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ARTICLE

Association of Geriatric Nutritional Risk Index Scores with Outcomes in Patients Undergoing Maintenance Hemodialysis

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Abstract

Aims/Background The Geriatric Nutritional Risk Index (GNRI) is an effective tool for identifying malnutrition, and helps monitor the prognosis of patients undergoing maintenance hemodialysis. However, the association between the GNRI and cardiovascular or all-cause mortality in hemodialysis patients remains unclear. Therefore, this study investigated the correlation of the GNRI with all-cause and cardiovascular mortality in patients undergoing maintenance hemodialysis.

Methods This study included 402 incident hemodialysis patients. Based on the first-dialysis GNRI quartile, the patients were divided into four groups: N1 (GNRI ≤85.04), N2 (GNRI 85.05–91.04), N3 (91.05–96.49), N4 (GNRI ≥96.5) groups. The risk of all-cause and cardiovascular mortality among the different GNRI groups was compared using the Kaplan-Meier survival curve analysis through log-rank tests. Furthermore, Cox regression analysis was used to assess the association between the GNRI groups and all-cause mortality. Additionally, the predictive capability of the GNRI groups on the prognosis was evaluated by employing receiver operating characteristic (ROC) curve analysis.

Results Patients in the N1 group exhibited a significantly higher risk of all-cause mortality ($p < 0.001$) and cardiovascular mortality ($p = 0.004$) compared to the other groups. ROC curve analysis revealed that GNRI, age, and serum creatinine had moderate predictive value for mortality, with GNRI indicating an area under the curve (AUC) of 0.605 for all-cause mortality and 0.565 for cardiovascular mortality. Moreover, the N2 and N3 groups had a significantly reduced risk of cardiovascular mortality compared to the N1 group.

Conclusion A lower GNRI is closely associated with a higher risk of all-cause and cardiovascular mortality in hemodialysis patients.

Key words: hemodialysis; Geriatric Nutritional Risk Index; malnutrition; cardiovascular disease; mortality

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Introduction

The International Society of Renal Nutrition and Metabolism (ISRNM) defined protein-energy wasting (PEW) as an impaired nutritional condition commonly observed in patients with chronic kidney disease (CKD) (Fouque et al, 2008). PEW is highly prevalent among hemodialysis patients, affecting 40–70% of this population. PEW's progression is linked to compromised immunity, increased hospitalization rates, reduced survival, and increased mortality in CKD patients. Specifically, in hemodialysis patients, PEW significantly increases the risk of cardiovascular

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complications, reduces quality of life, and contributes to overall mortality rates. Given its high prevalence and severe consequences, assessing and managing the nutritional status is crucial for improving patient outcomes. Furthermore, PEW is closely associated with an increased risk of dialysis-related complications (Fouque et al, 2011). The Geriatric Nutritional Risk Index (GNRI) is a modified nutritional assessment tool that evaluates nutritional status based on body weight, height, and serum albumin levels. Unlike other approaches that usually need subjective assessments, the GNRI offers a simple and objective approach to assess the nutritional status. Initially established by Bouillanne et al (2005) and later modified by Yamada et al (2008), the current GNRI formula is derived as follows: (14.89 × serum albumin in g/dL) + (41.7 × [current body weight in kg/standard body weight in kg]).

The modified formula demonstrated that the GNRI is the simplest and most accurate nutritional screening approach for hemodialysis patients, performing better than the other commonly used methods (Yamada et al, 2008). Furthermore, GNRI scores were recognized as crucial predictors of mortality in hemodialysis patients (Kobayashi et al, 2010). Moreover, these findings have been validated by various studies conducted in Japan, Italy, the Netherlands, and France (de Roij van Zuijdewijn et al, 2015; Fujioka et al, 2022; Harada et al, 2020; Maenosono et al, 2022; Panichi et al, 2014; Sirajedine et al, 2012).

In addition to nutritional screening, GNRI has been applied to predict cardiovascular outcomes. Previous studies have revealed a strong association between GNRI scores and cardiovascular event incidence in patients with chronic heart failure (Maenosono et al, 2022; Narumi et al, 2013). Xiong et al (2020) reported that the GNRI score strongly predicts all-cause and cardiovascular mortality in hemodialysis patients, suggesting its utility beyond nutritional assessment as an overall prognostic indicator. Similarly, Ren et al (2020) observed a close association between GNRI scores and mortality in patients receiving peritoneal dialysis. Furthermore, Liao et al (2023) examined elderly patients with acute kidney injury (AKI) in the Intensive Care Unit (ICU) and highlighted the GNRI as a crucial prognostic marker upon hospital admission.

Currently, limited studies have specifically investigated the relationship between GNRI scores and cardiovascular mortality in hemodialysis patients. To address this gap, this correlation study assessed the association between the GNRI and mortality risk in patients undergoing maintenance hemodialysis. These findings are expected to improve the prediction of long-term prognosis and inform clinical decision-making in these patients.

Methods

Patient Selection

The present study enrolled incident hemodialysis patients from the Hemodialysis Center of the First Affiliated Hospital of Nanchang University between 1 May 2010, and 30 June 2019. The predetermined exclusion criteria for patient selection were as follows: patients with a history of renal transplantation; patients who

switched from peritoneal dialysis to hemodialysis; those younger than 18 years; patients who switched to peritoneal dialysis or received combined peritoneal dialysis and hemodialysis; patients who recently relocated from another hemodialysis center; patients with incomplete follow-up data; and those with a dialysis duration of $<$3 months. These patients were followed up until 30 June 2020.

The study design complied with the ethical principles outlined in the Declaration of Helsinki (World Medical Association, 2013). The study protocol was approved by the Institutional Review Board of the First Affiliated Hospital of Nanchang University (Approval Number: IIT [2023] Ethical Review No. 401). An informed consent was obtained from each patient.

Cohort Design, Baseline Data Collection, and Outcome Definition

A retrospective study approach was used to assemble the cohort, with patient follow-up continuing until the development of the study endpoints, withdrawal from hemodialysis, patient death, transfer to another center, or the end of the follow-up period on 30 June 2020. The data were collected from the medical records of patients in the Hemodialysis Center, including age, gender, dialysis duration, height, weight, primary cause of end-stage renal disease (ESRD), and relevant clinical, demographic, and laboratory data, such as blood routine examination, liver function, kidney function, and lipid profiles. Body mass index (BMI) was calculated using the following formula: BMI = weight (kg)/height $(m)^2$.

