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The new score predicts 1-year poor outcome in patients with successful percutaneous coronary intervention: Naples prognostic score

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ABSTRACT

Aims: This study investigated the relationship between Naples prognostic score (NPS) and 1-year poor clinical outcomes in patients presenting with non-ST-segment elevation myocardial infarction (NSTEMI).

Methods: The study included 121 patients who had NSTEMI and received successful PCI treatment. The researchers calculated NPS using the neutrophil/lymphocyte ratio, lymphocyte/monocyte ratio, serum albumin level, and total cholesterol. The patients were divided into two groups based on their NPS scores: those with scores of 0.1 and 2 and those with scores of 3 and 4. The study compared the occurrence of major cardiovascular events (MACE) such as 1-year all-cause mortality, 1-year nonfatal recurrent MI, and stroke between the two groups.

Results: Patients with high NPS scores were observed to have significantly higher all-cause mortality than those with low NPS scores (23.9% vs. 9.3%, p=0.029). When the MACEs of the patients were compared, significantly higher MACE was observed in the high NPS group (39.1% vs. 18.7%, p=0.013).

In multivariate logistic regression analysis, creatinine (OR:4,914, CI 95%: 1.310-18,433, p=0.018) and NPS 3-4 (OR:2.565, CI 95%: 1.093-6.017, p=0.030) were independent predictors of MACE.

Conclusion: Composite MACEs of non-fatal recurrent MI, cerebrovascular accident, and all-cause death were higher at one year in patients with high NPS who underwent successful percutaneous intervention. High NPS is an indicator of MACE.

Keywords: Naples prognostic score, acute coronary syndrome, mortality

INTRODUCTION

Despite significant progress in diagnosis and treatment, acute coronary syndrome (ACS) remains a leading cause of morbidity and mortality worldwide. Previous studies have shown that inflammation is essential in atherosclerosis.[1] Inflammation and oxidative stress can trigger plaque rupture, leading to ACS.[2] Although mortality and morbidity in patients with acute coronary syndrome have decreased thanks to the development of PCI techniques and medical treatments, it is essential to predict adverse events that will develop during the follow-up of these patients in terms of follow-up and treatment strategy. Many computational tools have been developed to determine the prognosis of patients with ACS. Many of these tools are impractical to use. New scoring systems are needed to avoid wasting time and to obtain accurate prognostic value.

Previous studies have shown that neutrophil/lymphocyte ratio (NLR) and lymphocyte/monocyte ratio (LMR), which are inflammatory markers, together with albumin and total cholesterol, which are used as indicators of nutritional status and inflammation, can be used as prognostic indicators in patients presenting with ACS.[3-5] The Naples prognostic score (NPS) combines NLR, LMR, serum albumin level, and total cholesterol levels. It has previously been used as a valuable prognostic tool in cancer patients.[6] NPS provides nutritional status and inflammation information. The long-term prognostic value of NPS has been previously demonstrated in a study of ST-segment elevation myocardial infarction (STEMI) patients.[7] Our study aimed to investigate the relationship between NPS and MACE within one year in patients with non-ST-segment elevation myocardial infarction (NSTEMI). The NPS score is a simple way of measuring

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inflammation and was intended to explore its potential as a prognostic marker for patients with NSTEMI. Previous studies have not investigated the relationship between NPS and 1-year prognosis in NSTEMI patients undergoing successful PCI. This study aims to fill this gap and emphasize the importance of NPS in patient follow-up.

METHODS

The study was carried out with the permission of Health Sciences Non-interventional Researches Ethics Committee (Date: 21.06.2023, Decision No: 2023-96). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study was designed retrospectively and included 121 patients who applied to a Training and Research Hospital with NSTEMI and underwent successful percutaneous intervention with PCI between June 2019 and June 2022. In the study, Patients with severe intolerance or allergy to dual antiplatelet therapy, receiving anticoagulant therapy for mechanical heart valve or atrial fibrillation, acute coronary syndrome in the last 1 year, patients with coronary artery bypass graft operation in the last 1 year, history of hematological disease, chronic kidney disease, severe liver disease, patients using anticoagulants, patients with active infection and patients with a history of infectious disease in the last one month, and malignancy were excluded from the study.

