Research Article

The effect of GNRI score on prognosis in patients with multivessel disease

GNRI skorunun çok damarlı hastalığı olan hastalarda prognoz üzerindeki etkisi

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ABSTRACT

Background: Geriatric Nutrition Risk Index (GNRI) is a simple and practical method used to evaluate the nutritional status of patients. Low GNRI scores are associated with poor outcomes and increased mortality. The aim of the study was to evaluate the association of the GNRI score with adverse outcomes in patients with multivessel disease.

Materials and Methods: Our study included 232 patients with multivessel disease from 2 centers between 01.01.2019-01.01.2021. Patients were divided into 2 groups according to GNRI score; GNRI > 98 normal nutrition and GNRI ≤98 malnutrition. All-cause mortality and major adverse cardiovascular events (MACE) rates were assessed at 36 months of follow-**up**.

Results: Approximately one third of the patients were in the low GNRI group (GNRI \leq 98, n = 81, 34.9%). The low GNRI group had higher rates of MACE (45.7% vs. 21.9%, p < 0.001) and mortality (22.2% vs. 8.6%, p = 0.004). In multivariate Cox regression analysis, GNRI was identified as an independent predictor of both mortality and MACE (HR: 0.908, 95% CI: 0.864-0.954, p<0.001 and HR: 0.903, 95% CI: 0.873-0.934, p<0.001, respectively). In Kaplan-Meier analysis, both MACE and mortality were higher in the low GNRI group over time (Log-Rank Test=20.481, p<0.001 and Log-Rank Test=8.287, p=0.004, respectively).

Conclusion: In conclusion, this study demonstrated that GNRI is an independent predictor of MACE and all-cause mortality in patients with multivessel disease. Closer monitoring of patients with low GNRI and interventions to improve their nutritional status may contribute to improving their long-term prognosis.

Keywords: Multivessel disease, mortality, geriatric nutrition risk index, major adverse cardiovascular events.

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ÖZ

Geriatrik Beslenme Risk İndeksi (GNRI), hastaların beslenme durumunu değerlendirmek için kullanılan basit ve pratik bir yöntemdir. Düşük GNRI skorları kötü sonuçlar ve artmış mortalite ile ilişkilidir. Çalışmanın amacı, GNRI skorunun çok damarlı hastalığı olan hastalarda olumsuz sonuçlarla ilişkisini değerlendirmekti.

Gereç ve Yöntemler: Çalışmamıza 01.01.2019-01.01.2021 tarihleri arasında 2 merkezden çok damarlı hastalığı olan 232 hasta dahil edildi. Hastalar GNRI skoruna göre 2 gruba ayrıldı; GNRI >98 normal beslenme ve GNRI≤98 yetersiz beslenme. Her nedene bağlı mortalite ve majör olumsuz kardiyovasküler olay (MACE) oranları 36 aylık takipte değerlendirildi.

Bulgular: Hastaların yaklaşık üçte biri düşük GNRI grubundaydı (GNRI ≤ 98, n=81, %34,9). Düşük GNRI grubunda daha yüksek MACE oranları (%45,7'ye karşı %21,9, p<0,001) ve mortalite (%22,2'ye karşı %8,6, p=0,004) vardı. Çok değişkenli Cox regresyon analizinde, GNRI hem mortalite hem de MACE'nin bağımsız bir öngörücüsü olarak tanımlandı (sırasıyla HR: 0,908, %95 CI: 0,864-0,954, p<0,001 ve HR: 0,903, %95 CI: 0,873-0,934, p<0,001). Kaplan-Meier analizinde, hem MACE hem de mortalite düşük GNRI grubunda zaman içinde daha yüksekti (sırasıyla Log-Rank Test=20,481, p<0,001 ve Log-Rank Test=8,287, p=0,004).

Sonuç: Sonuç olarak, bu çalışma GNRI'nin çoklu damar hastalığı olan hastalarda MACE ve tüm nedenlere bağlı mortalitenin bağımsız bir öngörücüsü olduğunu göstermiştir. Düşük GNRI'li hastaların daha yakından izlenmesi ve beslenme durumlarını iyileştirmeye yönelik müdahaleler uzun vadeli prognozlarının iyileştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: Çoklu damar hastalığı, mortalite, geriatrik beslenme risk indeksi, majör olumsuz kardiyovasküler olaylar.

