# Predictive Value of the Naples Score for In-Hospital Mortality in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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## ABSTRACT

**Introduction:** ST-segment elevation myocardial infarction (STEMI) is a significant contributor to mortality. The identification of high-risk patients holds great importance for prognosis. The development of a scoring system that incorporates both inflammatory and nutritional status components can provide valuable insights into prognosis.

**Patients and Methods:** This is a retrospective observational study comprising 570 consecutive ST-elevation myocardial infarction patients who underwent primary coronary intervention between 2018 and 2020. Patient data were obtained from the electronic database of the hospital.

**Results:** The incidence of in-hospital mortality rate was 4.9%. The entire group was then divided into two groups based on the presence of in-hospital mortality: 542 patients without in-hospital mortality constituted group 1, while 28 patients with in-hospital mortality formed group 2. In the multivariate logistic regression analysis, the Naples score was identified as an independent predictor of in-hospital mortality.

**Conclusion:** A higher Naples score is associated with increased in-hospital mortality in patients with STelevation myocardial infarction who undergo primary coronary intervention.

Key Words: ST-elevation myocardial infarction; inflammation; mortality; risk scores

# ST-Elevasyonlu Miyokard İnfarktüsü Nedeniyle Primer Perkütan Koroner Girişim Yapılan Hastalarda Naples Skorunun Hastane İçi Mortaliteyi Öngördürücü Değeri

# ÖZET

**Giriş:** ST segment elevasyonlu miyokard infarktüsü mortalitenin önemli bir nedenidir. Yüksek riskli hastaları tespit etmek prognoz için çok önemlidir. İnflamasyon ve nutrisyonel durumu gösteren skorlama sistemleri prognozu öngörmede daha fazla bilgi sağlayabilir.

**Hastalar ve Yöntem:** 2018 ve 2020 yılları arasında, ST elevasyonlu miyokard infarktüsü nedeniyle primer perkütan girişim yapılan ardışık 570 hasta retrospektif olarak incelendi. Hasta verileri hastanenin elektronik veri tabanından elde edildi.

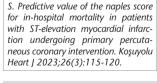
**Bulgular:** Hastane içi mortalite insidansı %4.9 idi. Tüm grup hastane içi mortalite olmasına göre ikiye ayrıldı; hastane içi mortalite olmayan 542 hasta grup 1 ve hastane içi mortalite olan 28 hasta grup 2 olarak adlandırıldı. Çok değişkenli lojistik regresyon analizinde Naples skoru hastane içi mortalitenin bağımsız öngördürücüsü olarak bulundu.

**Sonuç:** ST elevasyonlu miyokard infarktüsü nedeniyle primer koroner girişim yapılan hastalarda yüksek Naples skorları daha fazla hastane içi mortalite ile ilişkilidir.

Anahtar Kelimeler: ST-elevasyonlu miyokard infarktüsü; inflamasyon; mortalite; risk skorları

# INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is a critical condition often caused by an interruption of coronary artery flow. Reperfusion therapy including percutaneous coronary intervention (PCI) should be performed as soon as possible<sup>(1)</sup>. Mortality rates after STEMI are reported as 6-14% in hospital and 12% at six months<sup>(2)</sup>. These rates may vary among different subsets of patients<sup>(3)</sup>. Identifying the high-risk patients with STEMI is of great significance in prognosis<sup>(4)</sup>.



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Current scoring systems do not include inflammatory markers and nutritional status, which play a critical role in the prognosis of STEMI<sup>(5)</sup>.

The Naples score (NS) is a multidimensional, comprehensive prognostic evaluation system based on serum albumin levels, serum cholesterol levels, neutrophil/lymphocyte ratio (NLR), and lymphocyte/monocyte ratio (LMR)<sup>(6)</sup>. Preoperative NS was first established as an independent prognostic factor for colorectal cancer patients by Galizia et al<sup>(6)</sup>. This score can assess both the inflammatory and nutritional status of patients. Inflammation is a well-known risk factor for atherosclerosis<sup>(7)</sup>. Low serum albumin level is also a risk factor for coronary artery disease<sup>(8)</sup>. The NS can be useful for a more comprehensive risk assessment of STEMI patients. Subsequent studies demonstrated the prognostic value of the NS in patients with STEMI<sup>(9,10)</sup>.

