RESEARCH

THE EFFECT OF NUTRITIONAL STATUS ON LONG-TERM MORTALITY IN VERY ELDERLY PATIENTS WITH ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Abstract

Introduction: This study aimed to evaluate the predictive role of the Geriatric Nutrition Risk Index in long-term mortality of very elderly patients with ST-segment elevation myocardial infarction and to compare it with the other known objective nutritional indices, namely the Prognostic Nutritional Index and Controlling Nutritional Status.

Materials and Methods: A total of 212 eligible patients, aged 80 years or older, who were hospitalized with a diagnosis of ST-segment elevation myocardial infarction and underwent primary percutaneous coronary intervention were included in the study. Baseline patient characteristics, echocardiographic assessments, laboratory findings, and nutritional indices were assessed.

Results: During the median follow-up period of 34 months, 60 (28.3%) all-cause mortalities were identified, and event-free cumulative rates were 46.3%, 81.4%, and 90.1% for Geriatric Nutrition Risk Index <100.5, 100.5–112.6, and >112.6, respectively (log-rank test, $p < 0.0001$). Receiver operating characteristic curve comparison analysis revealed that the Geriatric Nutrition Risk Index was a better predictor than the Controlling Nutritional Status, Prognostic Nutritional Index, Body Mass Index, and serum albumin ($p < 0.001$ for each pairwise comparison of Receiver operating characteristic curves).

Conclusion: It is important to evaluate malnutrition that is known to be associated with mortality in very elderly patients with ST-segment elevation myocardial infarction, who are more fragile than young people, and Geriatric Nutrition Risk Index -a simple and easy-to-calculate index- can be a guide in this regard.

Keywords: Nutritional Status; Mortality; Myocardial Infarction; Aged

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is one of the leading causes of death worldwide, with in-hospital mortality ranging between 4% and 12% and 1-year mortality 10%(1, 2). It has been shown that the mortality rate of elderly patients with STEMI is significantly higher than that of young patients because of their comorbidities and delayed diagnosis of myocardial infarction(3, 4). In addition, a higher proportion of elderly patients is anticipated to present with STEMI because of aging, so special consideration should be given to the risk assessment and care of these patients.

Malnutrition is a common problem affecting the elderly population and has been shown to be associated with worse clinical outcomes in patients with cancer, heart failure, and stable coronary artery disease (CAD)(5-7). To evaluate nutritional status, some indices have been developed, including the Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT), and Geriatric Nutrition Risk Index (GNRI)(8-10). Of these, CONUT and PNI have been shown to be related to prognosis in patients with acute coronary syndrome (ACS)(11, 12). Although GNRI has been validated by previous studies to assess the nutritional status of patients and predict adverse outcomes, there are limited data available in the literature on the predictive value of GNRI in patients with ACS and its comparison with other scores(7, 13).

This study aimed to evaluate the predictive role of GNRI in long-term mortality of very elderly patients with STEMI and to compare it with the other known objective nutritional indices, namely PNI and CONUT.

MATERIALS AND METHODS

Study population

This study was conducted retrospectively by analyzing 293 patients, aged 80 years or older, who were hospitalized with a diagnosis of STEMI and underwent primary percutaneous coronary intervention (PCI) between January 2016 and December 2018 in the cardiology departments. Exclusion criteria included active inflammatory and neoplastic disease (8), end-stage renal and liver disease (6), failed primary PCI (7), and pretreatment with fibrinolytic drugs (2). A total of 58 patients who had missing laboratory or file data were excluded, and 212 patients were eligible for the analysis. In-hospital follow-up data were obtained from hospital file records, and post-discharge follow-up data were obtained by contacting the patients or their relatives. For patients who could not be reached, information was obtained from the National Statistical Institute and Birth Records Registry to determine if they were dead. The study protocol was reviewed and approved by the Ethics Committee of University in accordance with the Declaration of Helsinki.