INTRODUCTION

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide (1). Multivessel disease represents a severe clinical picture in which there is more than 70% stenosis in more than one major coronary artery, and these patients are at higher risk of cardiovascular events(2-3). The frequency and severity of cardiovascular events in these patients may be exacerbated by both the nature of the disease and by comorbid conditions such as malnutrition. Individuals with multivessel disease often require more aggressive treatment approaches and their quality of life is severely affected.

Malnutrition is a widespread yet often overlooked issue among hospitalized patients, leading to significant and broad-ranging negative impacts on clinical outcomes (4). This situation results in high economic burden, longer hospital stays and higher mortality rates (5). Previous studies have reported that malnutrition leads to increased inflammatory response and progression of arterial calcification and atherosclerosis (6-7). This indicates that malnutrition may be a critical factor in the formation and progression of cardiovascular diseases, thus emphasizing the negative effects of nutritional deficiencies on cardiovascular risk factors. As a result, evaluating the nutritional status could play a crucial role in accurately determining risk stratification in patients with CAD.

The geriatric nutritional risk index (GNRI), developed by Bouillanne et al., is a simple and practical method that evaluates the nutritional status of patients using parameters such as serum albumin level and body weight(8).GNRI is an index developed to comprehensively assess the nutritional status of elderly patients and to predict the morbidity and mortality risks that may develop due to nutritional deficiencies. According to this new nutritional tool, a low GNRI score is considered an indicator of malnutrition (9). Several studies have shown that GNRI predicts mortality in patients with chronic diseases such as chronic kidney disease, heart failure, and malignancies (10-12). In addition, there are some studies that have associated GNRI with adverse outcomes in patients with coronary artery disease (CAD) (13-15). However, the prognostic value of GNRI in CAD patients with multivessel disease has still not been fully elucidated.

The aim of this study is to comprehensively evaluate the prognostic value of GNRI in individuals with multivessel disease and also to determine the effect of GNRI on major adverse cardiovascular events (MACE) and all-cause mortality, thus revealing the contributions of this index to clinical practice.

MATERIALS AND METHODS

Study design

Patients who underwent coronary angiography in 2 centers between 01.01.2019 and 01.01.2021 and were detected to have multivessel disease were consecutively included in our study. A total of 255 patients were studied in a retrospective review, but 23 of these patients were excluded from the study because they did not meet the specified inclusion criteria, leaving the remaining 232 patients eligible for study analysis and included in the study (Figure. 1).



Figure 1. Study flowchart

The study group consisted of patients who underwent CAG for any reason and were diagnosed with multivessel disease. Multivessel disease was defined as the presence of two or more main coronary branches (vessel diameter ≥ 2.5 mm) with $\geq 70\%$ stenosis degree(2). Patients with diagnoses of malignancy, severe liver and kidney disease, pregnancy, autoimmune diseases, severe valve disease, and severe pulmonary hypertension were excluded from the study. The study was conducted meticulously in accordance with the Declaration of Helsinki, which sets international ethical standards and research practice(2013). The local ethics committee approval required for the study was obtained (Diyarbakır Gazi Yaşargil Training and Research Hospital Ethics Committee, with date and number: 04/10/2024 and 173).

Assessment of patient characteristics

demographic clinical Data on and characteristics of patients were collected (e.g. gender, age, height, weight, BMI (body mass index), heart rate, blood pressure, medical history, family history and medical treatment received, etc.). Body mass index (BMI) was calculated by dividing individuals' body weight in kilograms by the square of their height in meters (kg/m2). Hypertension was defined as the use of antihypertensive medication to control blood pressure or the presence of blood pressure above 140/90 mm Hg. Patients with hemoglobin A1c >6.5%or those receiving antidiabetic therapy (treatment with diet, insulin, or oral agents) were considered to have Diabetes Mellitus. Patients with an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m² were defined as having chronic kidney disease. Peripheral blood samples were taken from the patients and basic metabolic parameters (glucose, urea, creatinine, etc.), complete blood count (white blood cell count, hemoglobin, hematocrit, etc.) and lipid profile were examined. Blood tests were taken at the time the patients were admitted to the hospital. All participants underwent echocardiography using the Vivid 7 (GE Vingmed Ultrasound, Horton, Norway) ultrasound system, and LVEF (left ventricular ejection fraction) was calculated with the modified Simpson method. Discharge medications [aspirin, clopidogrel, statins, β -blockers and angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB)] were recorded.