The primary outcomes of the present study were all-cause mortality and cardiovascular mortality. Cardiovascular mortality was defined as death resulting from cardiovascular illnesses, including myocardial infarction, heart failure, unstable angina, peripheral vascular events, and sudden death.

Patient Grouping

The GNRI was calculated using the serum albumin levels and anthropometric parameters following a previous study (Bouillanne et al, 2005): GNRI = (14.89 $\times$ serum albumin in g/dL) + (41.7 $\times$ [current body weight in kg/standard body weight in kg]). If the patient's body weight exceeded the ideal weight, the ratio of actual weight to ideal weight was recorded as 1. If the actual weight was below the ideal weight, the ratio was documented as the original value. For patients undergoing maintenance hemodialysis, the dry weight was used as the actual body weight, while the ideal body weight was calculated based on a BMI of 22 kg/m^2, which indicates the lowest BMI threshold for identifying morbidity in Asians.

Based on the GNRI quartiles, participants were divided into four groups: N1 group: GNRI $\leq$85.04, N2 group: GNRI 85.05–91.04, N3 group: GNRI 91.05–96.49, and N4 group: GNRI $\geq$96.5.

Statistical Analysis

Data analysis was performed using the IBM SPSS 26.0 statistical software (version 26.0, IBM Corp., Armonk, NY, USA). Data following the normal distribution was expressed as mean $\pm$ standard deviation, while non-normally distributed was expressed as median with interquartile ranges. Categorical data were expressed in

percentages (%). One-way analysis of variance (ANOVA) was used to compare normally distributed continuous variables. Moreover, the Kruskal-Wallis test was used for non-normally distributed continuous variables. The chi-square test was used to compare the categorical data between groups. When significant results were identified in ANOVA, post-hoc multiple comparisons were performed by applying Tukey's Honest Significant Difference (HSD) test to detect specific group differences.

Furthermore, the Kaplan-Meier method was used to analyze the all-cause mortality and cardiovascular mortality and to generate the survival curves for the different GNRI groups. Survival curves were compared employing the Log-rank test. The correlation between the GNRI groups and all-cause mortality or cardiovascular mortality in hemodialysis patients was evaluated using Cox regression models, which provided hazard ratio (HR) and 95% confidence interval (CI). A p-value of <0.05 was considered statistically significant.

In the multivariate Cox regression model, variables were selected based on their clinical relevance and statistical significance in univariate analyses ($p < 0.05$). Critical Variables, such as age, diabetes status, serum creatinine, hemoglobin, and serum cholesterol, were included due to their established roles as mortality predictors in hemodialysis patients. This approach ensured that the model appropriately accounted for potential confounders, providing a robust estimation of the independent effect of GNRI on mortality. Receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of the included indicators.

Results

Baseline Characteristics of the Participants

Applying the predetermined inclusion-exclusion criteria, 402 hemodialysis patients were finally included in this study. The study cohort included 250 males (62.19%) and 152 females (37.81%), with an average age of 60.19 ± 15.03 years. Among these patients, 104 (25.87%) had diabetes mellitus, and 285 (70.90%) had hypertension. The mean duration of dialysis was 27.93 months (14.66–48.52), and the median GNRI was 91.043. During the follow-up period, 102 (25.37%) patients died, of whom 47 (11.69%) deaths were due to cardiovascular origins (Table 1).

Comparison of Baseline Characteristics and Laboratory Indicators among Patients in the GNRI Groups

A comparison of clinical and baseline characteristics among the study participants, grouped by GNRI quartiles, is summarized in Table 2. Significant differences were observed across several variables. Notably, total protein and serum albumin levels were significantly lower in the N1 group compared to the N4 group ($p < 0.001$), indicating that lower GNRI scores are associated with poorer nutritional status. Furthermore, age also showed substantial variation between groups ($p = 0.005$), with younger patients predominantly observed in the higher GNRI quartiles suggesting a potential age-related impact on nutritional status. Additionally, serum creatinine levels were significantly higher in the N4 group ($p < 0.001$), indicating better muscle mass and overall nutritional status in patients with higher

Table 1. Baseline characteristics of the study participants (n = 402).

Baseline Characteristics	n (%) or mean ± SD
Gender	
Male	250 (62.19)
Female	152 (37.81)
Average Age (years)	60.19 ± 15.03
Duration of dialysis (months)	27.93 (14.66, 48.52)
Diabetes Mellitus	104 (25.87)
Hypertension	285 (70.90)
Median GNRI	91.04
Total Deaths	102 (25.37)
Cardiovascular Deaths	47 (11.69)

GNRI, Geriatric Nutritional Risk Index; SD, standard deviation.

GNRI scores. Post-hoc analysis utilizing Tukey's HSD test demonstrated significant differences between the N1 and N4 groups ($p < 0.001$).

These findings underscore the significance of nutritional status as a prognostic factor in hemodialysis patients, particularly those in lower GNRI quartiles.

Kaplan-Meier Survival Curves for All-Cause Mortality in Patients in Different GNRI Groups

The association between GNRI groups and all-cause mortality in hemodialysis patients was analyzed using the Kaplan-Meier method (Fig. 1). The risk of all-cause mortality was significantly higher in the N1 group than in other groups (Log-rank value: 19.619, $p < 0.001$).

Kaplan-Meier Survival Curves for Cardiovascular Mortality in the Different GNRI Groups

The association between GNRI groups and cardiovascular mortality in hemodialysis patients was assessed using the Kaplan-Meier method (Fig. 2). The risk of cardiovascular mortality was significantly higher in the N1 group compared to the other groups (Log-rank value: 13.11, $p = 0.004$).

Univariate Cox Regression Analysis for All-Cause Mortality

Univariate Cox regression analysis revealed that age, diabetes, serum albumin, creatinine, total bilirubin, hemoglobin, uric acid, and total cholesterol were all significantly associated with overall mortality (Table 3). Furthermore, the higher GNRI scores (HR: 0.97, 95% CI: 0.95–0.99, $p = 0.002$) in the N2 (HR: 0.40, 95% CI: 0.24–0.67, $p = 0.001$), N3 (HR: 0.42, 95% CI: 0.25–0.72, $p = 0.001$), and N4 (HR: 0.43, 95% CI: 0.25–0.75, $p = 0.003$) groups compared to the N1 group, were significantly linked to lower risk of all-cause mortality.