Data collection and definitions

The patients' baseline clinical data, demographic data, and detailed biochemical markers—measured within 24 hours of admission—were recorded from patient files. Their height and weight were obtained from patient care forms. Detailed echocardiographic assessments were executed 24–48 hours after primary PCI, and the left ventricular ejection fraction (LVEF) values were calculated by the modified Simpson technique. The estimated glomerular filtration rate (eGFR) was calculated from the serum creatinine levels taken on admission by the Modification of Diet in Renal Disease Study equation.

Definition and calculation of nutritional scores

Body Mass Index (BMI) was obtained for each patient by dividing the body weight (kg) by the square of the height (m^2). GNRI was calculated as follows: GNRI = 14.89 × Serum albumin (g/dL) + 41.7 × Body weight/ideal body weight, and ideal body weight

= (Height [cm] − 100) − (Height [cm] − 150)/4 for men and (Height [cm] − 100) − (Height [cm] − 150)/2 for women(10). Subsequently, the GNRI values were divided into tertiles. CONUT (=Serum albumin [g/dL] + Total lymphocyte count [per mL] + Total cholesterol [mg/dL]) and PNI (=10 × Serum albumin [g/dL] + 0.005 × Total lymphocyte count [per mL]) were calculated as previously described(9, 14).

Statistical analysis

Data analysis was performed using SPSS Statistics (v.22.0; SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as numbers and percentages. The Kolmogorov–Smirnov test was used to evaluate the distribution of continuous variables. If the variables had a normal distribution, they were presented as mean ± standard deviation; if they did not have a normal distribution, they were presented as the median (interquartile range). Categorical variables were compared using a Chi-squared test or the Fisher exact test. The Student *t*test or Mann–Whitney *U*-test were used to compare the continuous variables. A two-tailed *p*-value of <0.05 was considered statistically significant. Univariate and multivariate Cox proportional hazard analyses were performed to identify the predictors of mortality. The Kaplan–Meier method was used to obtain the association between GNRI and all-cause mortality at follow-up. A receiver operating characteristic (ROC) curve was used to determine the best cutoff value for PNRI to predict all-cause mortality. Multicollinearity between GNRI and its components (albumin and BMI) was assessed by Eigenvalue and Condition Index. Linearity was tested by interacting with the logarithmic transformation of each parameter itself. To compare the area-under-the-curve (AUC) values of nutritional scores, ROC curve comparison analysis was performed using the DeLong method.

RESULTS

Of the 212 eligible patients with STEMI who underwent primary PCI, with the mean age 86 ± 5 years, 18.2% were females, and the mean GNRI was 108 ± 14. There was no significant difference between tertiles in terms of diabetes mellitus, hypertension, dyslipidemia, smoking status, and family history of CAD. The hemodynamic parameters and rates of patients with Killip class >1 on admission were also not significantly different between the groups. The patients on the lowest GNRI levels had lower baseline levels of serum albumin, total cholesterol, and triglycerides—as well as lower eGFR and higher C-reactive protein (CRP) levels—on admission. When the other nutritional indices—PNI and CONUT—were evaluated, they were found to be in parallel with GNRI, and they increased as GNRI increased **(Table 1)**.

Multivariate Cox regression analyses revealed that systolic blood pressure (SBP) (hazard ratio [HR]: 0.992, 95% confidence interval [CI]: 0.985–0.999, $p = 0.031$), eGFR (HR: 0.983, 95% CI: 0.970–0.996, $p = 0.010$), LVEF (HR: 0.906, 95% CI: 0.869–0.944, $p < 0.001$), and GNRI (HR: 0.968, 95% CI: 0.945–0.992, $p = 0.008$) were related with all-cause mortality **(Table 2)**. Albumin and BMI were not included in the Cox regression analysis because of collinearity, which was observed between BMI, albumin, and GNRI.