We aimed to investigate the prognostic impact of NS at admission on in-hospital mortality among patients with STEMI who underwent PCI.

## **PATIENTS and METHODS**

We collected data from 570 consecutive STEMI patients who underwent PCI between January 2018 and September 2020 for this retrospective observational analysis. Patients with active cancer, active autoimmune disease, active infections, and chronic renal disease requiring hemodialysis and peritoneal dialysis were excluded. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The ethics committee of our hospital approved the study (Decision no: 2023-04-53, Date: 16.05.2023). Due to the study's retrospective nature, written informed consent from the patient was not required.

## **Definitions and Risk Factors**

The diagnostic criteria for STEMI were as follows: typical chest pain for more than 20 minutes and ST-segment elevation in at least two contiguous leads with the following cut-off points:  $\geq 0.2 \text{ mV}$  in men  $\geq 40$  years old;  $\geq 0.25 \text{ mV}$  in men <40 years old or  $\geq 0.15 \text{ mV}$  in women in leads V2 to V3 and/or  $\geq 0.1 \text{ mV}$  in the other leads as well as posterior (V7-V9) and right derivations (V3R-V4R)<sup>(11)</sup>.

Demographic and clinical parameters were recorded from the hospital database. Biochemical analyses including complete blood count, serum creatinine, serum albumin, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and serum electrolyte levels were assessed. The blood samples were obtained at the time of hospital admission to the emergency service.

Hypertension was defined as a systolic blood pressure of >140 mmHg and/or diastolic blood pressure of >90 mmHg, requiring antihypertensive medication. Diabetes mellitus (DM) was defined as a fasting glucose level of  $\geq$ 126 mg/dL or receiving antidiabetic therapy. Coronary angiography was performed via femoral or radial access within 90 minutes of admission for each patient.

The NS was calculated using serum albumin and serum total cholesterol levels, NLR, and LMR ratios as described in Figure 1.

Variable	Cut-off	Points	NS group
Albumin (g/L)	≥40	0	Group 0: 0 points
	<40	1	
Total cholesterol (g/dL)	>180	0	Group 1: 1 or 2 points
	≤180	1	
NLR	≤2.96	0	Group 3: 3 or 4 points
	<2.96	1	
LMR	>4.44	0	
	≤4.44	1	

Figure 1. Formulation of Naples score.

NLR: Neutrophil to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio, NS: Naples score.

## **Statistical Analyses**

Statistical analysis was conducted using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York, USA). Pearson Chi-square analysis was used for categorical variables. Fitness to normal distribution was analyzed with the Kolmogorov-Smirnov test. Mann-Whitney U test was performed for variables without normal distribution and Student's t-test was used for the variables with normal distribution. Data were expressed as "mean  $\pm$  standard deviation (SD)" for normal distribution and "median ( $25^{th}$ - $75^{th}$  percentiles)" for abnormal distribution while "n (%)" for categorical variables. Univariate and multivariate logistic regression analyses were used for predicting in-hospital mortality. A p-value of <0.05 was considered statistically significant.

## RESULTS

A total of 570 patients who were admitted with STEMI undergoing primary PCI were retrospectively included in this study. The incidence of in-hospital mortality rate was 4.9% (28 patients). The entire group was divided into two groups based on the presence of in-hospital mortality: group 1 consisted of 542 patients without in-hospital mortality, and group 2 included 28 patients with in-hospital mortality. The baseline demographic and clinical variables are demonstrated in Table 1. There were

no differences in terms of gender, smoking status, hypertension, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, ejection fraction, and culprit vessel between groups. However, the mean age was higher in group 2 compared to group 1.

The laboratory parameters are demonstrated in Table 2. There were no significant differences in high-density cholesterol (HDL), glucose, C-reactive protein, alanine aminotransferase, hemoglobin, leukocyte, neutrophil, and thrombocyte between groups. The total cholesterol, low-density lipoprotein cholesterol (LDL), triglyceride, and lymphocyte levels were lower in group 2, while creatinine level, and NS were higher in group 2. The incidence of patients with higher (>2.96) NLR, lower (<4.44) LMR, lower (<180 mg/dL) total cholesterol, and lower (<4 g/dL) serum albumin were also demonstrated in group 2 compared to group 1. Additionally, the incidence of patients with NS 0 and 1 or 2 was lower in group 2 while the incidence of patients with NS three or four was higher in group 2.