The NPS score is determined by using NLR, LMR, serum albumin level, and total cholesterol. If a person has an albumin level of less than 4 mg/dl, a total cholesterol level of 180 mg/dl or less, an NLR level greater than 2.96, or an LMR level of 4.44 or less, they are assigned one point when calculating the NPS score. However, if a person has an albumin level of greater than or equal to 4 mg/dl, a total cholesterol level greater than 180 mg/dl, an NLR level of 2.96 or less, or an LMR level greater than 4.44, they are assigned a score of 0. To determine the NPS score, all of these scores are added together.[6] In the study, patients were categorized into two groups based on their NPS score: those with a score of 0.1 to 2, and those with a score of 3 to 4. Major cardiovascular event (MACE) was defined as 1-year all-cause mortality, 1-year stroke, nonfatal recurrent MI, stroke, and MACEs were compared between the groups.

We used IBM SPSS Statistics 23 for analysis. Continuous variables were presented as mean±standard deviation if normally distributed, and median [IQR] if not. Student t-test compared normally distributed independent groups, while Mann-Whitney U test compared non-normally distributed. Categorical variables were presented as percentages and compared using chi-square test. A multivariate logistic regression model was created with significant variables from univariate regression. p values below < 0.05 were considered significant.

RESULTS

In a retrospective analysis of 121 patients, the study grouped them into two categories based on their NPS scores. Group 1 included 75 patients who scored 0-1-2, while Group 2 comprised 46 patients who scored 3-4. The average age of patients in Group 1 was 71.2±11.5, while in Group 2, it was 71.3±11 years. Interestingly, there were no significant differences between the two groups in terms of gender, age, presence of diabetes mellitus, hypertension, and previous coronary artery disease (CAD) left ventricular ejection fractions. However, Group 2 displayed significantly higher levels of WBC and neutrophils, and lower levels of lymphocyte, total cholesterol, and serum albumin. **Table 1** provides an overview of the study participants' laboratory, clinical, and demographic data and the drugs they used.

Table 1. Demographic, clinical, and laboratory characteristics of the patients

Variables	All (121)	Grup 1 (75)	Group 2 (46)	p
Age, year	76.3±7.0	71.2±11.5	71.3±11.0	0.951
Male gender, n (%)	64 (52.9)	38 (50.7)	26 (56.5)	0.531
Hypertension, n (%)	97 (80.2)	63 (84.0)	34 (73.9)	0.177
Diabetes mellitus, n (%)	44 (36.4)	27 (36.0)	17 (37.0)	0.915
Smoke, n (%)	31 (25.6)	17 (22.8)	14 (30.4)	0.342
Hyperlipidemia, n (%)	41 (33.9)	24 (32)	17 (37)	0.576
Previous CAD, n (%)	42 (34.7)	24 (32.0)	18 (39.1)	0.424
ASA, n (%)	45 (37.2)	27 (36.0)	18 (39.1)	0.729
Statin, n (%)	28 (23.1)	16 (21.3)	12 (26.1)	0.346
ACEi, n (%)	65 (53.7)	42 (56.0)	23 (50.0)	0.521
Beta-Blocker, n (%)	35 (28.9)	22 (29.3)	13 (28.3)	0.899
OAD, n (%)	37 (30.6)	22 (29.3)	15 (32.6)	0.428
OAD + Insulin, n (%)	17 (14.0)	12 (16.0)	5 (10.9)	0.430
LvEF, %	52.2±8.4	51.3±8.5	53.8±8.1	0.122
WBC, (103/µl)	7.4±2.4	9.3±3.3	11.4±4.9	0.005
Hemoglobin, g/dl	12.3±1.1	12.3±1.2	12.1±1.1	0.255
Lymphocyte, (10^3/µl)	1.6±0.6	2.3±0.9	1.6±0.7	<0.001
Neutrophil, (10^3/µl)	5.0±2.2	6.1±3.0	8.9±4.4	<0.001
Monocyte, (10^3/µl)	0.5±0.2	0.7±0.3	0.9±0.4	0.053
Platelet count, (10^3/µl)	235.0±82.2	223.3±67.8	232.1±71.1	0.496
Creatinine, mg/dl	1.1±0.32	1.07±0.31	1.16±0.33	0.162
Total cholesterol, mg/dl	163.6±42.9	182.1±48.8	142.9±23.8	<0.001
Albumin, (mg/dl)	4.2±0.4	4.2±0.3	4.0±0.5	0.024

