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Original Article

The Value of Naples Prognostic Score in Predicting Ischemia on Myocardial Perfusion Scintigraphy

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Abstract

Objectives: Naples prognostic score (NPS) is a recently established score that measures inflammation and nutritional conditions. This score includes lymphocyte-to-monocyte ratio, neutrophil-to-lymphocyte ratio, total cholesterol levels, and serum albumin levels. Initial studies have shown that the NPS score has more prognostic value than other inflammatory parameters in some cancer diseases. Recently, the association of the NPS score with various cardiovascular diseases has started to be evaluated. The association between ischemia in myocardial perfusion scanning and the Naples score has not yet been investigated. In this study, we evaluated if the NPS may help predict ischemia in myocardial perfusion scanning.

Methods: This study included a total of 110 patients. All patients underwent myocardial perfusion scintigraphy (MPS) at the nuclear medicine department, with dipyridamole or adenosine administered as the pharmaceutical stressor. The subjects were divided into two groups according to the presence or absence of ischemia on gated single-photon emission computed tomography (SPECT) MPI. Laboratory values within the past month before MPS were obtained from digital records for both groups. The NPS was calculated for each group. Laboratory values and NPSs of the groups were compared.

Results: All individuals in the trial had gated SPECT MPI. The average age of individuals was 59.8±11.1 years, with 62 patients (56%) being male. Subjects were divided into two groups according to the presence or absence of ischemia on gated SPECT MPI. Table 1 displays the demographics of the whole study population. Based on the laboratory data (Table 2), there was no significant difference in the demographic features of the groups. The ischemia group had significantly higher levels of white blood cell count (cells/μL), neutrophil count (cells/μL), hemoglobin (g/dL), CRP (mg/L), and NPS (8.6±2.2, 7.7±1.9, p=0.040; 5.0±2.1, 4.1±1.3, p=0.014; 12.6±1.7, 13.4±1.8, p=0.025; 8.2±2.0, 7.9±2.0, p=0.004; 2.6±1.0, 1.5). Other laboratory results did not differ across the groups.

Conclusion: Our findings indicated an association between NPS and the detection of ischemia in MPS. NPS is an independent variable for diagnosing myocardial ischemia in stable coronary artery disease patients.

Keywords: Myocardial ischemia; myocardial perfusion scintigraphy; naples prognostic score; single-photon emission computed tomography.

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Naples Prognostik Skorunun Miyokardiyal Perfüzyon Sintigrafisindeki İskemiyi Öngörmedeki Değeri

Özet

Amaç: Naples Prognostik Skor (NPS), inflamasyon ve beslenme durumunu değerlendiren yeni tanımlanmış bir skordur. NPS skorunun çeşitli kardiyovasküler hastalıklarla ilişkisi araştırılmaya başlanmıştır. Miyokard perfüzyon taramasında iskemi olması ile Naples skoru arasındaki ilişki henüz araştırılmamıştır. Bu çalışmada, Naples prognostik skorunun miyokard perfüzyon taramasında iskemi tahminine yardımcı olup olamayacağını değerlendirdik.

Gereç ve Yöntem: Bu çalışma toplam 110 hastayı içermektedir. Tüm hastalara, nükleer tıp bölümünde farmakolojik stresör olarak dipyridamol veya adenosin kullanılarak miyokard perfüzyon sintigrafisi (MPS) yapılmıştır. Hastalar, gated SPECT MPI'daki iskemi varlığına göre iki gruba ayrıldı. MPS yapılmasından önceki son bir ay içindeki laboratuvar değerleri her iki grup için dijital kayıtlardan elde edildi. Her bir grup için Naples Prognostik Skoru (NPS) hesaplandı. Grupların laboratuvar değerleri ve Naples Prognostik Skorları karşılaştırıldı.