Multicollinearity was assessed using the variance inflation factor (VIF). Most variables had VIF values below 10, indicating no significant multicollinearity. However, serum albumin (VIF = 22.84) and GNRI (VIF = 25.97) showed significantly

Table 2. Comparison of clinical and baseline characteristics among the patients in the GNRI groups.

Category	Total (n = 402)	GNRI				$F/\chi^2/z$	p-value
		N1 (n = 101)	N2 (n = 100)	N3 (n = 98)	N4 (n = 103)		
Age (year)	60.19 ± 15.03	61.88 ± 14.36	61.12 ± 14.35	62.20 ± 15.81	55.70 ± 14.84	4.36	**0.005**
Duration of dialysis (months)	27.93 (14.66, 48.52)	25.03 (11.88, 38.65)	37.92 (17.28, 65.40)	29.28 (14.08, 59.40)	25.70 (13.43, 42.87)	15.72	**0.026**
Male gender (%)	250 (62.2)	65 (64.36)	61 (61.00)	60 (61.22)	64 (62.14)	0.30	0.960
Total protein (g/L)	59.86 ± 8.90	54.84 ± 12.60	57.59 ± 5.81	60.85 ± 4.53	66.06 ± 5.80	38.33	<**0.001**
Serum albumin (g/L)	33.93 ± 5.99	26.39 ± 4.38	32.67 ± 2.31	31.03 ± 1.77	40.53 ± 2.86	413.25	<**0.001**
Serum creatinine (μmol/L)	679.50 (515.55, 888.50)	612.90 (418.00, 793.80)	643.95 (518.05, 848.00)	706.00 (544.22, 912.70)	760.70 (599.00, 997.95)	23.32	<**0.001**
Blood urea nitrogen (mmol/L)	24.55 (18.00, 33.30)	21.00 (15.40, 28.10)	22.35 (16.38, 32.65)	26.45 (19.55, 34.02)	27.60 (22.05, 35.20)	20.36	<**0.001**
Uric acid (μmol/L)	444.25 ± 137.47	404.20 ± 127.93	444.53 ± 132.39	445.73 ± 138.25	481.84 ± 141.60	5.47	<**0.001**
Total cholesterol (mmol/L)	4.23 ± 1.28	4.49 ± 1.24	4.16 ± 1.55	4.09 ± 1.29	4.19 ± 0.96	2.08	0.124
Serum triglycerides (mmol/L)	1.30 (0.90, 1.75)	1.36 (1.04, 1.78)	1.30 (0.88, 1.66)	1.16 (0.8525, 1.6275)	1.39 (0.90, 1.84)	4.91	0.179
Total bilirubin (μmol/L)	3.30 (2.50, 4.50)	3.20 (2.20, 4.40)	3.15 (2.50, 4.30)	3.30 (2.340, 4.28)	3.70 (2.80, 5.15)	15.30	**0.035**
Serum calcium (mmol/L)	1.96 ± 0.27	1.91 ± 0.22	1.95 ± 0.24	1.96 ± 0.31	2.04 ± 0.29	4.35	**0.008**
Hemoglobin (g/L)	78.12 ± 18.53	78.74 ± 18.20	71.85 ± 15.47	77.53 ± 8.08	84.17 ± 20.14	8.18	<**0.001**
Dry weight (Kg)	61.59 ± 12.39	59.82 ± 12.17	60.91 ± 13.54	60.95 ± 10.02	64.58 ± 13.11	0.40	0.464
Height (cm)	163.87 ± 9.44	164.05 ± 7.09	163.54 ± 7.65	164.19 ± 7.46	163.71 ± 13.81	0.30	0.957
BMI (kg/m^2)	23.18 ± 9.50	22.14 ± 3.86	22.63 ± 3.99	22.50 ± 2.70	25.37 ± 17.72	2.08	0.305
Systolic blood pressure (mmHg)	145.37 ± 26.81	144.41 ± 27.28	148.17 ± 27.71	145.49 ± 28.28	143.50 ± 24.06	0.48	0.635
Diastolic blood pressure (mmHg)	82.12 ± 16.26	79.95 ± 15.76	81.39 ± 14.65	80.41 ± 17.30	86.54 ± 16.58	3.47	**0.013**
GNRI	91.04 (85.04, 96.52)	79.97 (75.87, 82.87)	88.01 (86.37, 89.49)	93.89 (92.47, 95.18)	99.92 (98.08, 103.05)	521.09	<**0.001**
Diabetes [n (%)]	104 (25.87)	40 (39.60)	26 (26.00)	27 (27.55)	11 (10.68)	22.47	<**0.001**
Hypertension [n (%)]	285 (70.90)	65 (64.36)	73 (73.00)	71 (72.45)	76 (73.79)	2.84	0.417

Values with $p < 0.05$ are indicated in bold to emphasize clinical statistical significance. GNRI, Geriatric Nutritional Risk Index; BMI, body mass index.