Assessment of nutritional status

In our study, the nutritional status of the patients was analyzed with the GNRI score. The following formula was used to calculate the GNRI (8): $GNRI = 41.7 \times (weight/idealweight) (kg) + 1.489 \times albumin (g/L).$

Ideal body weight was calculated according to the participants' height, and was obtained by multiplying the square of the height in meters by 22, using the generally accepted method (16). In this score calculated, the weight/ideal body weight ratio is taken as 1 when the patient's' weight exceeds the ideal body weight (17). According to GNRI cut-off values, nutritional risk levels are as follows (9):

- -GNRI >98: no risk
- GNRI 92–98: low risk
- GNRI 82-92: moderate risk
- GNRI<82: severe risk

According to the above values, GNRI >98 indicates that the patients have normal nutritional status, so we used 98 as the cut-off value in our study. Thus, patients were divided into two different groups in terms of nutritional status: GNRI >98 with normal nutrition and GNRI \leq 98 with malnutrition.

Follow-up and endpoints

The results of 36 months follow-up from the date of inclusion were reviewed. The endpoints of our study were all-cause death and MACE. All-cause death, nonfatal acute myocardial infarction, revascularization, and stroke were considered

MACE. Patient data were obtained from hospital digital databases and the national registry.

Statistical analysis

Statistical analysis of the data obtained in our study was performed using SPSS 22.0 (IBM Corp., Armonk, New York, USA) software. Kolmogorov-

distribution were described as mean \pm standard deviation, and variables with abnormal distribution were described as median (interquartile range) values. In order to compare categorical variables, the Chisquare test was applied to determine the distribution differences between the groups. Kaplan-Meier analysis was performed to evaluate the 3-year survival probability of patients with low and high GNRI scores. In addition, the log-rank test was applied to determine the statistical significance of survival differences between the groups. To determine independent predictors of mortality and MACE, both univariate and multivariate Cox regression analysis models were applied to perform a Table 1. Basic clinical and laboratory characteristics of patients according to GNRI groups

Smirnov test was performed to determine whether continuous variables showed normal distribution. Student t-test, a parametric test, was used to compare variables with normal distribution. On the other hand, Mann-Whitney U test, one of the non-parametric methods, was preferred for variables without normal distribution. Variables with normal

comprehensive statistical analysis. In the statistical analyses, it was determined that the p value should be below 0.05 in order for the results to be considered statistically significant.

RESULTS

A total of 232 consecutive patients who underwent coronary angiography between January 1, 2019 and January 1, 2021 and were diagnosed with multivessel disease were included in the study. Patients were divided into two different groups based on GNRI values to determine their nutritional status: low GNRI group (GNRI \leq 98, n=81, 34.9%) and high GNRI group (GNRI > 98, n=151, 65.1%). The basic characteristics, demographic data and results of these groups are summarized in Table 1.

	Low GNRI score (GNRI≤98, n= 81)	High GNRI score (GNRI>98, n= 151)	<i>p</i> value
GNRI	91.1±4.3	106.4±5.6	<0.001
Gender (Female), n(%)	30(37.0)	49(32.5)	0.482
Age, (years)	70.8±7.1	65.4±8.0	<0.001
Body mass index, (kg/m2)	26.4±3.1	29.1±5.0	<0.001
Heart Rate (minute)	84.9±15.3	78.4±12.9	0.001
Systolic Blood Pressure (mmHg)	123.9±13.0	130.0±16.4	0.005
Diastolic Blood Pressure(mmHg)	76.7±9.7	80.3±10.4	0.012
Diagnosis -STEMI, n(%) -NSTEMI, n(%) -Unstable angina, n(%) -Stable CAD, n(%)	9(11.1) 22(27.2) 30(37.0) 20(24.7)	22(14.6) 35(23.2) 48(31.8) 46(30.5)	0.602
Angiography result, n(%) -Medical therapy -PCI	17(21.0) 50(61.7)	17(11.3) 101(66.9)	0.125