Bulgular: Çalışmamızda tüm hastalara gated SPECT MPI testi yapılmıştı. Hastaların ortalama yaşı 59.8±11.1 yıl olup, 62 hastanın (%56) erkek olduğu görüldü. Hastalar, gated SPECT MPI'daki iskemi varlığına göre iki gruba ayrıldı. Grupların demografik özelliklerinde anlamlı fark yoktu. Laboratuvar verilerine dayanarak iskemi grubunda ; beyaz kan hücresi sayısı (hücreler/µl), nötrofil sayısı (hücreler/µL), hemoglobin (g/dL), CRP (mg/L) ve Naples prognostik skoru (8.6±2.2, 7.7±1.9, p=0.040; 5.0±2.1, 4.1±1.3, p=0.014; 12.6±1.7, 13.4±1.8, p=0.025; 8.2±2.0, 7.9±2.0, p=0.004; 2.6±1.0, 1.5) anlamlı derecede yüksekti. Diğer laboratuvar sonuçları gruplar arasında farklılık göstermedi.

Sonuç: Bulgularımız, NPS ile miyokard perfüzyon sintigrafisinde iskemi olması arasında bir ilişki olduğunu gösterdi. NPS, stabil koroner arter hastalığı olan hastalarda miyokard iskemisini teşhis etmek için bağımsız bir değişkendir.

Anahtar sözcükler: Miyokard iskemisi; miyokard perfüzyon sintigrafisi; naples prognostik skoru; tek foton emisyonlu bilgisayarlı tomografi.

Introduction

Ischemic heart disease is known as the leading cause of mortality worldwide. Angina pectoris is the predominant symptom of ischemic heart disease. In patients with stable angina pectoris, non-invasive imaging tests are first performed to diagnose coronary artery disease (CAD). Myocardial perfusion scintigraphy (MPS) and stress echocardiography are recommended in the latest guidelines due to the high rate of false positive results in the treadmill exercise test. Myocardial perfusion scintigraphy using single-photon emission computed tomography (SPECT) is still widely used as the principal approach for detecting ischemia of the myocardium in patients with suspected CAD.[1,2] The inflammatory process, lipid metabolism, and immunological variables all play essential roles in the pathogenesis of atherosclerosis in cardiovascular diseases.[3,4] In previous research, inflammatory or biochemical indicators such as high-sensitivity C-reactive protein (hs-CRP), serum albumin levels, neutrophil count, lymphocyte count, lymphocyte-to-monocyte ratio (LMR), and neutrophil-to-lymphocyte ratio (NLR) were found to be possibly associated with CAD.[5,6] The Naples Prognostic Score (NPS) is a recently established score that measures inflammation and nutritional conditions. This score includes LMR, NLR, total cholesterol (TC) levels, and serum albumin (Alb) levels. Initial studies have shown that the NPS score has more prognostic value than other inflammatory parameters in some cancer diseases[6,7] Recently, the association of the NPS score with different diseases has started to be evaluated. Studies have demonstrated that NPS is associated with the prognosis of acute pulmonary embolism (PE), transcatheter aortic valve replacement treatment, mortality due to heart failure (HF), and long-term outcomes in patients with ST-segment elevation myocardial infarction. [8–11] The association between ischemia in myocardial perfusion scanning and the Naples score has not yet been investigated. In this study, we evaluated if the Naples score may help predict ischemia in myocardial perfusion scanning.

Materials and Methods

We retrospectively evaluated 1848 patients referred for gated SPECT MPI from a cardiology outpatient clinic between October 2020 and June 2022. Out of these, we enrolled patients who had complete blood count (CBC) TC and albumin levels measured within 30 days before MPI. After applying exclusion criteria, we examined 134 patients who satisfied the criteria. We called these people to learn about their cardiovascular risks and disorders that may influence acute-phase reactants. Individuals with a prior diagnosis of CAD (including revascularization), chronic kidney failure (glomerular filtration rate <60 mL/min), hepatic disease (aspartate aminotransferase and alanin aminotransferase levels that are more than twice the normal limits), significant anemia (hemoglobin <10 g/dL), white blood cell count (>11,000/mL), neutrophilia (>70%), thrombocyte count (<100,000/dL), history of cancer or systemic inflammatory disease, or who used statins, anti-inflammatory drugs, or antibiotics a month before the study were excluded. As a result, 110 appropriate individuals remained for the study (Fig. 1). All patients underwent MPS at the nuclear medicine department, with dipyridamole or adenosine administered as the pharmaceutical stressor. Patients were divided into two groups based on the presence or absence of ischemia on MPS. Laboratory values within the past month before MPS were obtained from digital records for both groups. NPS was calculated for each group. Laboratory values and NPS of the groups were compared. Before the study, every patient gave written informed permission. The study was authorized by the Local Ethics Committee (decision number 2024/05/791).