CAD, coronary artery disease; ASA, Acetylsalicylic acid; OAD, Oral antidiabetic drug; LvEF, Left ventricular ejection fraction; WBC, White blood cell

Adverse cardiovascular events developed in the 1-year follow-up of the patients were compared and are given in **Table 2**. All-cause mortality in Group 2 was significantly higher than in Group 1 (23.9% vs 9.3%, p=0.029). When MACEs consisting of all-cause mortality, recurrent

MI, and development of cerebrovascular accident were compared, a significantly higher MACE was observed in Group 2 (39.1% vs 18.7%, p=0.013).

Table 2. Clinical outcomes of the groups at 1-year follow-up

Variables	All (121)	Group 1 (75)	Group 2 (46)	p
Composite MACE, n (%)	32 (26.4)	14 (18.7)	18 (39.1)	0.013
All-cause death, n (%)	18 (14.9)	7 (9.3)	11 (23.9)	0.029
Non-fatal recurrent MI, n (%)	10 (8.3)	5 (6.7)	5 (10.9)	0.415
Stroke, n (%)	12 (9.9)	7 (9.3)	5 (10.9)	0.784

MACE, Major cardiovascular event; MI, Myocardial Infarction

In multivariate logistic regression analysis, creatinine (OR:4,914, CI 95%: 1.310-18,433, p=0.018) and NPS 3-4 (OR:2.565, CI 95%: 1.093-6.017, p=0.030) were found to be independent predictors of the development of MACE (**Table 3**).

Table 3. Univariate and multivariate regression analysis for detecting mace

	Univariate	Multivariate
	OR (95% confidence interval)	OR (95% confidence interval)
Age	0.973 (0.938-1.010, p=0.145)	
Hypertension	2.025 (0.636-6.472, p=0.232)	
Diabetes mellitus	1.280 (0.559-2.934, p=0.559)	
LvEF	0.962 (0.918-1.009, p=0.110)	
Creatinine	5.638 (1.516-20.966, p=0.010)	4.914 (1.310-18.433, p=0.018)
NPS (3-4)	2.801 (1.222-6.420, p=0.015)	2.565 (1.093-6.017, p=0.030)

NPS, Naples Prognostic Score

DISCUSSION

Looking at previous studies, no study was observed showing the relationship between NPS and 1-year prognosis in patients who presented with NSTEMI and underwent successful PCI. Our study determined that more MACE was detected with a higher NPS score in patients with successful PCI due to NSTEMI. NPS was an independent predictor of MACE.

Inflammation is known to be the most critical component of the pathogenesis of CAD. White blood cell count has been used as an inflammatory biomarker in many studies to predict outcomes and prognosis in patients with ACS.[8] Although thrombosis leading to the development of ACS is a process different from inflammation, inflammation also causes thrombosis.[9] In addition to thrombosis, inflammatory cells also cause plaque rupture. Especially neutrophils have an active role in all stages of formation, development, and rupture of atheroma plaque in the coronary vessels in ACS patients. It is known that neutrophils use local chemicals that facilitate the rupture of atheromatous plaque and cause cell aggregation, especially leukocytes, and thrombocytes, in the coronary vessel.[10] On the contrary, it has been shown in previous studies that low lymphocyte levels cause an increase in mortality and morbidity in patients with CAD.[11,12] The relative decrease in lymphocyte levels is thought to be caused by endogenous cortisol, which increases due to stress, and inflammation causes lymphocyte apoptosis.

NLR is a marker of inflammation and a prognostic indicator in cancer, infectious diseases, and cardiovascular diseases.[13-15] It has been shown that NLR, which is used as an inflammation marker, can predict mortality in ACS patients.[16] Similarly, in LMR, the myelodysplastic syndrome is used as a prognostic indicator in ovarian cancers but has been associated with the presence and severity of CAD.[17-19] Yılmaz et al.[20] showed that NLR combining these two blood parameters could be a prognostic value in ACS patients.

