by longer time to hospital admission of elderly individuals and diabetic patients requiring insulin therapy. In the study of Gradišer et al,[30] patients who underwent primary PCI with STEMI were divided into 2 groups according to the presence of DM. Symptom-admission times were compared between the groups. Although there was no statistical difference between the groups, the late admission rate tended to be high in the DM group. In the study, the reason why the symptom-balloon time was not different between the groups, although there was a trend, was attributed to the well-done diabetes education. In addition, regardless of EF, angina balloon time was found to be associated with an increase in mortality in our study, and considering that this situation may be associated with an increase in mortality, it should be taken into account that medical treatments that have a positive effect on mortality should be more carefully regulated and followed.

Conclusion

Mortality in elderly patients with STEMI is like a multivariate equation. Although positive improvements in mortality have been achieved in the general population with early diagnosis and interventional treatment, mortality is still high in the elderly patient population and the number of studies is limited. In these patients, important results can be obtained in reducing mortality by detecting many factors before and during the STEMI. It should not be forgotten that in addition to the obvious deterioration of thyroid functions, subclinical values are also important. When thyroid functions are evaluated together with other parameters, important data about the prognosis of elderly patients can be obtained and significant gains can be achieved with interventions in this direction. In elderly patients, serious improvements in prognosis can be achieved with interventions and changes in dietary habits that affect thyroid functions, renal status, uric acid level, accompanying DM, and albumin level, which is an indicator of negative catabolism.

Limitations

The main limitations of our study are single centered recruitment of the study group and a limited number of patients. More reliable results can be obtained with multicenter studies and with a larger random sample. Since the last patient included in the study had a PCI date in 2014, the old stent technology can be considered as another limitation.

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Kocaeli University (Approval Number: KÜ GOKAEK-2022/20.08, Date: 20.08.2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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