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Combined effects of nutritional status on long-term mortality in patients with non-st segment elevation myocardial infarction undergoing percutaneous coronary intervention

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SUMMARY

OBJECTIVE: The aim of this study was to investigate the performance of controlling nutritional status (CONUT) index, geriatric nutritional risk index (GNRI), and prognostic nutritional index (PNI) scores in predicting the long-term prognosis of patients with non-ST-elevated myocardial infarction (NSTEMI) who underwent percutaneous coronary intervention (PCI).

METHODS: A total of 915 patients with NSTEMI (female: 48.4%; mean age: 73.1±9.0 years) who underwent PCI at Adana Numune Training and Research Hospital, Cardiology Clinic between January 2014 and January 2015 were included in this cross-sectional and retrospective study. CONUT, GNRI, and PNI scores were calculated based on the admission data derived from samples of peripheral venous blood. The mean follow-up duration was 64.5±15.4 months.

RESULTS: During follow-up (mean 64.5±15.4 months), 179 patients (19.6%) died. The mean GNRI and PNI scores were significantly lower in the nonsurvivor group; however, the median CONUT score was significantly higher in the nonsurvivor group compared with the survivor group. The receiver operating characteristic (ROC) curve analyses have shown that GNRI score has similar performance to the CONUT score and has better performance than PNI score in predicting 5-year mortality. The Kaplan–Meier curve analysis has shown that patients with lower PNI or GNRI had higher cumulative mortality than the patients with higher PNI or GNRI. Also, the patients with higher CONUT scores had higher cumulative mortality compared with those with lower scores. The multivariate analyses have shown that GNRI (HR: 0.973), PNI (HR: 0.967), CONUT score (HR: 1.527), and body mass index (BMI) (HR: 0.818) were independent predictors of the 5-year mortality in patients with NSTEMI.

CONCLUSION: In this study, we have shown that CONUT score, GNRI, and PNI values were associated with the long-term mortality in patients with NSTEMI who underwent PCI, and GNRI yielded similar results to CONUT score but was better than PNI.

KEYWORDS: Controlling Nutritional Status, Geriatric Nutritional Risk Index, Prognostic Nutritional Index, Non-ST-Elevated Myocardial Infarction, Percutaneous Coronary Intervention

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INTRODUCTION

Despite the evolving pharmacological treatments and reperfusion strategies, cardiovascular diseases still remain to be the leading cause of overall morbidity and mortality in the world. The majority of deaths linked to cardiovascular diseases is caused by acute coronary syndromes categorized into three conditions, namely, unstable angina pectoris, non-ST-elevated myocardial infarction (NSTEMI), and ST-elevated myocardial infarction (STEMI). Although patients with STEMI have higher in-hospital mortality, the long-term follow-up studies showed that the mortality rates increased significantly in NSTEMI cases over time[1,2]. Comprehensively designed studies that include the nutritional status indicate that the coexistence of cardiovascular diseases and malnutrition results in higher mortality rates[3]. In earlier studies, it has been shown that the malnutrition rate in hospitalized patients ranges 20–50% in developed countries and is higher in some geographical regions[4,5]. Controlling nutritional status (CONUT) index, geriatric nutritional risk index (GNRI), and prognostic nutritional index (PNI) are reliable and easily calculated nutritional indicators and have shown to have prognostic values in multiple chronic conditions[6,7]. In various studies, these indicators have demonstrated a strong association with the prognosis of patients with cardiovascular diseases and conditions, including coronary artery disease and congestive heart failure[8,9]. Among these studies, the researchers focused exclusively on acute myocardial infarction (AMI) or STEMI cases[10,11]. The clinical characteristics, risk factors, and prognosis of the NSTEMI differ significantly than the STEMI. The main differences are the increased mean age and the number of comorbid chronic diseases[12]. There are reports assessing the association of these nutritional indicators with the prognosis of NSTEMI cases exclusively. Given the noticeable differences compared with STEMI cases, the lack of a study including an analysis of CONUT score, GNRI, and PNI together may have foreclosed valuable information. The aim of this study was to investigate the performance of CONUT score, GNRI, and PNI in predicting the long-term prognosis of the patients with NSTEMI who underwent percutaneous coronary intervention (PCI).