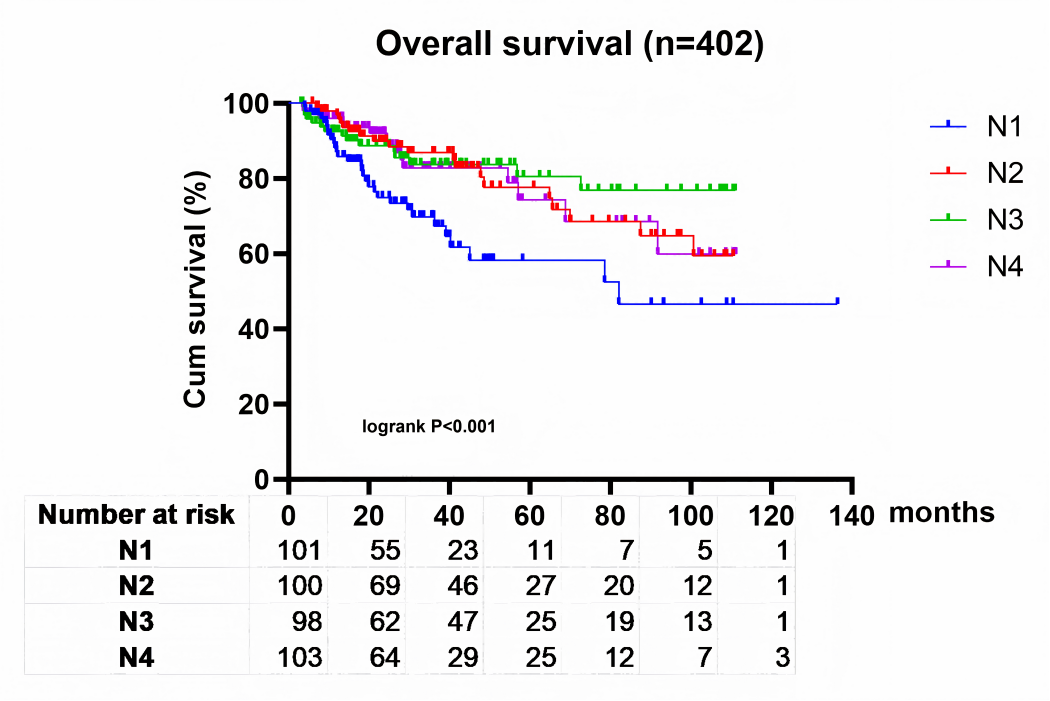

Fig. 1. Kaplan-Meier curves for all-cause mortality stratified by GNRI groups. GNRI, Geriatric Nutritional Risk Index.

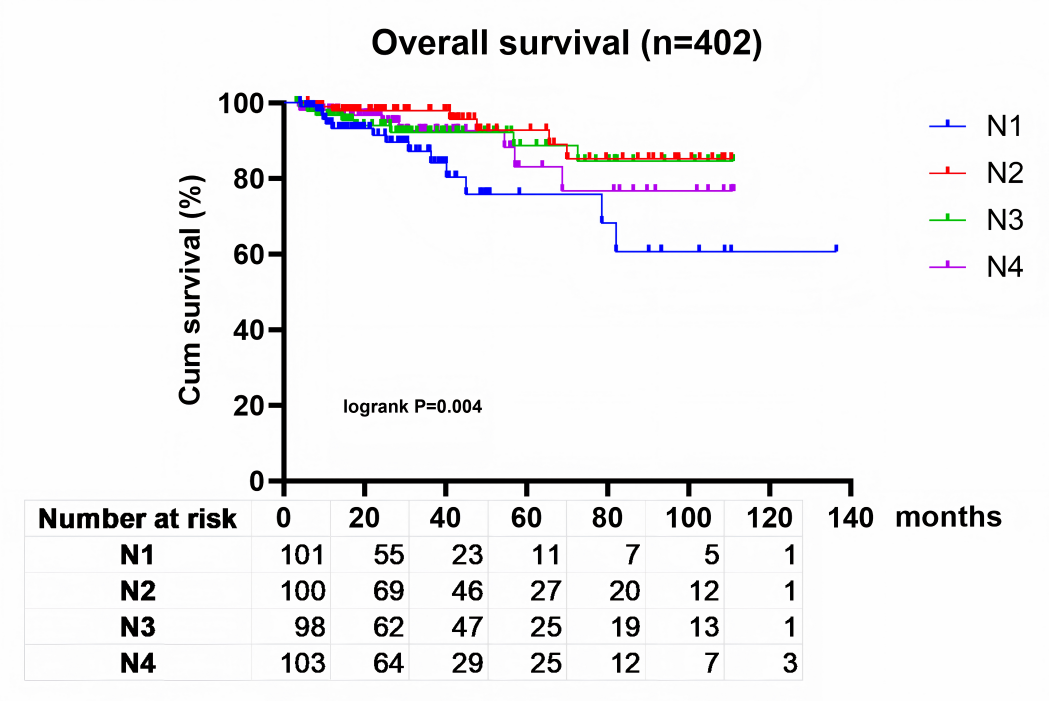

Fig. 2. Kaplan-Meier curves for cardiovascular mortality stratified by GNRI groups. GNRI, Geriatric Nutritional Risk Index.

high VIF values, suggesting potential multicollinearity. Despite this, these variables were retained in the model due to their clinical significance and relevance to

Table 3. Univariate Cox regression analysis for all-cause mortality.

Category	HR	95% CI	VIF	*p*-value
Age (year)	1.04	1.02–1.06	1.611	**0.000**
Gender (male)	1.14	0.76–1.71	2.48	0.517
Total protein (g/L)	0.98	0.96–1.01	1.53	0.157
Serum albumin (g/L)	0.94	0.91–0.97	22.84	**0.000**
Serum creatinine (μmol/L)	0.999	0.998–0.999	1.89	**0.000**
Blood urea nitrogen (mmol/L)	0.98	0.96–1.00	1.68	0.063
Total bilirubin (μmol/L)	1.09	1.02–1.17	1.17	**0.012**
Hemoglobin (g/L)	1.01	1.00–1.02	1.31	**0.011**
Uric acid (μmol/L)	0.998	0.996–1.000	1.18	**0.017**
Total cholesterol (mmol/L)	1.18	1.03–1.36	1.39	**0.018**
Serum triglyceride (mmol/L)	0.94	0.77–1.16	1.28	0.590
Serum calcium (mmol/L)	1.59	0.78–0.23	1.32	0.201
Weight (Kg)	1.01	1.00–1.03	5.06	0.095
Height (m)	1.01	0.99–1.04	6.19	0.251
BMI (kg/m^2)	1.00	0.98–1.01	3.40	0.687
Systolic blood pressure (mmHg)	1.003	0.996–1.01	2.12	0.402
Diastolic blood pressure (mmHg)	0.998	0.975–1.000	2.53	0.051
GNRI	0.97	0.95–0.99	25.97	**0.002**
GNRI quartile (compared to N1)	Reference		5.82	**0.000**
N2	0.40	0.24–0.67		**0.001**
N3	0.42	0.25–0.72		**0.001**
N4	0.43	0.25–0.75		**0.003**
Diabetes	1.73	1.15–2.61	1.35	**0.008**
Hypertension	1.08	0.70–1.66	1.10	0.730
End-stage kidney disease origin				
Chronic glomerulonephritis	0.68	0.46–1.01	1.10	0.054
Diabetic nephropathy	1.50	0.99–2.28	1.11	0.058
Others	1.08	0.70–1.67	1.43	0.711

Values with $p < 0.05$ are indicated in bold to emphasize clinical statistical significance. HR and 95% CI values are presented with three decimal places where applicable for precision. HR, hazard ratio; 95% CI, 95% confidence interval; BMI, body mass index; GNRI, Geriatric Nutritional Risk Index; VIF, variance inflation factor.

the outcomes. While multicollinearity may affect the precision of the estimates, it does not reduce their overall significance.