Myocardial Perfusion Imaging (MPI)

For the evaluation of the perfusion of the myocardium, a 2-day stress/rest scanning method utilizing Technetium-99m methoxy isobutyl isonitrile (Tc-99m MIBI) was used. Patients ate anything for at least 6 h before the process. Stress imaging was done using an exercise treadmill test with radiopharmaceutical substances administered at the peak of exertion. Imaging began 30–45 min after the administration of 15–20 mCi of Tc-99m MIBI. If any perfusion irregularities were seen in the stress pictures, a corresponding amount was administered during rest imaging. SPECT pictures were obtained using the IQ-SPECT Symbia S system (Siemens, USA) with specific multi-focused SMARTZOOM™ collimators for cardio-centric collection. Two experienced readers scored the images, and the results were established by consent. To establish the existence and severity of ischemia, the regional perfusion was assessed using a semi-quantitative analysis of the Total Stress Score (TSS), Total Rest Score, and Total Difference Score. TSS levels below 4 indicated normal perfusion, while scores of 4–8 denoted mild, 9–13 indicated moderate, and values exceeding 13 signified severe abnormal perfusions.

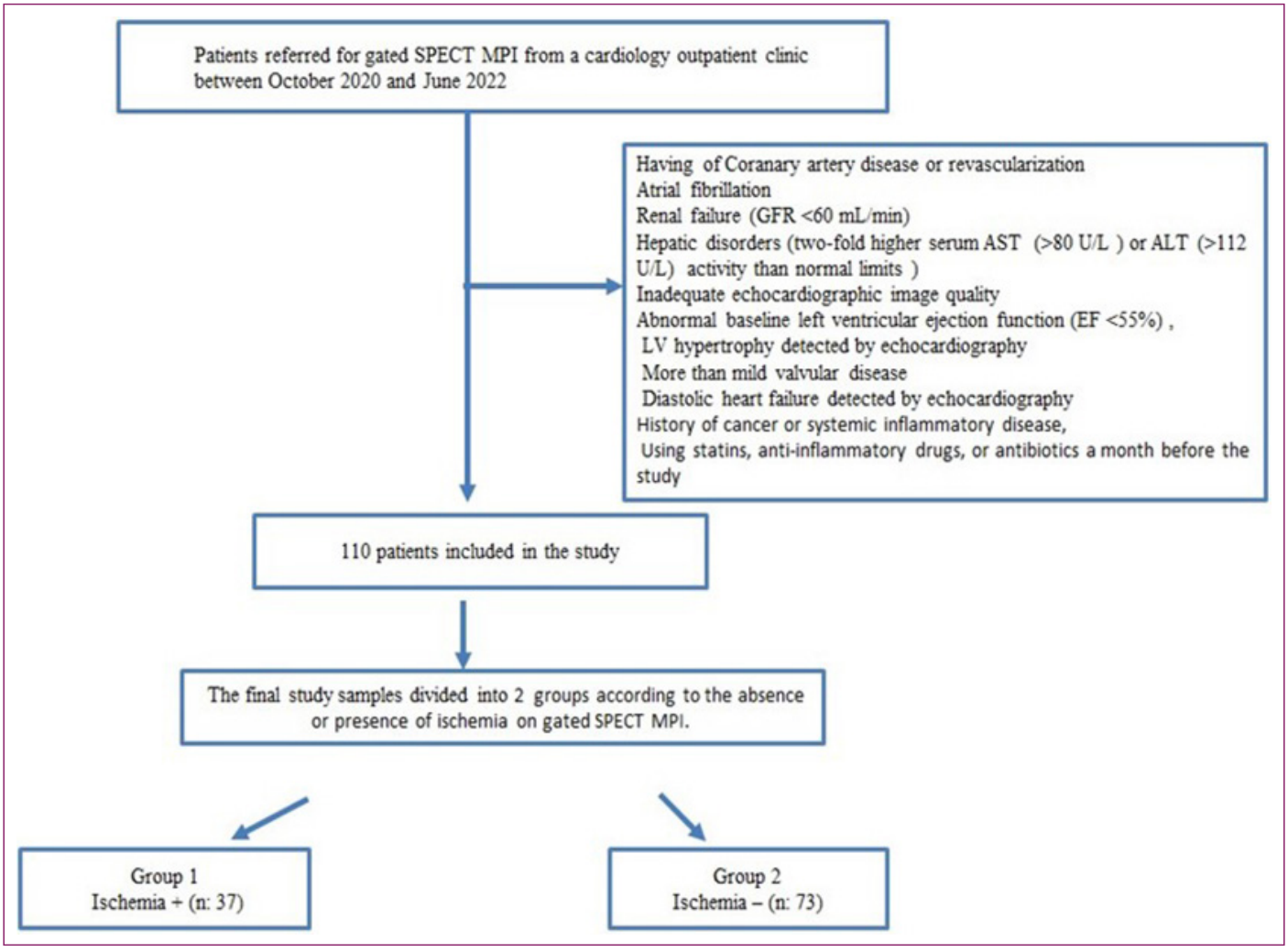

Figure 1. Consort diagram of study.

SPECT: Single-photon emission computed tomography; MPI: Myocardial perfusion imaging; GFR: Glomerular filtration rate; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; EF: Ejection fraction; LV: Left ventricle.

Laboratory Measurements