METHODS

A total of 915 NSTEMI patients who underwent PCI at Adana Numune Training and Research Hospital, Cardiology Clinic between January 2014 and January 2015 were included in this cross-sectional and retrospective study. The diagnosis of NSTEMI was made according to the global myocardial infarction guide[13]. The data at the time of hospitalization, including age, gender, height, weight, body mass index (BMI), smoking, diabetes mellitus (DM), coronary artery disease, hypertension (HT), stroke, and cerebrovascular disease were collected from the patient profiles. The patients with congestive heart failure, malignancy, chronic kidney failure, nephrotic syndrome, liver failure, hematological disease, autoimmune disease, and rheumatological disease were excluded.

According to the standard criteria, admission values of patients with DM, HT, hyperlipidemia, and smoking were considered for selection. The subjects with HbA1c >6.5%, fasting blood glucose >126 mg/dL, or being on antidiabetic medication were considered as DM patients. The patients with arterial blood pressure >140/90 mmHg or being on antihypertensive medication were considered having HT. The patients with serum total cholesterol levels >200 mg/dL or on antilipidemic medicines were regarded having hyperlipidemia. The CONUT, GNRI, and PNI scores were calculated based on the admission data derived from samples of peripheral venous blood. GNRI=14.89×albumin (g/dL) + 41.7×body weight (kg)/ideal body weight (kg). The ideal body weight was calculated as follows: body height−100−[(body height−150)/4] for males and body height−100−[(body height−150)/2.5] for females. The CONUT scores (0–10, varying from nourishment to malnutrition) were calculated using serum albumin level and lymphocyte count. CONUT: serum albumin ≥3.5 g/dL=0 points, 3.0–3.4 g/dL=2 points, 2.5–2.9 g/dL=4 points, and <2.5 g/dL=6 points; total cholesterol ≥180 mg/dL=0 points, 140–179 mg/dL=1 point, 100–139 mg/dL=2 points, and <100 mg/dL=3 points; and total lymphocyte count ≥1600/mL=0 points, 1200–1599/mL=1 point, 800–1199/mL=2 points, and <800/mL=3 points (Table 1). PNI: 10×serum albumin value (g/dL) + 0.005 × total lymphocyte count (per mm^3). BMI: weight (in kg)/$(height)^2$ (in m). As the primary end point in this study, nonsurvivor details

Table 1. Controlling nutritional status (CONUT) score calculation.

Score	0	2	4	6
Serum albumin (g/mL)	≥3.5	3.0–3.49	2.5–2.99	<2.50
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140–179	100–139	<100
Score	0	1	2	3
Lymphocytes (count/mL)	≥1600	1200–1599	800–1199	<800

were collected from the National Health Insurance System in July 2020, including the date of death, and all causes of death were accepted.

Statistical analyses

The continuous variables were represented as mean (± standard deviation) or median (25th–75th quartile). The distribution was analyzed with the Kolmogorov–Smirnov test. The Student's *t*-test was used to analyze the normally distributed variables, and the Mann–Whitney *U* test was used for the non-normal distributions. The variables with normal distribution were represented as mean (± standard deviation) and with non-normal distribution as median (25th–75th quartile).

The categorical variables were summarized as percentages and number. Categorical variables between the groups were compared by using the chi-squared test or Fisher's exact test. To demonstrate the sensitivity and specificity of the GNRI, PNI, and CONUT scores and their cut-off values for predicting the long-term mortality, the receiver operating characteristic (ROC) curves were used. The DeLong's method was used to compare area under the curve (AUC) of these nutritional indexes. The Kaplan–Meier analysis and log-rank test were performed to determine whether the nutritional indexes could help predict the long-term mortality. The multivariate Cox proportional hazards model was created to calculate the hazard ratios for all-cause mortality. Variables with p≤0.1 in the univariate analysis were included in the multivariate Cox proportional hazards model.

The statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS 20.0) for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc 15 statistical software (Ostend, Belgium). A p<0.05 was considered statistically significant.

RESULTS

Totally, 915 patients (female: 48.4%; mean age: 73.1±9.0 years) were included in this study. The mean follow-up duration was 64.5±15.4 months. During the follow-up period, 179 patients (19.6%) died. The baseline demographic and clinical characteristics of the patients were summarized in Table 2. Despite the

Table 2. Baseline characteristics of the study population.

	Survivor Group (n=736)	Nonsurvivor Group (n=179)	p
Age, year (mean ± SD)	72.8±9.4	74.1±7.1	0.084
Sex/female, % (n)	47.8 (352)	51.4 (92)	0.391
BMI (kg/m^2)	25.6±2.6	23.7±2.0	<0.001
Weight (kg)	71.4±8.2	70.1±7.4	0.055
Height (m)	1.67±7.2	1.77±8.1	<0.001
SBP (mmHg)	125±18	131±19	<0.001
DBP (mmHg)	78±10	78±11	0.638
Hypertension, % (n)	51.0 (375)	55.9 (100)	0.238
Diabetes mellitus, % (n)	32.3 (238)	33.0 (59)	0.873
Hyperlipidemia, % (n)	33.2 (244)	31.8 (47)	0.738
Stroke, % (n)	3.0 (22)	4.5 (8)	0.319
COPD, % (n)	7.2 (53)	3.9 (7)	0.130
Smoker, % (n)	36.0 (265)	34.6 (62)	0.732
Family history, % (n)	30.7 (226)	26.3 (47)	0.243
Previous myocardial infarction, % (n)	22.3 (164)	201. (36)	0.529
AF, % (n)	7.2 (52)	7.3 (13)	0.977
ASA, % (n)	20.1 (148)	22.9 (41)	0.407
ACEI/ARB, % (n)	32.1 (236)	28.5 (51)	0.355
Beta-blockers, % (n)	17.1 (126)	19 (34)	0.544
Diuretics, % (n)	5.2 (38)	7.8 (14)	0.168
Statins, % (n)	18.1 (133)	21.2 (38)	0.331

ACEI: angiotensin-converting enzyme inhibitors; ASA: acetylsalicylic acid; ARB: angiotensin receptor blockers; BMI: body mass index; CONUT: controlling nutritional status; GNRI: geriatric nutritional risk index; PNI: prognostic nutritional index; COPD: chronic obstructive pulmonary disease; AF: atrial fibrillation; SBP: systolic blood pressure; DBP: diastolic blood pressure. Statistically significant values are given in bold.

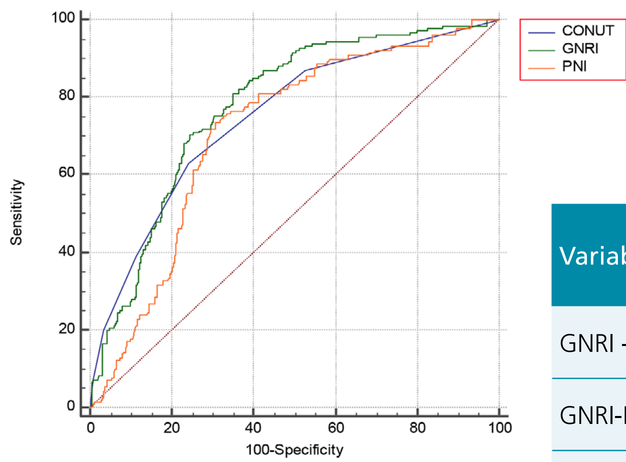
significantly higher mean age, height, and systolic blood pressure values in the nonsurvivor group, the survivor group displayed a higher mean BMI. The laboratory parameters of the two groups were summarized in Table 3. The median total cholesterol and mean albumin levels were significantly lower in the nonsurvivor group than the survivor group. The mean GNRI and PNI values were significantly lower in the nonsurvivor group; however, the median CONUT scores were significantly higher in the nonsurvivor group compared with the survivor group (Table 3). Figure 1 shows the ROC curve analyses of the scores. To predict mortality, the cut-off value for the PNI was ≤50.65, with 73.7% sensitivity and 69.4% specificity (AUC 0.714; 95%CI 0.684–0.744; p<0.001), the cut-off value for the GNRI was ≤114.77, with 81.0% sensitivity and 65.27% specificity (AUC 0.778; 95%CI 0.750–0.805; p<0.001), and the cut-off value for the CONUT score was >3, with 63.1% sensitivity and 76.0% specificity (AUC 0.751; 95%CI 0.722–0.779; p<0.001). The comparison of the ROC curve analyses shown that GNRI has similar performance to the CONUT score and has better performance than PNI in predicting 5 years mortality. Also, in predicting 5 years mortality, the prognostic values of the PNI and the CONUT scores were found similar (Figure 1).