Multivariate Cox Regression Analysis for All-Cause Mortality

In multivariate Cox regression analysis, variables were initially selected based on significance in univariate analysis ($p < 0.05$). However, in subsequent analyses, it was found that there were potential multicollinearities for indicators such as diabetes, serum creatinine, total bilirubin, uric acid, serum albumin, and hemoglobin, and to address this issue, these several variables were excluded from the final model. Higher age and total cholesterol levels were significantly associated with an in-

creased risk of all-cause mortality. Compared with patients in the N1 group, the risk of all-cause mortality was significantly reduced in the N2 (HR: 0.37, 95% CI: 0.22–0.64, p <0.001), N3 (HR: 0.37, 95% CI: 0.21–0.65, p <0.001) and N4 (HR: 0.50, 95% CI: 0.28–0.87, p = 0.014) groups (Table 4).

Table 4. Multivariate Cox regression analysis for all-cause mortality.

Category	HR	95% CI	p-value
Age (year)	1.04	1.02–1.06	**0.000**
Total cholesterol (mmol/L)	1.19	1.03–1.37	**0.017**
GNRI quartiles	Reference		**0.000**
N2	0.37	0.22–0.64	**0.000**
N3	0.37	0.21–0.65	**0.000**
N4	0.50	0.28–0.87	**0.014**

Values with $p < 0.05$ are indicated in bold to emphasize clinical statistical significance. HR, hazard ratio; 95% CI, 95% confidence interval; GNRI, Geriatric Nutritional Risk Index.

Univariate Cox Regression Analysis for Cardiovascular Mortality

The findings on the univariate Cox regression analysis revealed that the age, serum creatinine, blood urea nitrogen, hemoglobin, serum albumin, and total cholesterol and the N2 (HR: 0.25, 95% CI: 0.10–0.59; p = 0.002) and N3 (HR: 0.43, 95% CI: 0.20–0.91, p = 0.027) groups were associated with risk of cardiovascular mortality in hemodialysis patients (Table 5).

Multivariate Cox Regression Analysis for Cardiovascular Mortality

In the multivariate Cox regression analysis for cardiovascular mortality, variables were initially selected based on their significance in the univariate analysis ($p < 0.05$). However, to address multicollinearity, several variables, including blood urea nitrogen and hemoglobin, were excluded due to their association with factors such as GNRI and age. This approach ensured that only the most relevant and independent predictors were incorporated into the final model. Furthermore, high serum creatinine levels were associated with a reduced risk of cardiovascular mortality. Age is associated with the risk of cardiovascular mortality. Compared to patients in the N1 group, those in the N2 (HR: 0.27, 95% CI: 0.11–0.66, p = 0.004) and N3 (HR: 0.45, 95% CI: 0.20–0.97, p = 0.043) groups demonstrated a substantially lower risk of cardiovascular mortality (Table 6).

ROC Curves for All-Cause Mortality Predictive Ability

ROC curves were used to assess the predictive ability of the GNRI scores (Fig. 3), age (Fig. 4), and total cholesterol (Fig. 5) for all-cause mortality. The area under the ROC curve for age, GNRI, and total cholesterol were >0.5, indicating their accuracy in predicting all-cause mortality. The p-values for the GNRI scores, age, and total cholesterol were <0.05, with area under the curve (AUC) values of 0.605 for GNRI and 0.696 for age, respectively. The AUC for total cholesterol was

Table 5. Univariate Cox regression analysis for cardiovascular mortality.

Category	HR	95% CI	*p*-value
Age (year)	1.04	1.02–1.06	**0.001**
Gender (male)	0.97	0.72–1.30	0.842
Total protein (g/L)	0.99	0.96–1.03	0.721
Serum albumin (g/L)	0.95	0.90–0.99	**0.026**
Serum creatinine (μmol/L)	0.998	0.997–0.999	**0.001**
Blood urea nitrogen (mmol/L)	0.97	0.94–1.00	**0.025**
Total bilirubin (μmol/L)	1.04	0.93–1.16	0.499
Hemoglobin (g/L)	1.02	1.01–1.04	**0.007**
Uric acid (μmol/L)	0.998	0.996–1.000	0.104
Total cholesterol (mmol/L)	1.24	1.02–1.50	**0.030**
Serum triglycerides (mmol/L)	1.02	0.77–1.34	0.917
Serum calcium (mmol/L)	1.53	0.54–4.32	0.419
Weight (Kg)	1.01	0.98–1.03	0.522
Height (m)	1.02	0.99–1.04	0.187
BMI (kg/m^2)	1.00	0.98–1.02	0.841
Systolic blood pressure (mmHg)	1.00	1.00–1.02	0.306
Diastolic blood pressure (mmHg)	1.00	0.97–1.01	0.618
GNRI	0.97	0.94–1.00	0.079
GNRI quartile (compared to N1)	Reference		**0.008**
N2	0.25	0.10–0.59	**0.002**
N3	0.43	0.20–0.91	**0.027**
N4	0.47	0.22–1.01	0.052
Diabetes	1.50	0.81–2.77	0.197
Hypertension	1.14	0.60–2.16	0.687
End-stage kidney disease origin			
Chronic glomerulonephritis	0.64	0.36–1.16	0.139
Diabetic nephropathy	1.56	0.84–2.88	0.160
Others	1.11	0.59–2.09	0.739

Values with $p < 0.05$ are indicated in bold to emphasize clinical statistical significance. HR and 95% CI values are presented with three decimal places where applicable for precision. HR, hazard ratio; 95% CI, 95% confidence interval; BMI, body mass index; GNRI, Geriatric Nutritional Risk Index.