During the median follow-up period of 34 months (interquartile range: 11–41 months), 60 (28.3%) all-cause mortalities were identified, of which 23 (10.8%) were in-hospital. The Kaplan–Meier analysis was performed to evaluate cumulative survival rates **(Fig. 1)**. During the follow-up, event-free cumulative rates were 46.3%, 81.4%, and 90.1% for GNRI <100.5, 100.5–112.6, and >112.6, respectively (log-rank test, $p < 0.0001$).

ROC curve analysis revealed that the optimal cut-off value of GNRI for all-cause mortality was 99.4, with 63.3% sensitivity and 82.2% specificity

Table 1. The baseline characteristics and laboratory results of all patients and patients classified in accordance with tertiles of GNRI

	All patients (n: 212)		Patients with GNRI < 100.5 (n: 70)		Patients with GNRI 100.5-112,6 (n: 71)		Patients with GNRI > 112.6 (n: 71)		p value
Age, years	86	±5	87	±5	86	±4	85	±5	0.046
Female gender, n (%)	96	(45.3)	27	(38.6)	31	(43.7)	38	(53.5)	0.195
Diabetes mellitus, n (%)	65	(30.7)	22	(31.4)	24	(33.8)	19	(26.8)	0.655
Hypertension, n (%)	130	(61.3)	44	(62.9)	43	(60.6)	43	(60.6)	0.950
Dyslipidemia, n (%)	71	(33.5)	23	(32.9)	24	(33.8)	24	(33.8)	0.991
Smoking, n (%)	45	(21.2)	16	(22.9)	16	(22.5)	13	(18.3)	0.764
Family history of CAD, n (%)	33	(15.6)	7	(10.0)	13	(18.3)	13	(18.3)	0.295
Killip > 1 on admission, n (%)	51	(24.1)	20	(28.6)	18	(25.4)	13	(18.3)	0.348
Systolic blood pressure, mmHg	137	±39	134	±42	137	±40	141	±36	0.551
Heart rate, bpm	79	±19	77	±21	81	±18	78	±17	0.365
White blood cell count, 10^3/μL	11.6	±4.0	12.4	±4.6	10.8	±3.5	11.7	±3.8	0.072
Lymphocyte count, 10^3/μL	1.3	(1.0-2.0)	1.2	(1.0-1.9)	1.4	(1.0-1.9)	1.5	(1.1-2.1)	0.361
Hemoglobin, g/dL	12.4	±1.8	12.0	±1.9	12.7	±1.8	12.6	±1.6	0.028
eGFR, ml/min	71.3	±26.6	64.4	±26.0	75.3	±27.0	74.0	±25.6	0.029
C-Reactive protein, mg/dL	13.6	(7.9-21.2)	16.9	(10.2-32.5)	12.1	(7.1-20.0)	13.3	(7.4-16.7)	<0.001
Serum albumin, g/dL	3.48	±0.44	3.22	±0.38	3.52	±0.35	3.69	±0.44	<0.001
Total cholesterol, mg/dL	170	±45	160	±44	172	±44	179	46	0.038
LDL, mg/dL	110	±39	104	±40	109	±40	116	±38	0.206
HDL, mg/dL	41	±14	38	±12	42	±14	42	±17	0.138
Triglycerides, mg/dL	106	±61	90	±39	110	±50	117	±84	0.030
LVEF, %	45	±9	43	±10	45	±8	46	±8	0.060
BMI, kg/m^2	29.0	±5.4	25.1	±2.7	28.9	±3.5	34.2	±5.5	<0.001
PNI score	34.8	±4.4	32.2	±3.8	35.2	±3.6	36.9	±4.4	<0.001
CONUT score	175	±45	164	±44	177	±44	185	±46	0.033
GNRI score	108	±14	93	±6	107	±4	123	±8	<0.001
In hospital death, n (%)	23	(10.8)	13	(18.6)	6	(8.5)	4	(5.6)	0.034
Long-term death, n (%)	37	(19.6)	26	(45.6)	8	(12.3)	3	(4.5)	<0.001
Total death, n (%)	60	(28.3)	39	(55.7)	14	(19.7)	7	(9.9)	<0.001

Abbreviations: GNRI; Geriatric Nutritional Risk Index, CAD; coronary artery disease, eGFR; estimated glomerular filtration rate, LDL; low density lipoprotein, HDL; high density lipoprotein, LVEF; left ventricular ejection fraction, PNI; prognostic nutritional index, CONUT; controlling nutritional status.