Logistic regression analysis was performed, and significant variables identified in the univariate analysis were included in the multiple logistic regression analysis to predict the independent risk factors for in-hospital mortality. In the multivariate logistic regression analysis, NS was identified as an independent predictor of in-hospital mortality (Table 3).

	Patients without in-hospital	Patients with in-hospital		
	mortality (n= 542)	mortality (n= 28)	р	
Age (years)	55.2 ± 11.2	59.8 ± 10.5	0.034	
Gender (female), n (%)	104 (19.2)	7 (25.0)	0.449	
Smoking, n (%)	260 (48.0)	11 (39.3)	0.370	
Hypertension, n (%)	182 (33.6)	9 (32.1)	0.875	
Diabetes mellitus, n (%)	111 (20.5)	5 (17.9)	0.737	
Peripheral arterial disease, n (%)	19 (3.5)	0 (0)	0.378	
Chronic obstructive pulmonary disease, n (%)	17 (3.1)	1 (3.6)	0.602	
Ejection fraction (%)	$46.8 \pm 9.8$	$48.1 \pm 1.8$	0.523	
Culprit vessel, n (%)				
LAD	285 (52.6)	12 (42.9)	0.550	
CXA	84 (15.5)	6 (21.4)		
RCA	173 (31.9)	10 (35.7)		

	Patients without in-hospital mortality	Patients with in-hospital mortality	
	(n= 542)	(n= 28)	р
Total cholesterol (mg/dL)	$202.2 \pm 43.5$	158.1 ± 25.9	<0.001
LDL cholesterol (mg/dL)	$123 \pm 38$	85 ± 23	< 0.001
HDL cholesterol (mg/dL)	39 (34-46)	43.5 (37.5-47)	0.212
Triglyceride (mg/dL)	182 (120-260)	130.5 (100-200.5)	0.018
Creatinine (mg/dL)	0.84 (0.73-1.0)	0.93 (0.80-1.13)	0.048
Glucose (mg/dL)	135 (110-194)	145 (102-212)	0.736
ALT (U/L)	20 (15-29)	18 (14-29)	0.663
C-reactive protein (mg/dL)	3.83 (1.82-8.37)	4.77 (2.28-38.61)	0.100
Hemoglobin (g/dL)	$14.43 \pm 1.81$	$14.08 \pm 1.90$	0.329
Leukocyte x 10 <sup>3</sup> /mm <sup>3</sup>	11.9 (9.6-14.0)	12.1 (10.3-1.43)	0.589
Lymphocyte (10 <sup>9</sup> /L)	2.5 (1.8-3.7)	1.8 (1.5-2.6)	0.002
Neutrophil (10 <sup>9</sup> /L)	7.3 (5.5-10.0)	8.5 (6.5-10.6)	0.191
Thrombocyte x 10 <sup>3</sup> /mm <sup>3</sup>	261 (222-318)	266.5 (234-312.5)	0.795
NAPLES score	1 (0-1)	3 (2-3)	< 0.001
NLR, n (%)			
≤2.96 (0 point)	293 (54.1)	5 (17.9)	< 0.001
>2.96 (1 point)	249 (45.9)	23 (82.1)	
LMR, n (%)			
>4.44 (0 point)	529 (97.6)	22 (78.6)	< 0.001
≤4.44 (1 point)	13 (2.4)	6 (21.4)	
Total cholesterol, n (%)			
>180 (0 point)	379 (69.9)	5 (17.9)	< 0.001
≤180 (1 point)	163 (30.1)	23 (82.1)	
Serum albumin, n (%)			
≥4 (0 point)	506 (93.4)	11 (39.3)	<0.001
<4 (1 point)	36 (6.6)	17 (60.7)	
NAPLES group, n (%)			
Group 1 (0 point)	195 (63.0)	4 (14.3) <sup>a</sup>	
Group 2 (1 or 2 points)	311 (57.4)	6 (21.4) <sup>a</sup>	< 0.001
Group 3 (3 or 4 points)	36 (6.6)	18 (64.3) <sup>b</sup>	

 $^{a}$ = Significantly lower in group 2,  $^{b}$ = Significantly higher in group 2.