All laboratory findings were collected retrospectively using computerized recordings. We accomplished standard CBC and blood chemistry tests, comprising TC and albumin. To compute NLR and LMR, divide the complete neutrophil count by the lymphocyte count and the complete lymphocyte count by the monocyte count, respectively. The NPS was determined as previously stated in the literature.[12] The NPS is made up of four components: the neutrophil/lymphocyte ratio, the lymphocyte/monocyte ratio, the TC level, and the serum albumin level. Each parameter value is either 0 or 1 point, and the total of these values is computed. Patients with NPS levels of 0, 1, or 2 are classified as low NPS, but those with NPS values of 3 or 4 are categorized as high-NPS. Figure 2 illustrates the calculation of the NPS.

Statistical Analysis

The statistical analysis was conducted using R Studio version 4.1 (Vienna, Austria). Numerical variables were shown as mean±standard deviation whereas discrete data were represented as absolute numbers. The one-way ANOVA or Wilcoxon rank and the χ^2 statistics were used to evaluate the baseline and clinical characteristics among patients based on the non-ischemia versus ischemia group.

The primary outcome of the study was ischemia on SPECT. The main predictor was the NPS. Statistical modeling was done using logistic regression. Finally, we assessed the predictive accuracy (Nagelkerke's R2) of variables. P<0.05 was accepted as statistically significant. All statistical analyses were performed using the "Hmisc" and "rms" packages with the R studio 4.2 version.

Results

All individuals in the trial had gated SPECT MPI. The average age of individuals was 59.8±11.1 years, with 62 patients (56%) being male. Subjects were divided into two groups according to the presence or absence of ischemia on gated SPECT MPI. Table 1 presents the demographic characteristics of the entire study population. There was no significant difference in the demographic features of the groups. The ischemia group had significantly high-