0.557, suggesting a reduced predictive ability for this variable. Both GNRI and age were significant predictors of all-cause mortality, with age reflecting greater predictive value. The cut-off values for the GNRI and age were 86.83 and 70.5, respectively.

ROC Curves for Cardiovascular Mortality Predictive Ability

ROC curves were used to evaluate the predictive ability of the GNRI scores (Fig. 6), creatinine (Fig. 7), and age (Fig. 8) for cardiovascular mortality. The AUC for the GNRI scores, age, and creatinine was >0.5, indicating their predictive accuracy for cardiovascular mortality. The AUC values for the GNRI scores, age, and

Table 6. Multivariate Cox regression analysis for cardiovascular mortality.

Category	HR	95% CI	*p*-value
Age (year)	1.03	1.01–1.06	**0.011**
Serum creatinine (μmol/L)	0.999	0.997–1.000	**0.028**
GNRI quartile (compared to N1)	Reference		**0.025**
N2	0.27	0.11–0.66	**0.004**
N3	0.45	0.20–0.97	**0.043**
N4	0.61	0.27–1.38	0.236

Values with $p < 0.05$ are indicated in bold to emphasize clinical statistical significance. HR and 95% CI values are presented with three decimal places where applicable for precision. HR, hazard ratio; 95% CI, 95% confidence interval; GNRI, Geriatric Nutritional Risk Index.

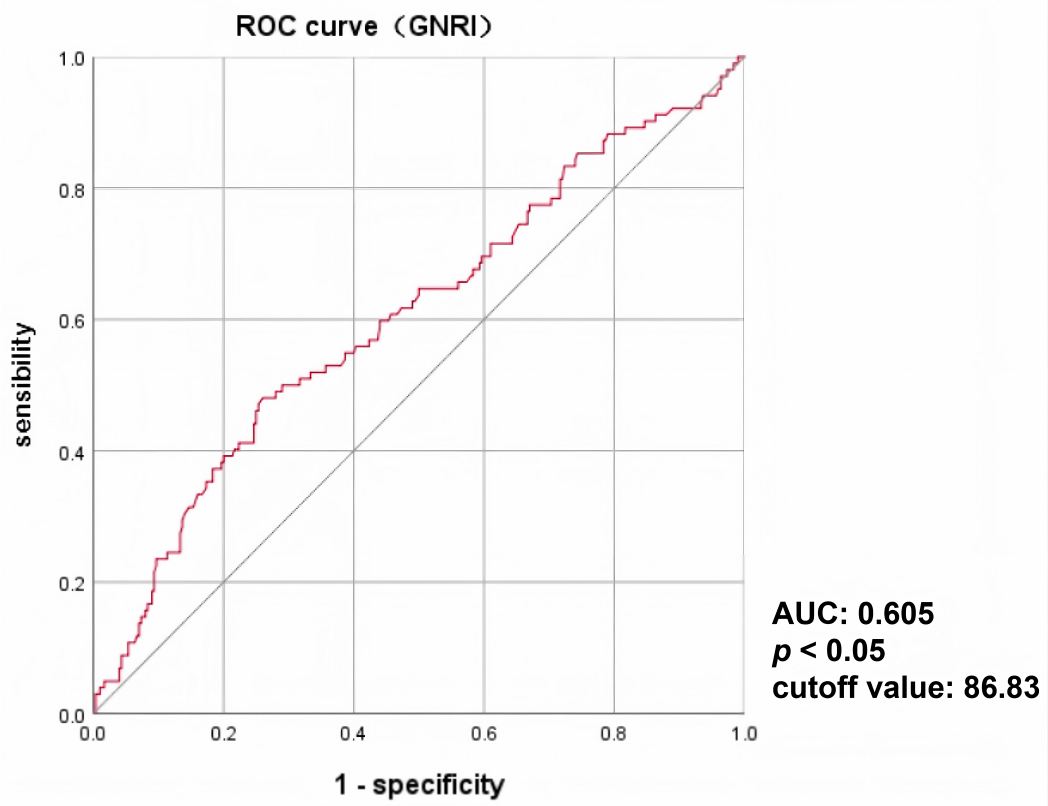

Fig. 3. ROC curve for GNRI scores to predict all-cause mortality. GNRI, Geriatric Nutritional Risk Index; ROC, receiver operating characteristic; AUC, area under the curve.

creatinine were 0.565, 0.652, and 0.635, respectively. These findings suggest that the GNRI has relatively limited predictive ability compared to age and creatinine.

Discussion

The GNRI is a simple and objective approach for assessing the nutritional status of patients using their body weight, body height, and serum albumin levels. A prior study demonstrated a strong association between GNRI scores and lean tissue indices, indicating that the baseline GNRI score can accurately predict the future

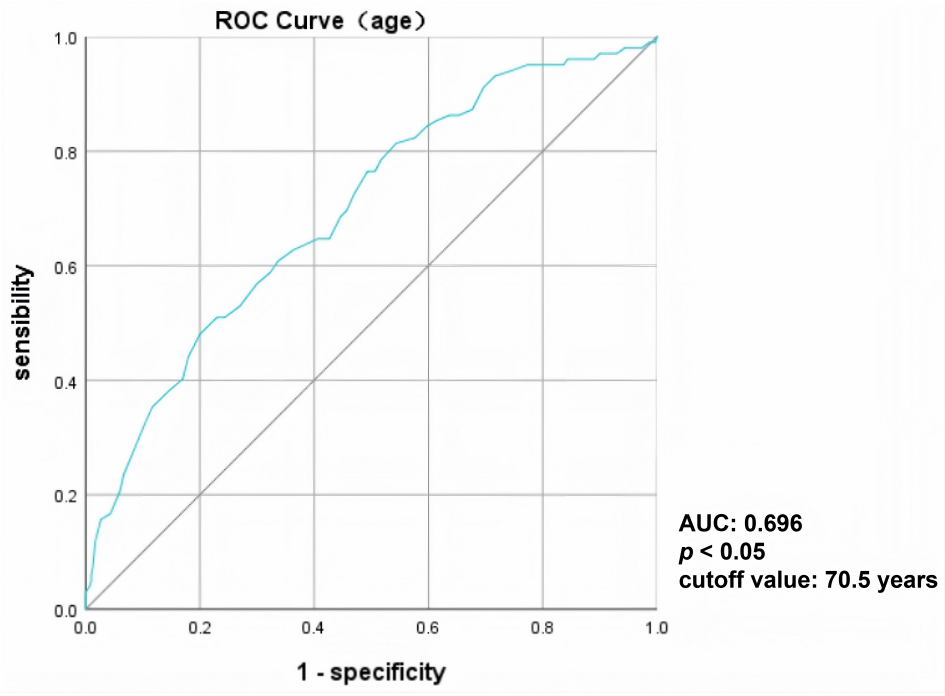

Fig. 4. ROC curve for age to predict all-cause mortality.