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, ALT: Alanine transaminase, NLR: Neutrophil to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio.

Table 3. Multivariate logistic regression	analysis to r	predict the inde	nendent predicto	rs of in-hospital mortality

	Odds ratio	95% CI (Lower-Upper)	р
NAPLES score	4.368	2.881-6.625	<0.001
Age	1.018	0.982-1.054	0.330
Creatinine (mg/dL)	0.791	0.335-1.872	0.594

The present study revealed that higher NS is associated with higher in-hospital mortality in STEMI patients treated with PCI. STEMI is a complex clinical scenario that requires rapid therapeutic management and early risk stratification. The identification of high-risk patients with STEMI is of great significance in guiding medical management. Inflammatory processes are believed to trigger cardiovascular disease development and final clinical events. Neutrophils drive the early inflammatory response following myocardial infarction, and a high neutrophil count is an important marker for cardiovascular mortality<sup>(12)</sup>. Lymphocytes have inflammationsuppressing properties, which leads to a lower immune response and suppressed myocardial damage<sup>(13)</sup>. Inflammatory responses induce lymphopenia due to increased lymphocyte apoptosis. Lower lymphocyte levels are associated with a higher risk of cardiovascular mortality<sup>(14)</sup>. Monocytes have a role in inflammation and the procoagulant state observed during STEMI<sup>(15)</sup>. Monocytes actively bind to platelets, forming highly thrombotic monocyte-platelet aggregates, and markers of monocyte and platelet activation involved in regulating their function are also increased in STEMI<sup>(16)</sup>. Albumin has many functions that affect the cardiovascular system besides regulating osmotic pressure in extracellular fluid. Decreased levels of albumin lead to an increase in blood viscosity and impaired endothelial dysfunction<sup>(17)</sup>. Albumin has antioxidant properties and an inverse relationship with inflammation<sup>(18)</sup>. Biccire et al.<sup>(19)</sup> demonstrated that a low level of albumin was associated with mortality in STEMI patients. Hypercholesterolemia is a well-known risk factor for the development of coronary artery disease<sup>(20)</sup>. However, some studies showed an inverse association between TC and mortality, mostly attributable to concomitant conditions such as advanced age, frailty, and poor health status<sup>(21)</sup>. However, the explanation for this paradigm remains elusive.

The NS is a useful prognostic scoring model for determining survival in various types of cancer<sup>(22)</sup>. Recent studies showed the efficacy of the NS in predicting the prognosis of STEMI patients<sup>(9,10)</sup>. All individual components of the NS have a prognostic value for the in-hospital survival of STEMI patients. Simultaneous assessment of these components might provide complementary information to predict mortality. Routine blood tests obtained from STEMI patients can contribute to identifying patients who should be followed more closely and treated more aggressively.

This study has several limitations, with the first being its retrospective and single-center design. Secondly, we did not compare our results with well-known scoring systems, such as the Global Registry of Acute Coronary Events (GRACE). Thirdly, this study involved only STEMI patients. Therefore, the results might only apply to some of the spectra of acute coronary syndrome.

## CONCLUSION

The Naples score (NS), which reflects the inflammation and nutritional status of patients, can serve as a predictor of in-hospital mortality among STEMI patients treated with PCI.

**Informed Consent:** This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - EÖ; Analysis/Interpretation - SK; Data Collection - SK; Writing - EÖ; Critical Revision - EÖ; Final Approval - EÖ; Statistical Analysis -SK; Overall Responsibility - EÖ.

Conflict of Interest: The authors have no conflicts of interest to declare.