The Kaplan–Meier curve analysis was performed for each nutritional index according to the cut-off value for all-cause mortality (Figure 2). Patients with lower PNI or GNRI had higher cumulative mortality than those with higher PNI or GNRI (37.0 *vs.* 8.4%, p<0.001; 36.2 *vs.* 6.6%, p<0.001, respectively). Patients with higher CONUT scores had higher cumulative mortality compared with those with lower scores (10.6 *vs.* 39.0%, p<0.001). Moreover, the cumulative 5-year mortality was higher in patients with the lowest quartile of GNRI (≤107.4) or PNI (≤46.43) than in patients with the top quartile of GNRI (≥125.1) or PNI (57.36). Furthermore, the cumulative 5-year mortality was higher in patients with the top quartile of CONUT score (≥4.0) than in patients with the lowest quartile (≤2.0) (Figure 3). The univariate and multivariate Cox proportional hazard analyses of predictors on mortality were summarized in Table 4. The multivariate analyses have shown that GNRI (HR: 0.973; 95%CI 0.964–0.982; p<0.001), PNI (HR 0.967; 95%CI 0.947–0.988; p<0.001), CONUT score (HR 1.527; 95%CI 1.404–1.661; p<0.001), and BMI (HR 0.818; 95%CI 0.767–0.872; p<0.001) were independent predictors of 5-year mortality in patients with NSTEMI.

Table 3. Baseline laboratory and echocardiography parameters of the study population.

	Survivor Group (n=736)	Nonsurvivor Group (n=179)	p
Albumin (g/mL)	4.1±0.58	3.9±0.32	<0.001
Total protein (g/mL)	7.6±0.6	7.5±0.30	0.104
Total cholesterol (mg/dL) median (25th–75th)	183 (155–210)	182 (163–207)	0.072
LDL-C (mg/dL) median (25th–75th)	123 (99–145)	122 (106–138)	0.602
HDL-C (mg/dL) median (25th–75th)	39 (34.2–47)	40.0 (35.0–45.0)	0.476
White blood count (×10^3)	8.2±3.2	9.2±2.7	0.458
Platelet count (×10^3)	245±65	233±91	0.053
Hemoglobin (mg/dL)	13.8±1.7	13.7±2.1	0.322
CRP (mg/dL) median (25th–75th)	0.7 (0.3–1.50)	1.0 (0.6–1.60)	0.558
Creatine median (25th–75th)	0.8 (0.7–1.0)	0.9 (0.7–1.1)	0.581
Urea (mg/dL) median (25th–75th)	29.9 (23.5–36.4)	38.5 (29.9–51.3)	0.604
LVEF, %	49.7±6.1	48.7±9.3	0.059
PNI, mean	53.2±7.4	47.9±6.7	<0.001
GNRI, mean	117±13.8	104±15.2	<0.001
CONUT score, median (25th–75th)	3.0 (2.0–3.0)	4.0 (3.0–5.0)	<0.001

LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; CRP: C reactive protein; LVEF: left ventricular ejection fraction; PNI: prognostic nutritional index; GNRI: geriatric nutritional risk index; CONUT: controlling nutritional status. Statistically significant values are given in bold.