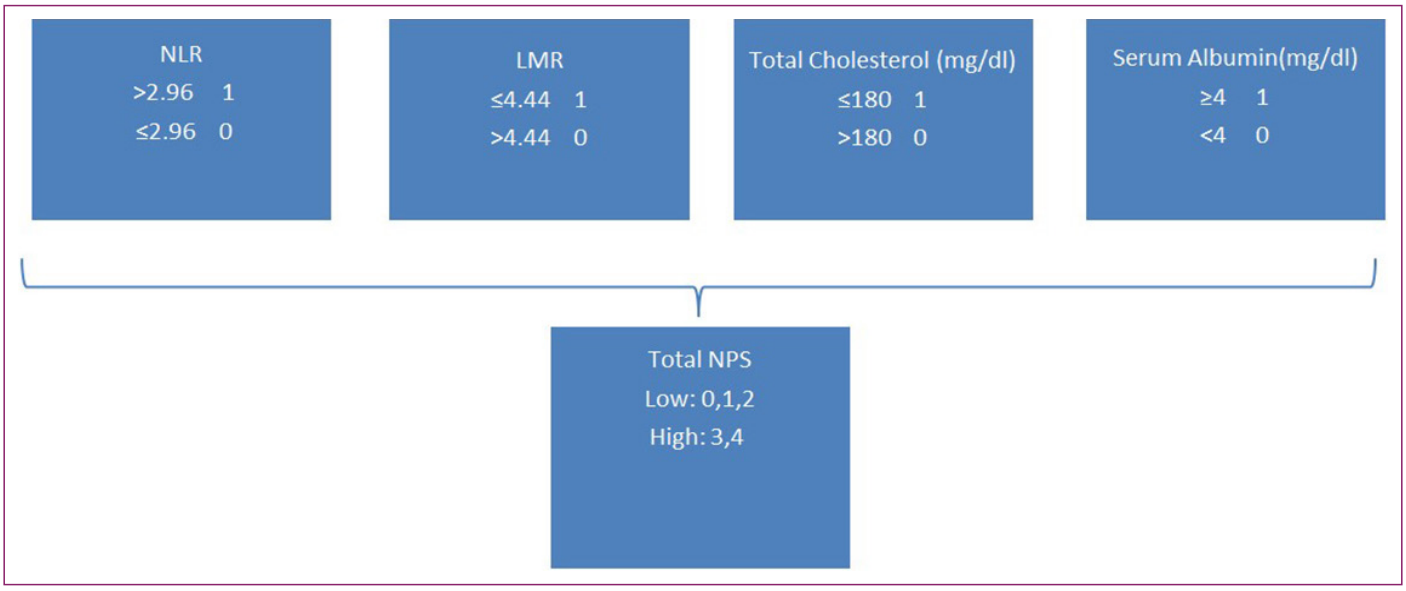

Figure 2. The calculation of the Naples prognostic score.

NLR: Neutrophil-to-lymphocyte ratio; LMR: Lymphocyte-to-monocyte ratio; NPS: Naples prognostic score.

er levels of white blood cell count (cells/μL), neutrophil count (cells/μL), hemoglobin (g/dL), CRP (mg/L), and NPS (8.6 ± 2.2, 7.7 ± 1.9, p: 0.040; 5.0 ± 2.1, 4.1 ± 1.3, p: 0.014; 12.6 ± 1.7, 13.4 ± 1.8, p: 0.025; 8.2 ± 2.0, 7.9 ± 2.0, and p: 0.004; 2.6 ± 1.0, 1.5). Other laboratory results did not differ across the groups (Table 2).

To determine the roles of NPS in predicting ischemia detected by SPECT MPI, the predictors related to ischemia were evaluated by logistic regression. NPS (OR: 1.86, 95% CI 1.16 – 2.96), and albumin (cathegoric) (OR; 2.82, 95% CI 1.24–6.36) were statistically significantly related to ischemia (Table 3). However, other variables were not associated with ischemia. Furthermore, when each component of the NPS was separately included in the model to determine which variable was more closely associated, it was observed that albumin had the highest explanatory power (Nagelkerke's R2: 0.078), while the explanatory powers of NLR, LMR, and TC were lower (Nagelkerke's R2: 0.012, 0.06, 0.013; respectively). However, these values were lower than those of the NPS alone (Nagelkerke's R2: 0.089). A marginal mean plot for the NPS was created to predict ischemia, revealing that as the Naples score increased, the probability of ischemia detected by SPECT MPI also increased (Fig. 3).