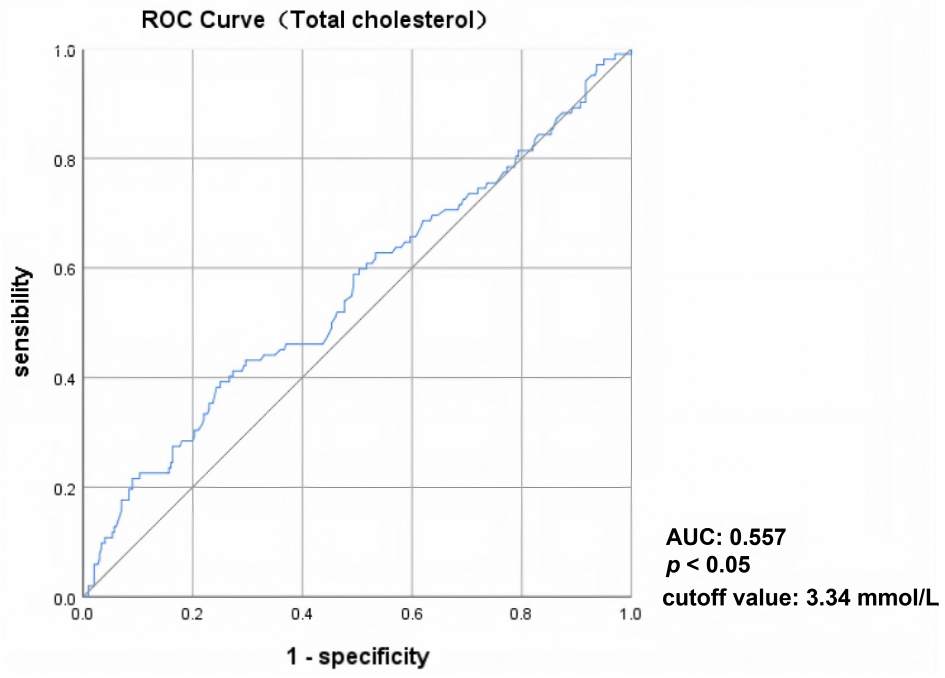

Fig. 5. ROC curve for total cholesterol to predict all-cause mortality.

nutritional status of hemodialysis patients (Mizuiri et al, 2021). Another group of researchers reported that hemodialysis patients with higher GNRI scores, indicating better nutrition status, showed higher bone mineral density and lean BMI compared to those with low scores (Chen et al, 2019). Additionally, changes in GNRI score have been closely aligned with variations in other nutritional biomarkers, body composition parameters, and serum interleukin-6 levels in patients un-

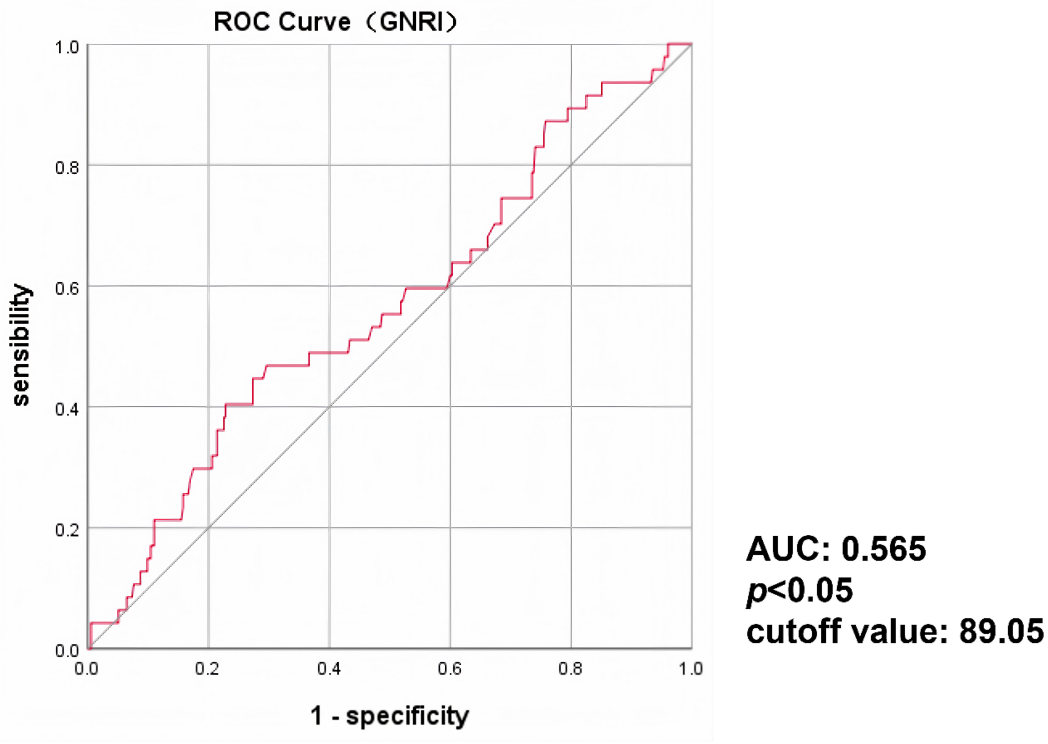

Fig. 6. ROC curve analysis of GNRI for predicting cardiovascular mortality.