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-CABG	14(17.3)	33(21.9)	
HT, n(%)	50(61.7)	113(74.8)	0.037
DM, n(%)	49(60.5)	83(55.0)	0.418
Dyslipidemia, n(%)	37(45.7)	97(64.2)	0.006
CKD, n(%)	21(25.9)	22(14.6)	0.034
Smoking, n (%)	44(64.3)	60(39.7)	0.033
LVEF, (%)	48.5±9.4	53.2±7.9	<0.001
WBC, (x10 ³ /uL)	10.5±2.1	9.8±1.8	0.011
Hgb, (gr/L)	11.7±2.2	12.6±2.0	0.006
Glucose, (mg/dl)	132(116-161)	128(115-148)	0.415
Creatinine, (mg/dL)	0.92(0.80-1.25)	0.88(0.75-1.04)	0.042
GFR, (mL/min)	72.8±21.8	82.4±20.6	0.001
Albumin, (gr/L)	33.2±2.9	43.5±3.7	<0.001
CRP, (mg/dL)	1.10(0.17-2.50)	0.71(0.10-2.50)	0.149
Total cholesterol, (mg/dl)	176.6±33.5	194.3±44.1	0.002
HDL cholesterol, (mg/dl)	36.5±6.5	37.2±6.3	0.448
LDL cholesterol, (mg/dl)	108.1±26.1	121.1±39.2	0.003
Triglyceride(mg/dl),	159.5±62.5	179.7±59.2	0.016
Uric acid, (mg/dl)	6.0±1.6	5.8±1.4	0.327
Medical treatment, , n(%)			
-Aspirin	80(98.8)	150(99.3)	0.653
-P2Y12 inhibitors	62(76.5)	118(78.1)	0.780
-Beta-blocker	50(61.7)	108(71.5)	0.127
-ACEI/ARB	35(43.2)	72(47.7)	0.515
-Statins	68(84.0)	132(87.4)	0.465
MACE, n(%)	37(45.7)	33(21.9)	<0.001
Mortality, n(%)	18(22.2)	13(8.6)	0.004

Abbrevations: ACEI: Angiotensin Converting Enzyme Inhibitor, ARB: Angiotensin Receptor Blocker, BUN: Blood Urea Nitrogen, CABG: Coronary Artery Bypass Grafting, CAD: Coronary Artery Disease, CKD: Chronic Kidney Disease, CMP: Cardiomyopathy, CRP: C-Reactive Protein, DM: Diabetes Mellitus, GFR: Glomerular Filtration Rate, GNRI: Geriatric Nutritional Risk Index, HDL: High-density Lipoprotein, Hgb: Hemoglobin, HT: Hypertension, LDL: Low-density lipoprotein, LVEF: Left Ventricular Ejection Fraction, MACE: Major Adverse Cardiovascular Events, NSTEMI: Non- ST-Segment Elevation Myocardial Infarction, PCI: Percutaneous Coronary Intervention, STEMI: ST-Segment Elevation Myocardial Infarction, WBC: White Blood Cell

Patients in the low GNRI group were significantly older (70.8 \pm 7.1 vs. 65.4 \pm 8.0, p<0.001) and had a lower body mass index (26.4 \pm 3.1 vs. 29.1 \pm 5.0, p<0.001) compared to those in the high GNRI group. In addition, the low GNRI group had higher heart rate, lower systolic and diastolic blood pressure, and higher prevalence of smoking. Hypertension and dyslipidemia were higher, while chronic kidney disease was lower, in the high GNRI group. In patients in the low GNRI group, LVEF, hemoglobin, glomerular filtration rate (GFR), albumin, total cholesterol, triglyceride and LDL cholesterol levels were significantly lower. In contrast, white blood cell count and creatinine levels were higher. Importantly, the low GNRI group exhibited worse outcomes, with a significantly higher rate of MACE (45.7% vs. 21.9%, p<0.001) and mortality (22.2% vs. 8.6%, p=0.004).

As a result of 3 years follow-up, a total of 70 patients had MACE and 31 patients had mortality.