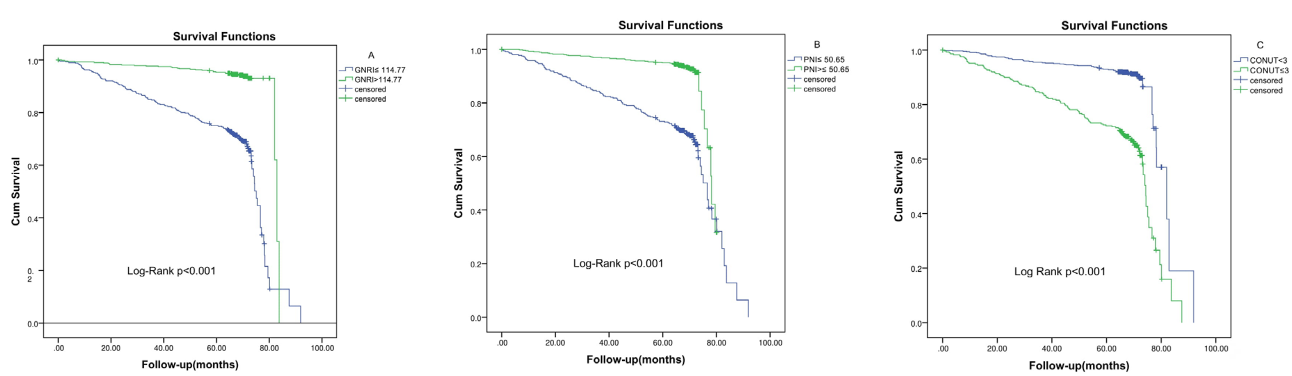


Variable	AUC	SE	95%CI
GNRI	0.778	0.018	0.750-0.805
CONUT	0.751	0.019	0.722-0.779
PNI	0.714	0.020	0.684-0.744

Variable	Differences between areas	SE	95%CI	Z statistic	P
GNRI - CONUT	0.027	0.0272	-0.0264-0.0804	0.992	0.321
GNRI-PNI	0.0635	0.0238	0.0169-0.1100	2.672	0.0075
PNI-CONUT	0.0365	0.0200	-.0002-0.0756	1.827	0.0677

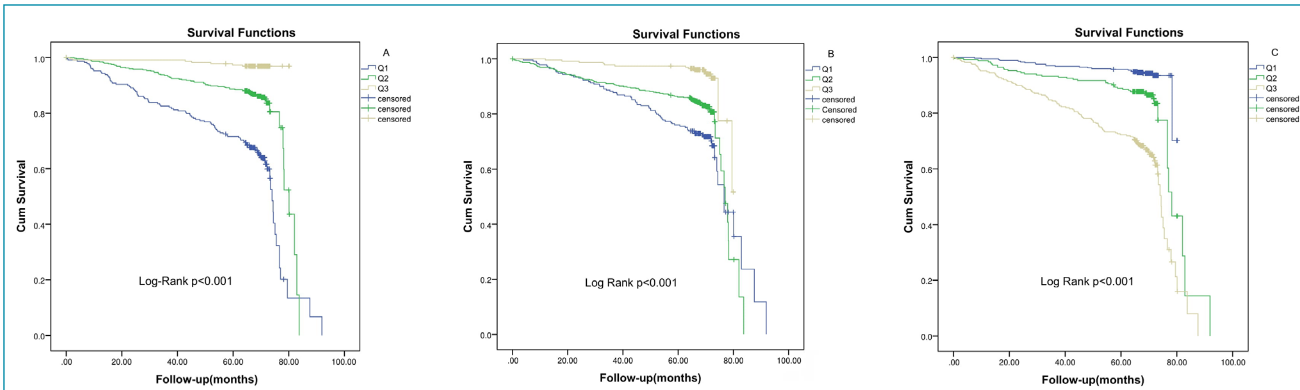
AUC: area under the curve; CI: confidence interval; CONUT: controlling nutritional status; GNRI: geriatric nutritional risk index; PNI: prognostic nutritional index; SE: standard error.

Figure 1. Comparison of receiver operating characteristic (ROC) curves for all-cause mortality.