(AUC: 0.791, 95% CI: 0.708–0.859, $p < 0.001$). ROC curve comparison analysis was performed to compare nutritional scores, as well as serum albumin and BMI. GNRI was found to be a better predictor than CONUT (AUC: 0.603, 95% CI: 0.510–0.690), PNI (AUC: 0.618, 95% CI: 0.526–0.704), BMI (AUC: 0.616, 95% CI: 0.524–0.702), and serum albumin (AUC: 0.624, 95% CI: 0.532–0.710; $p < 0.001$ for each pairwise comparison of ROC curves) **(Fig. 2)**.

DISCUSSION

This study evaluated the predictive value of GNRI in long-term mortality in patients, aged 80 years or older, with STEMI and the comparison of nutritional indices among themselves. Consequently, low GNRI was an independent predictor of long-term mortality and was superior to the other nutritional indices, namely BMI, PNI, and CONUT, in this age group.

Table 2. Univariable and multivariable Cox regression analysis for the prediction of total mortality

	Univariable analysis		Multivariable analysis	
	p value	HR (95% CI)	p value	HR (95% CI)
Systolic blood pressure	<0.001	0.986(0.979 -0.994)	0.031	0.992(0.985 -0.999)
Estimated glomerular filtration rate	<0.001	0.963(0.951 -0.976)	0.010	0.983(0.970 -0.996)
Left ventricular ejection fraction	<0.001	0.880(0.848 –0.913)	<0.001	0.906(0.869 –0.944)
GNRI	<0.001	0.928(0.906 -0.952)	0.008	0.968(0.945 -0.992)

All clinically relevant parameters were included in the model. **Abbreviations**: GNRI; Geriatric Nutritional Risk Index

Figure 1. Kaplan Meier survival analysis of long-term mortality in patients classified in accordance with tertiles of Geriatric Nutrition Risk Index

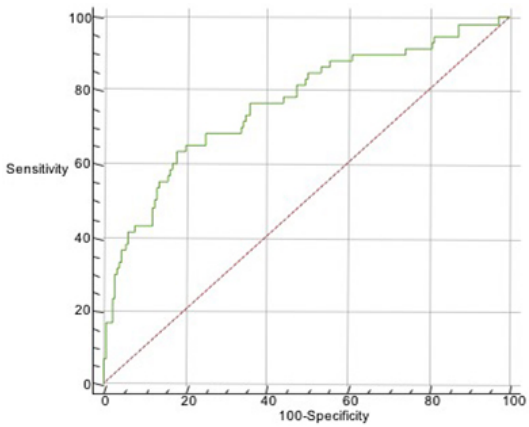
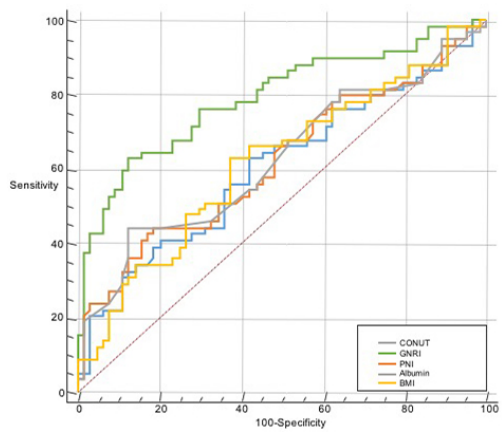


Figure 2. ROC curve comparison analysis of the nutritional scores and also serum albumin and Body Mass Index