Discussion

In this study, we examined the association between the NPS and ischemia detected on MPS in patients with stable CAD. Among the several inflammatory parameters, the NPS has been found to be superior in predicting myocardial ischemia, independently. Atherosclerosis is a frequent condition with substantial clinical effects, including CAD. CAD patients typically develop myocardial ischemia. The genesis of atherosclerosis and myocardial ischemia is complicated, including several biological mechanisms such as biomolecular and inflammatory processes.[13] During the early phases of myocardial ischemia, there are inflammatory responses in myocardial tissue. CRP, albumin, and the neutrophil-lymphocyte ratio (NLR) are suggested to be utilized to assess inflammation, particularly in acute coronary syndromes.[14] NLR has been identified as a key predictor in several investigations of individuals with acute and stable CAD.[15,16] CRP and neutrophil levels were also higher in patients with ischemia in our study. Studies have demonstrated that aberrant lipid metabolism causes accumulation of lipids and dysfunction of the mitochondria, both of which are significantly linked to myocardial ischemia.[17] It has been demonstrated that hypercholesterolemia is intimately connected with CAD and that reducing levels of cholesterol may decrease the incidence and death rates of CAD.[18] Ozdemir et al.[19] studied 262 patients who had abnormal and normal MPS and looked to determine the relationship between N/L ratio, P/L ratio, PDW, and RDW and myocardial perfusion. Neutrophil numbers and N/L ratios were considerably greater in individuals who had been confirmed to have myocardial ischemia or infarction. They discovered that the N/L ratio was linked with myocardial ischemia and connected with the left ventricular ejection fraction (LVEF). In our study, neutrophil and white blood cell levels were higher and hemoglobin levels were slightly lower in patients with ischemia in MPS. Efe et al.[20] examined CRP/albumin ratios in two groups of patients with and without ischemia in gated SPECT MPI and found that the CRP/albumin ratio was significantly correlated with ischemia in gated SPECT MPI. Similarly, although we found significantly higher CRP levels in patients with ischemia, we did not observe a significant difference in albumin levels. In a recent study, the neutrophil/HDL ratio was compared in patients with mild stenosis and moderate to advanced stenosis of coronary arteries. The neutrophil/HDL ratio increased with the increasing severity of coronary artery stenosis.[21] NPS is a scoring system that measures a patient's inflammatory and nutritional condition, including LMR, NLR, TC, and serum alpha levels. TC and serum albumin represent

Table 1. Baseline demographic characteristics findings of all patients

	Presence of ischemia (n=37)		Absence of ischemia (n=73)		p
	n	%	n	%	
Gender, male	20	54	42	57.5	0.728
Age (years)	59.5±10.4		60.2±11.8		0.593
Use of smoking	18	48.6	28	38.3	0.301
Hypertension	15	40.5	22	30.1	0.275
Diabetes mellitus	16	43.2	29	39.7	0.723
Dyslipidemia	3	8.1	15	20.5	0.096

Nominal variables presented as frequency (%)

Table 2. Laboratory and echocardiographic findings of patients

	Presence of ischemia (n=37)	Absence of ischemia (n=73)	p
EF % (teicholtz)	61.6±10.4	64.4±9.8	0.174
White blood cell count (cells/μL)	8.6±2.2	7.7±1.9	0.040
Neutrophil (cells/μL)	5.0±2.1	4.1±1.3	0.014
Lymphocyte (cells/μL)	2.5±0.8	2.5±0.8	0,714
Monocyte (cells/μL)	0.7±0.3	1.3±0.6	0,561
Hemoglobin (g/dL)	12.6±1.7	13.4±1.8	0.025
Creatinine (mg/dL)	0.8±0.3	0.8±0.2	0.283
Serum albumin, g/L	4.0±0.5	4.1±0.2	0.217
Total cholesterol (mg/dL)	185.3±87	193.2± 79	0.646
CRP, mg/L	8.20±2.02	7.90±2.00	0.004
Naples prognostic score	2.6±1.0	1.5±0.7	<0.001

Continuous variables are presented as mean±SD. EF: Ejection fraction; SD: Standard deviation; CRP: C-reactive protein; g: Grams; mg: Milligrams; dL: Deciliters; L: Liters.

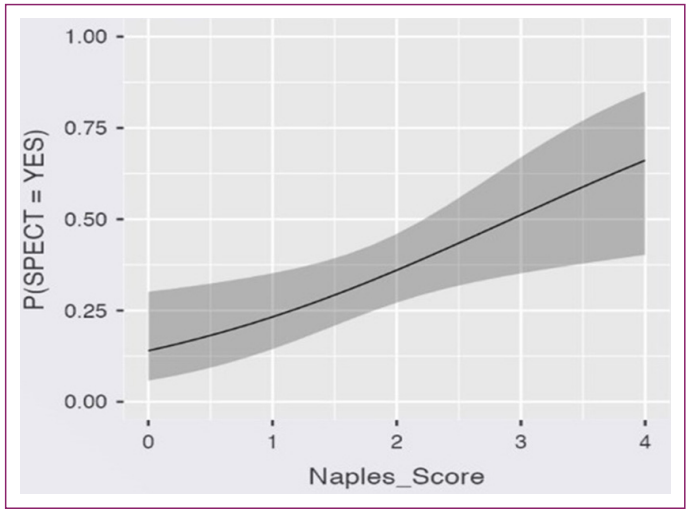

Figure 3. NPS in predicting ischemia detected by SPECT MPI.