(A) GNRI, geriatric nutritional index. (B) PNI, prognostic nutritional index. (C) CONUT, controlling nutritional status score.

Figure 2. The Kaplan–Meier analysis for all-cause mortality, according to the cut-off values of (A) GNRI, (B) PNI, and (C) CONUT scores.



(A) GNRI, geriatric nutritional index. (B) PNI, prognostic nutritional index. (C) CONUT, controlling nutritional status score.

Figure 3. The Kaplan-Meier analysis for all-cause mortality, according to interquartile of (A) GNRI, (B) PNI, and (C) CONUT scores.

Table 4. Univariate and multivariate Cox proportional hazard analysis of all-cause mortality.

Analysis	Univariate		Multivariate	
	p	HR [95%CI]	p	HR [95%CI]
Age	0.212	1.011 (0.994–1.029)		
Height	<0.001	1.134 (1.090–1.179)		
Weight	0.131	0.985 (0.966–1.004)		
BMI	<0.001	0.787 (739–839)	<0.001	0.818 (0.767–0.872)
Albumin	0.001	0.639 (0.495–0.825)		
SBP	0.003	1.012 (1.004–1.019)		
Total cholesterol	0.050	1.003 (1.00-1.006)		
Total protein	0.079	0.800 (0.624–1.026)		
LVEF	0.089	0.982 (0.963–1.003)		
PNI	<0.001	0.927 (0.910–0.945)	0.002	0.967 (0.947–0.988)
CONUT score	<0.001	1.494 (1.380–1.619)	<0.001	1.527 (1.404–1.661)
GNRI	<0.001	0.968 (0.962–0.973)	<0.001	0.973 (0.964–0.982)

BMI: body mass index; CI: confidential interval; CONUT: controlling nutritional status; EDV: end-diastolic volume, ESV: end-systolic volume; HR: hazard ratio; GNRI: geriatric nutritional risk index; PNI: prognostic nutritional index; LVEF: left ventricular ejection fraction; SBP: systolic blood pressure. Statistically significant values are given in bold.

DISCUSSION

This study was the first to examine the association of the CONUT, GNRI, and PNI scores with the long-term mortality in patients with NSTEMI who underwent PCI. It was noted that all the three indexes were significantly associated with the long-term all-cause mortality in patients involved in this study. Besides, in the comparison of predicting mortality, GNRI yielded similar results to CONUT score but was better than PNI. Malnutrition is a frequent and significant problem and is seen especially in hospitalized elderly patients. Earlier reports suggest that malnutrition is closely related to poor prognosis and mortality in terminal kidney failure, malignancy, and hematological diseases[6-8]. In search of a valuable marker, various nutritional indicators have been identified, including lymphocyte count, serum albumin levels, serum cholesterol levels, Mini-Nutritional Assessment (MNA)[14], and Subjective Global Assessment (SGA) in addition to the CONUT scores, GNRI, and PNI. Among these indicators, the ones with additional parameters put by the healthcare professionals, such as MNA and SGA, although expected to be more accurate, may be considered as potentially biased. On the other hand, CONUT scores, GNRI, and PNI include the objective quantitative data of the patient. In the calculation of the GNRI, only the height, weight, and serum albumin data of the patient are required. Similarly, the calculation of the PNI needs only the serum albumin level and the lymphocyte count of the patient. The calculation of the CONUT score requires the serum cholesterol level of the patient in addition to their serum albumin level and the lymphocyte count. These three indexes use different methods and variables and therefore have unique advantages and disadvantages. Nevertheless, serum albumin is the only common parameter, and its low levels alter the results of all the three indicators. A recent study suggested that in patients who underwent PCI, low serum albumin levels, independent of the traditional risk factors, were associated with major adverse cardiac event (MACE) development[15]. The association of the CONUT scores, GNRI, and PNI with the mortality in patients with AMI[16], cardiac failure[17], and chronic coronary syndrome who underwent elective PCI[18] was reported in earlier studies. In a retrospective study, including patients who underwent PCI due to stable coronary disease, the mean follow-up duration was 7.4 years and a high CONUT score was found to be associated with all-cause mortality and nonfatal MI in the long-term follow-up[19]. A research conducted in 802 patients who received elective PCI to the *de novo* lesions due to stable angina pectoris or objective ischemia showed a significant association between GNRI and poor cardiac prognosis following PCI[20]. Furthermore, the majority of the patients with chronic coronary syndrome were on an antilipidemic medication; the use of CONUT score on this particular group may seem erroneous. In this study, a low percentage of the patients were on statins, and the difference between the two groups was insignificant. Therefore, the CONUT scores in the study might be considered optimal[20]. In a recent report conducted on 2853 patients with first PCI procedure, 849 had acute coronary syndrome, suggesting that low GNRI scores were independent predictors of all-cause mortality[21].