Malnutrition is one of the reasons leading to worse outcomes in the elderly population, and the aging process itself is a cause for malnutrition, so the evaluation of nutritional status in elderly patients seems important. Basically, it has been demonstrated that serum albumin and BMI can be used to assess nutritional status. Low serum albumin and BMI have been associated with worse clinical outcomes, including mortality in patients with ACS(12, 15). In the present study, serum albumin and BMI were evaluated, and in parallel with the literature, they were significantly lower in patients with low GNRI. The relationship of low albumin and BMI with mortality may be related to the change in cardiometabolic demands and priorities in ACS. Because cardiometabolic demands are increased because of the activation of neurohormonal and inflammatory pathways in ACS, patients with low BMI who have low physiological reserves and fat stores may not be able to overcome these catabolic changes(16). Infection, heart failure, and other cardiac reasons may require hospitalization after discharge in patients with low BMI, which also leads to additional weight loss and, as a result, increases long-term mortality. Similarly, serum albumin is a widely used marker to assess nutritional status, and its level decreases as a result of malnutrition. Besides, it is a negative acute-phase reactant, and its decrease in an inflammatory state such as ACS may have had an additive effect and was significantly lower in patients with malnutrition. In addition, CRP is an inflammatory marker, and its increased level has been shown to be a predictor for worse clinical outcomes in patients with ACS(17). In accordance with the literature, we found higher CRP levels in patients with low GNRI. According to this result, it can be speculated that malnutrition aggregates the inflammatory state.

In the Cox regression analysis to predict total mortality, SBP, eGFR, and LVEF were found to be independent predictors, and this result is consistent with the literature(18, 19). In addition, we found that GNRI was an independent predictor of mortality in very old patients with STEMI. The assessment of nutritional status involves the process of obtaining, verifying, and interpreting the data needed to discover nutritional problems and their causes and importance(20). To ensure a structured assessment and documentation of nutritional status, it is important to identify which nutritional assessment tool is appropriate for use in that group. The prognostic value of PNI in predicting poor prognosis, including mortality, has been tested in patients with STEMI, and PNI has been found to be an independent predictor of mortality(11, 21). In another study, patients with severe CONUT—not those with severe PNI—had the highest event rate for all-cause mortality in patients with STEMI(12). In these studies, GNRI has not been tested, and patient groups were younger than the patients in the present study because the mean age of patients was between 58 and 65 years in the aforementioned studies. Therefore, considering that nutritional problems increase with age, it can be said that data on the evaluation and importance of this in the population, aged 80 years and older, with STEMI are limited. In the present study, we found that GNRI predicts mortality and is superior to PNI and CONUT in very elderly patients.

GNRI was specifically designed to assess the nutritional status of elderly patients and predict malnutrition-related complications, and its validity and reliability have been better studied in hospitalized elderly patients than in those with STEMI(7, 10, 22-24). In the present study, we found that low GNRI was an independent predictor of mortality and was superior to BMI, PNI, and CONUT in very old patients with STEMI. Recently, the Mini-Nutritional Short Form (MNA-SF) was used to evaluate the nutritional status of elderly patients with ACS, and it was found to be a useful predictor for all-cause mortalities(25). Although we did not evaluate the effectiveness of MNA-SF in the present study, it was found that GNRI was more appropriate than MNA-SF in assessing nutritional status and identifying nutritional complications in hospitalized elderly

patients(23). Moreover, using GNRI to evaluate malnutrition is a less time-consuming and easy tool that requires fewer medical staff.

Malnutrition is associated with mortality not only in hospitalized elderly patients but also in the normal population hospitalized with ACS. Moreover, albumin is used in addition to BMI in the calculation of GNRI, and albumin is both a negative acute-phase reactant and a marker of malnutrition. Depending on all this, it may have had an additive effect on GNRI being a strong predictor of mortality in elderly patients with STEMI.

As a conclusion, the number of elderly patients with STEMI is increasing because of aging, and it is important to evaluate these patients more meticulously and objectively. As malnutrition is a known predictor of mortality, it may be important to evaluate it with a simple, cost-effective, and easily calculated index.

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