SPECT: Single-photon emission computed tomography; MPI: Myocardial perfusion imaging; NPS: Naples prognostic score.

the body's nutritional condition, whereas NLR and LMR represent its immunoinflammatory condition. This allows for a more thorough assessment of the patient's physical state. NPS was originally investigated as a prognostic factor in gastrointestinal cancers.[22,23] It has been examined in the literature to determine the prognosis of various diseases.[24,25] Recently, this score has been examined in several cardiovascular diseases and has been associated with poor outcomes in patients.[26,27] Several studies have examined the Naples score in STEMI patients and found a correlation between NPS and in-hospital and follow-up mortality rates.[11,27] Kılıç et al.[28] and Erdoğan et al.[10] observed that mortality increased in HF patients with high Naples scores. In a study conducted on patients undergoing TAVR, the association of NPS with one-year mortality was examined, and it was found that NPS was an independent predictor of mortality in these patients.[9] Çetin et al.[8] examined the predictive efficacy of the NPS for 30-day total mortality in patients with APE and discovered a significant association between NPS and mortality in the findings of their research. Another study in STEMI patients showed that a significant inverse relationship was found between NPS and LVEF at discharge.[26] Karakoyun et al.[29] included 2901 patients with STEMI who underwent primary percutaneous coronary intervention and showed that NPS had predictive value in predicting the development of acute renal failure in these patients. Ozkan et al.[30] studied 1138 patients having coronary computed tomographic angiography and found that NPS and the systemic immune-inflammation index (SII) might predict coronary artery severity. Contrary to the previous research presented, they discovered that SII might have some predictive value, although NPS might not.

Table 3. Logistic regression for predicting ischemia

	Odds ratio, CI %95	p	Nagelkerke's R2
EF % (teicholtz)	0.97 (0.94–1.01)	0.19	
Naples prognostic score	1.86 (1.16–2.97)	0.009	0.089
Age (years)	0.99 (0.95–1.03)	0.58	
Use of smoking (%)	1.52 (0.68–3.38)	0.30	
Hypertension (%)	1.58 (0.69–3.60)	0.28	
Dyslipidemia (%)	0.34 (0.11– 1.26)	0.11	
Component of Naples prognostic score			
LMR	1.36 (0.60–3.09)	0.46	0.006
NLR	1.82 (0.56–5.80)	0.31	0.012
Albumin (cathegoric)	2.82 (1.24–6.36)	0.01	0.078
Total cholesterol (cathegoric)	1.53 (0.67–3.52)	0.31	0.013

CI: Confidence interval; EF: Ejection fraction; LMR: Lymphocyte-to-monocyte ratio; NLR: Neutrophil-to-lymphocyte ratio.

It is known that inflammatory and nutritional markers are associated with chronic CAD. In our study, we used the Naples score, which is calculated from NLR, LMR, albumin, and TC values and has been shown to be more sensitive than these markers individually. In our study, we demonstrated the usability of the Naples score as a predictor of ischemia in MPS.

Limitations

Some limitations of this study include the small sample size and the absence of coronary CT angiography or invasive coronary angiography tests in the patients, as well as the lack of clinical implications such as the association with clinical events. Furthermore, due to the retrospective nature of the study, we were unable to assess myocardial viability by MPI and therefore could not determine the percentage of ischemia from MPI reports.

Conclusion

Our findings indicated an association between NPS and the detection of ischemia in MPS. NPS is an independent variable for diagnosing myocardial ischemia in stable CAD patients.

Disclosures

Ethics Committee Approval: The study was approved by the Kartal Kosuyolu High Specialty Training and Research Hospital Clinical Research Ethics Committee (no: 2024/05/791, date: 05/03/2024).

Authorship Contributions: Concept – T.U., S.Ç.E., A.K.; Design – T.U., S.Ç.E., G.A.; Supervision – T.U.; Data collection and/or processing – T.U., S.F., B.G.Ş., M.A.; Data analysis and/or interpretation – T.U., S.Ç.E., A.K., M.S.; Literature search – S.T.D., T.U., B.Ö.; Writing – T.U.; Critical review – T.U., S.F., S.T.D., B.G.Ş., M.A., M.S., S.Ç.E., G.A., B.Ö., A.K.

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