Considering whether mortality and MACE developed, patients were compared in terms of GNRI scores. Significantly lower GNRI scores were found in patients who developed MACE and mortality [96.7(87.8-101.2) vs 104.2 (98.2-108.7), p<0.001 and 92.3 (86.3-101.2) vs 102.7(96.0-108.7), p<0.001, respectively] (Figure. 2)



Figure 2. Comparison of patients with and without mortality and MACE in terms of GNRI scores in a box plot graph

Using univariate and multivariate Cox regression analysis models, independent predictors of 3-year

mortality and MACE were determined in our study (Table 2).

Table 2. Independent	predictors of mortality	y and MACE in	Univariate and	Multivariate	Cox Regression	analysis models
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	Univariate analysis			Multivariate analysis			
Mortality	HR	95%CI	р	HR	95%CI	р	
Gender	1.811	0.781-4.204	0.167				
Age	1.072	1.023-1.125	0.004	1.031	0.983-1.082	0.206	
HT	0.903	0.425-1.917	0.790				
DM	2.200	0.984-4.918	0.055				
GNRI	0.898	0.857-0.940	<0.001	0.908	0.864-0.954	<0.001	
Smoking	1.121	0.554-2.268	0.750				
Dyslipidemia	1.947	0.954-3.973	0.067				
CKD	0.818	0.314-2.129	0.680				
BMI	0.960	0.8861040	0.319				
	Univariate analysis			Multivariate analysis			
MACE	HR	95%CI	Р	HR	95%CI	р	
Gender	0.984	0.601-1.613	0.950				

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Age	1.074	1.040-1.108	<0.001	1.032	1.000-1.065	0.052
HT	0.826	0.501-1.360	0.452			
DM	1.991	1.176-3.372	0.010	1.315	0.770-2.248	0.316
GNRI	0.888	0.860-0.916	< 0.001	0.903	0.873-0.934	< 0.001
Smoking	0.817	0.508-1.315	0.405			
Dyslipidemia	0.718	0.450-1.148	0.166			
CKD	1.015	0.555-1.853	0.962			
BMI	0.927	0.876-0.981	0.009	0.970	0.914-1.029	0.307

Abbrevations: BMI: Body Mass Index, CI: Confident Interval, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, GNRI: Geriatric Nutritional Risk Index, HT: Hypertension, OR: Odds Ratio

In the univariate analysis performed for mortality, age (HR: 1.072, 95% CI: 1.023-1.125, p=0.004) and GNRI value (HR: 0.898, 95% CI: 0.857-0.940, p<0.001) were determined as independent predictors. Multivariate analysis results showed that only GNRI (HR: 0.908, 95% CI: 0.864-0.954, p<0.001) was found to be significant as an independent predictor. For MACE, age (HR: 1.074, 95% CI: 1.040-1.108, p<0.001), DM (HR: 1.991, 95% CI: 1.176-3.372, p=0.010), GNRI (HR: 0.888, 95% CI: 0.860-0.916, p<0.001) and BMI (HR: 0.927, 95% CI: 0.876-0.981, p=0.009) were found to be independent predictors in univariate analysis. In multivariate analysis, GNRI (HR: 0.903, 95% CI: 0.873-0.934, p<0.001) was also found to be significant as an independent predictor.

Kaplan-Meier analysis was conducted to investigate the association between low and high GNRI groups and mortality and MACE during the 3year follow-up period. According to this analysis, both MACE and mortality were higher in the low GNRI group over time (Log-Rank Test=20.481, p<0.001 and Log-Rank Test=8.287, p=0.004, respectively) (Figure. 3).



Figure 3. Kaplan-Meier analysis of the association between low and high GNRI groups and MACE and mortality during the 3-year follow-up period

DISCUSSION

In our study, we examined the prognostic value of GNRI in patients diagnosed with multivessel coronary artery disease and its effect on the clinical outcomes of patients. Our study showed that both MACE and mortality were significantly higher in patients with low GNRI values. These results suggest that GNRI may be a prognostic indicator in patients with multivessel disease and that malnutrition may have a significant impact on clinical outcomes in this group of patients.