Moreover, these indicators have also been shown to yield different associations with poor prognosis and mortality in similar disease groups. In a study examining the prognostic values of CONUT score and PNI, conducted in 945 elderly STEMI patients who underwent PCI, at the end of a 2-year follow-up, CONUT scores were found to be associated with the increase in all-cause mortality rates, whereas PNI scores failed to present a predictive value[16]. Conversely, in a research carried out in 345 STEMI patients who underwent primary PCI assessing PNI predictivity only, it was found that PNI was an independent predictor of mortality in this group[22]. Similarly, in a study of 1823 STEMI cases who underwent primary PCI, it was proposed that low PNI values were associated with both in-hospital and 3-year long-term mortality[18]. In a study of 2251 patients, 975 had STEMI and 1276 had NSTEMI, and low GNRI scores were found to be significantly associated with post-MI complications and in-hospital mortality[23].

In the present study, low GNRI and PNI and high CONUT values were shown to predict the long-term mortality in NSTEMI patients. The multivariate analysis revealed that all the three indicators had independent prognostic values for mortality. Moreover, GNRI was demonstrated to have similar value compared with CONUT score and better than PNI. Since the serum albumin level is the common parameter, the different results were based on serum cholesterol levels and weight data. Lowering the cholesterol levels of the patients is one of the primary goals in coronary heart disease[24]. Low cholesterol levels before treatment in a patient attach particular importance, since the nutritional assessment will result in low nutrition status. According to the guidelines, patients with NSTEMI should receive antilipidemics even with low cholesterol levels[24]. However, the possibility of a poorer prognosis of the patients with low cholesterol levels at the time of the index event should always be noted. In the same manner, this study has revealed that low weight was associated with the long-term outcomes. Weight lower than the ideal is associated with fragility, which was reported as closely linked with the long-term poor prognosis in patients with cardiovascular diseases[25]. In patients with coronary heart diseases, overweight or underweight, the latter pointing fragility, both are undesirable. In this study, it was shown that the patients with low GNRI levels, indicating more fragility, were reported to have a higher mortality rate. In NSTEMI cases, the possibility of experiencing the long-term poor prognosis for patients with low weight at the time of index event should be considered.

Limitation

There were significant limitations to this study. This study was a single-centered retrospective study. Moreover, all-cause mortality was set as the primary end point and the effect of the indicators on cardiovascular-related mortality was not assessed exclusively. Moreover, not all AMI cases were included in this study. The aim of not involving STEMI patients was to form a relatively homogeneous study group due to the differences in the mean age, risk factors, and the comorbidities of the STEMI patients compared with the NSTEMI population. Larger study populations, including all AMI patients assessing the nutritional indicators, are required.

CONCLUSION

In this study, it was shown that CONUT score, GNRI, and PNI were associated with the long-term mortality in NSTEMI patients who underwent PCI. Furthermore, in the comparison of predicting mortality, GNRI yielded similar results to CONUT score but was better than PNI.

ETHICAL APPROVAL

All the procedures performed in this study involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all the individual participants included in this study.

AUTHORS' CONTRIBUTIONS

AY: Conceptualization, Investigation, Writing – Review & Editing. **MK:** Data Curation, Writing – Original Draft. **NYK:** Formal Analysis, Software. **YC:** Methodology, Validation. **MCB:** Project Administration, Visualization. **SK:** Resources, Supervision.

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