Albumin is a negative acute phase reactant produced by the liver. In addition to showing nutritional status, serum albumin is associated with chronic and acute inflammatory responses, and increased inflammation reduces serum albumin levels.[21,22]

Albumin is an antioxidant protein. Therefore, the amount of free oxygen radicals and reactive oxygen products increases in cases of hypoalbuminemia, which may have a role in the pathophysiology of ACS.[23] Another essential function is to prevent thrombotic events, ensure the proper functioning of endothelial functions, and ultimately preserve vascular integrity.[24] In previous studies, low serum albumin levels were associated with mortality in patients with ACS.[25]

Although total cholesterol levels are a risk for developing atherosclerotic plaque, previous studies have shown that low cholesterol levels are paradoxically associated with mortality, on the contrary.[26] It is known that it mainly occurs with the rupture of atheroma plaques in the coronary vessels, followed by the settlement of a thrombus. Inflammation is essential in the atheroma plaque's formation, progression, and rupture stages. In one study, it was shown that cytokines can cause a decrease in blood cholesterol levels by changing cholesterol metabolism.[27] Cholesterol level, one of the NPS parameters, may indicate the inflammation status in ACS patients. In our study, no significant difference was found between the groups regarding previous diagnosis of hyperlipidemia, use of statins, and diagnosis of diabetes mellitus, which has prognostic significance in patients with coronary artery disease. Initiation of statins after percutaneous coronary intervention is expected to affect the NPS of these patients in their follow-up, and prospective studies are needed to investigate the effect of this situation.

Since ACS is a vital disease, early diagnosis, and treatment should be planned. These patients present with mild chest pain and life-threatening arrhythmias and shock. Therefore, it is crucial to predict mortality in these patients. The biochemical parameter, troponin, increases approximately 3 hours after symptom onset and does not increase in all ACS. In ACS patients, markers with rapid response and high prognostic value, which can be easily used in any laboratory environment, continue to be investigated. In this sense, NPS is a scoring system that is easy to look at and predicts inflammation and prognosis, forming the basis of ACS pathophysiology. New scoring systems are needed to avoid wasting time and to obtain accurate prognostic value; NPS may be one of them. NPS, first associated with poor prognosis in cancer patients, provides valuable information regarding prognosis in STEMI patients in more recent studies.[28,29] Birdal et al.[30] showed a relationship between NPS and low ejection fraction in patients with STEMI. Karakoyun et al.[31] showed the relationship between NPS and acute kidney injury in patients with STEMI. In a previous study, a significant relationship was found between the severity of coronary artery disease and the systemic immune inflammation index, including NLR and platelet components in patients with stable coronary artery disease, but the relationship between NPS was not significant. The reason for this is that total cholesterol, which is an important substrate in the formation of atherosclerotic plaque, is used in the calculation of NPS. However, since our study is a study showing the prognosis in patients with coronary artery disease, it shows the prognostic value of NPS with inflammation and nutritional status.[32] NPS: It consists of NLR, LMR, serum albumin, and total cholesterol components. High NLR, low LMR, low serum albumin, and low total cholesterol levels have been associated with poor prognosis.[7] NPS, a combination of these, is thought to be a more robust prognostic marker and has been proven by studies. Similar to previous studies, higher composite MACE was observed in the high NPS group in our study.

Our study has limitations, such as being retrospective and being conducted in a small group of patients. The importance of prognostic markers in larger patient groups and prospective studies are needed.

CONCLUSION

As a result, composite MACEs consisting of non-fatal recurrent MI, cerebrovascular accident, and all-cause death were found to be higher in patients with high NPS who underwent successful percutaneous intervention due to NSTEMI at 1-year follow-up. High NPS can be said to be a predictor of MACE. NPS is an easily calculated inflammatory score and can be used as a prognostic marker in patients with NSTEMI.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Health Sciences Non-interventional Researches Ethics Committee (Date: 21.06.2023, Decision No: 2023-96).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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