GNRI is a score that indicates nutritional status and is calculated using routinely measured serum albumin, weight and height parameters in hospitalized patients (8). Serum albumin and BMI values used in GNRI measurement have also been evaluated as indicators of nutritional status in some studies (18-19). However, factors like inflammation, dehydration, and heart failure can influence these measurements (20). The GNRI covers more than just the overlap of these two parameters, hence serving as a more reliable indicator. The prognostic value of GNRI has been previously demonstrated in various studies in chronic diseases such as coronary artery disease, heart failure, and chronic kidney disease (15,17,21). However, the prognostic role of GNRI in CAD patients with multivessel disease has not been evaluated. Our study fills this gap, revealing that patients with low GNRI may experience higher MACE and mortality rates. In particular, the fact that patients in the low GNRI group are older, have lower body mass indexes, and have poor clinical features suggests that this patient group is more fragile.

The association of low GNRI with MACE and mortality suggests the adverse effects of malnutrition on cardiovascular events. Malnutrition may contribute to increased inflammation, progression of atherosclerosis, and acceleration of vascular calcification (22-23). Additionally, low albumin levels and loss of body weight can increase the risk of complications by weakening the body's defense mechanisms (24). The energy metabolism of cardiomyocytes plays a crucial role in the cardiac remodeling and heart failure processes that frequently occur following coronary artery disease (25). The occurrence of serious complications such as infection in individuals with multivessel disease may further reduce the already limited metabolic reserve. In addition, the inability of malnourished patients to perform recommended physical activities may increase the risk of hypercoagulation in this group, making them more vulnerable to coronary events (14). These findings emphasize that the nutritional status of patients with multivessel disease should be regularly assessed and patients with low GNRI should be closely followed.

Our study also revealed that patients with lower GNRI scores were older, had lower BMI, and presented with poorer clinical parameters such as low LVEF, low hemoglobin levels, and impaired renal function. These findings suggest that malnutrition may contribute to the poorer overall health status of further these patients, exacerbating existing cardiovascular burden. Interestingly, despite the wellknown role of traditional risk factors such as hypertension, dyslipidemia, and chronic kidney disease, our findings suggest that nutritional status assessed by the GNRI provides additional prognostic value beyond these factors. Kaplan-Meier survival analysis further clarified the clear distinction between patients with low and high GNRI scores, with the low GNRI group showing significantly higher rates of MACE and death over time. These results suggest that routine assessment of nutritional status using simple tools such as the GNRI may aid in risk stratification of CAD patients, allowing for more

targeted interventions aimed at improving both nutritional status and cardiovascular outcomes.

Studies have shown that well-implemented nutritional interventions can lead to notable reductions in both hospital stay durations and mortality rates among malnourished patients (26). However, nutritional support is often neglected by physicians in patients with coronary artery disease (27). This article highlights the significance of evaluating nutritional status in individuals with coronary artery disease. The findings of our study also indicate that GNRI is not limited to elderly patients but may be a valuable prognostic tool in a wider patient population. The clinical use of GNRI can be expanded due to its simplicity and easy calculation, allowing early identification and intervention of high-risk patients. However, further studies in larger patient groups and different populations are required for the full integration of GNRI into clinical practice.

Limitations

Our study has some limitations that should be taken into consideration in terms of validity and reliability of the results obtained. First of all, the fact that this study was retrospective and conducted in two centers may restrict the generalizability of the results. Second, the use of the GNRI as a nutritional assessment tool, although practical, may not capture all aspects of malnutrition. Third, the GNRI score was measured only at admission, and changes over time could not be assessed. Finally, we did not assess other potential factors that may have influenced nutritional status, such as inflammatory markers or socioeconomic status, which may have influenced the results.

CONCLUSION

This study demonstrates the prognostic value of GNRI in patients with multivessel disease. According to our findings, patients with low GNRI values are at higher risk for both MACE and mortality. The negative effects of malnutrition on clinical outcomes in this patient group indicate that GNRI may be a valuable tool in cardiovascular risk assessment. Integrating nutritional status assessed by GNRI into routine clinical practice may be beneficial for early diagnosis of high-risk patients and improvement of clinical outcomes with nutritional interventions. However, further studies in larger and more diverse patient populations will contribute to our better understanding of the prognostic value and clinical utility of GNRI.

Conflict of interest disclosure

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