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#### REFERENCES

- Zeymer U, Ludman P, Danchin N, Kala P, Laroche C, Sadeghi M, et al. Reperfusion therapies and in-hospital outcomes for ST-elevation myocardial infarction in Europe: The ACVC-EAPCI EORP STEMI registry of the European society of cardiology. Eur Heart J 2021;42(44):4536-49.
- Ibanez B, James S, Agewell S, Antunes MJ, Ducci CB, Byeno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119-77.
- Fox KA, Carruthers KF, Dunbar DR, Graham C, Manning JR, De Raedt H, et al. Underestimated and under-recognized: The late consequences of acute coronary syndrome (GRACE UK-Belgian Study). Eur Heart J 2010;(22):2755-64.
- Lin A, Devlin G, Lee M, Kerr AJ: Performance of the GRACE scores in a New Zealand acute coronary syndrome cohort. Heart 100: 1960-1966, 2014.
- Wong BW, Meredith A, Lin D, Mc Manus BM. The biological role of inflamation in atherosclerosis. Can J Cardiol 2012;28:631-41.
- Galizia G, Lieto E, Auricchio A, Cardella F, Mabilia A, Podzemny V, et al. Naples prognostic score, based on nutritional and inflammatory status, is an independent predictor of long-term outcome in patients undergoing surgery for colorectal cancer. Dis Colon Rectum 2017;60:1273-84.
- Madjid M, Willerson JT. Inflammatory markers in coronary heart disease. Br Med Bull 2011;100:23-38.
- Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and clinical significance. JPEN 2019;43:181-93.
- Şaylık F, Çınar T, Selçuk M, Akbulut T, Hayıroğlu Mİ, Tanboğa İH. Evaluation of Naples score for long-term mortality in patients with STsegment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Angiology 2023:33197231170982.

Ethics Committee Approval: This study was approved by the Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Ethics Committee (Decision no: 2023.04-53, Date: 16.05.2023).

- Erdoğan A, Genç Ö, Özkan E, Göksu MM, İbişoğlu E, Bilen MN, et al. Impact of Naples prognostic score at admission on in hospital and folllow up outcomes among patients with ST-segment elevation myocardial infarction. Angiology 2023;74:970-80.
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction. J Am Coll Cardiol 2018;72:2231-64.
- Shah AD, Denaxas S, Nicholas O, Hingorani AD, Hemingway H. Neutrophil counts and initial presentation of 12 cardiovascular diseases: A CA-LIBER Cohort Study. J Am Coll Cardiol 2017;69(9):1160-9.
- Kurtul A, Yarlioglues M, Murat SN, Ergun G, Duran M, Kasapkara, H et al. Usefulness of the platelet-to-lymphocyte ratio in predicting angiographic reflow after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction. Am J Cardiol 2014;114:342-7.
- Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al; Intermountain Heart Collaborative Study Group. Which white cell subtypes predict increased cardiovascular risk? J Am Cardiol 2005;45:1638-43.
- Shantsila E, Lip GY. The role of monocytes in thrombotic disorders. Insights from tissue factor, monocytes-platelet aggregates and novel mechanism. Thromb Haemost 2009;102:916-24.

- Tapp LD, Shantsila E, Wrigley BJ, Pamukcu B, Lip GY. The CD 14++ CD+ monocyte subset and monocyte-platelet interactions in patients with ST-elevation myocardial infarction. J Thromb Haemost 2012;10:1231-41.
- Joles JA, Willekes-Koolschijn N, Koomans HA. Hypoalbuminemia causes high blood viscosity by increasing red cell lysophosphatidylcholine. Kidney Int 1997;52(3):761-70.
- Don BR, Kaysen G. Serum albumin: Relationship to inflammation and nutrition. Semin Dial 20114;17(6):432-7.
- Biccire FG, Pastori D, Tanzilli A, Pignatelli P, Viceconte N, Barilla F, et al. Low serum albumin levels and in-hospital outcomes in patientswith ST segment elevation myocardial infarction. Nutr Metabol Cardiovasc Dis 2021;31:2904-11.
- Stamler J, Wentworth D, Neaton JD. Is relationship between serum cholesterol and risk of premature death from coronary artery disease continuous and graded? Findings in 356,222 primary screnees of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA 1980;256:2823-8.
- Iribarren C, Reed DM, Chen R, Yano K, Dwyer JH. Low serum cholesterol and mortality. Which is the cause and which is the effect? Circulation 1995;92:2396-403.
- Nakagawa N, Yamada S, Sonohara F, Takami H, Hayashi M, Kanda M, et al. Clinical implications of naples prognostic score in patients with resected pancreatic cancer. Ann Surg Oncol 2020;27:887-95.