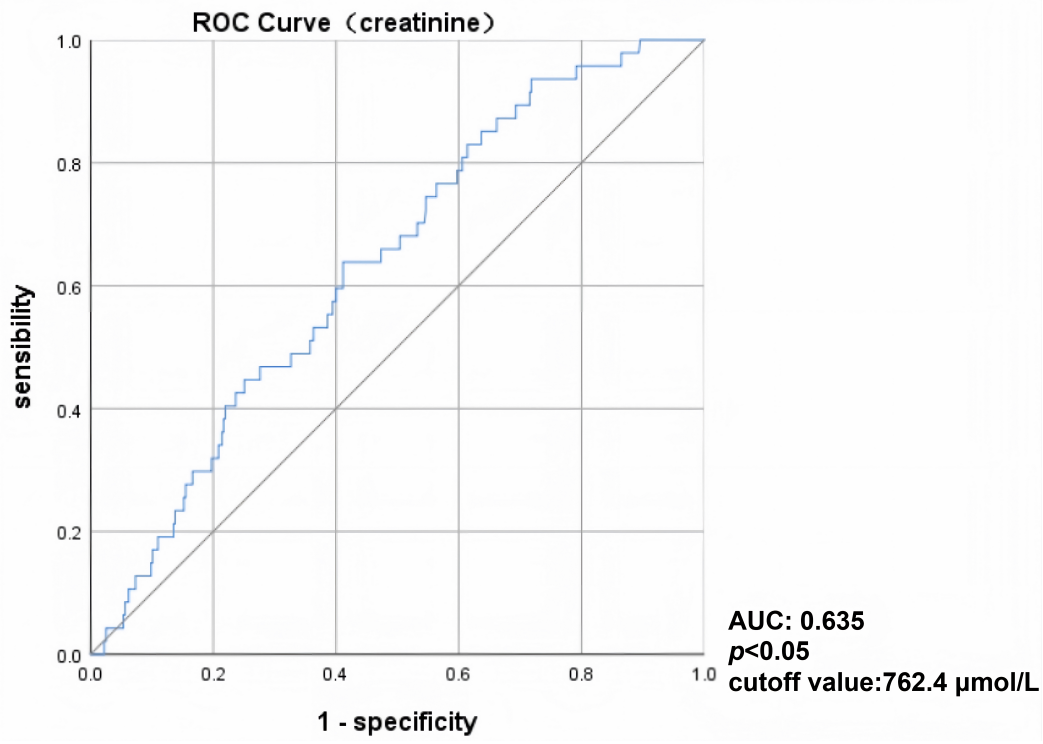

Fig. 7. ROC curve of creatinine for predicting cardiovascular mortality.

dergoing maintenance hemodialysis (Beberashvili et al, 2013). These observations highlight the significance of GNRI as a promising tool for assessing the nutritional status of hemodialysis patients. Additionally, numerous studies have validated the

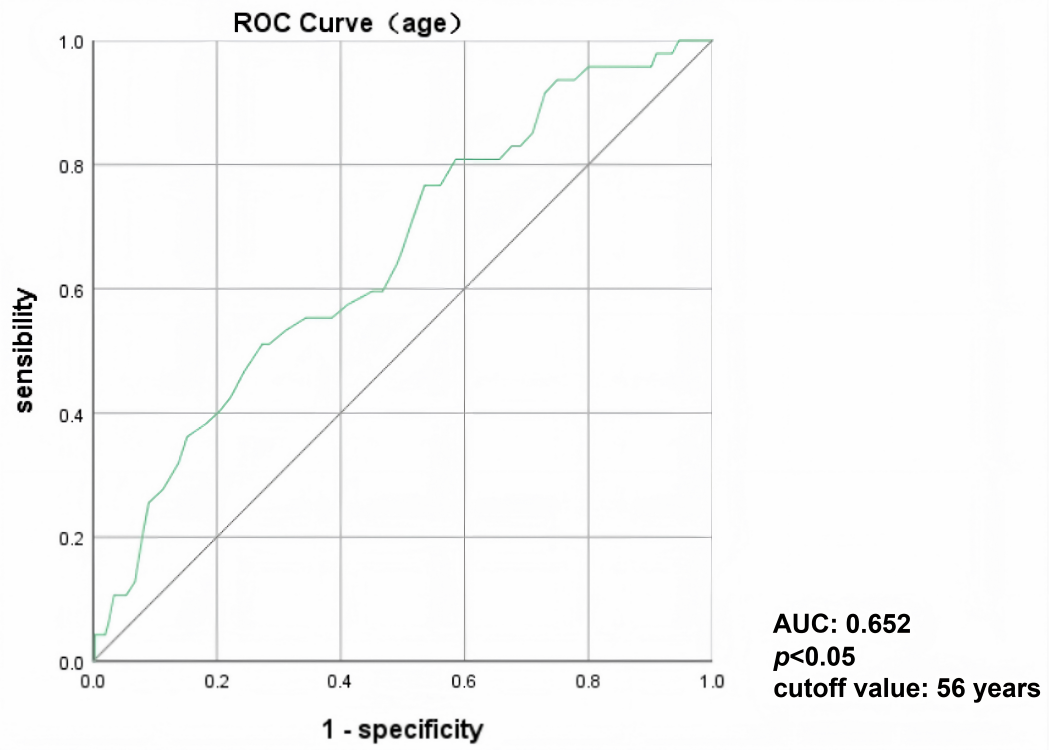

Fig. 8. ROC curve analysis of age for predicting cardiovascular mortality.

GNRI's efficacy in nutritional assessment and prognosis prediction among Asian patients undergoing maintenance dialysis (Jung et al, 2014; Kang et al, 2013; Takahashi et al, 2014; Tsai et al, 2014).

The present study revealed that lower GNRI scores were correlated with a higher risk of all-cause and cardiovascular mortality in patients undergoing maintenance hemodialysis. These findings align with the results reported by Yamada et al (2020), who reported that among 3536 maintenance hemodialysis patients, lower GNRI scores and creatinine indices were both associated with a higher risk of all-cause mortality. They suggested that the GNRI might be a reliable predictor of prognosis in hemodialysis patients due to its simplicity compared to the creatinine index. While serum creatinine was observed as an independent predictor of all-cause mortality in the univariate analysis, this association was no longer substantial in the multivariate analysis (Tables 3,4). Similarly, Xiong et al (2020) reported a significant association of low GNRI scores with elevated cardiovascular events, worsening of renal function, and all-cause mortality in 2791 patients with CKD. Our findings further validated that after adjusting for multiple confounders, age, serum cholesterol, and GNRI scores remained significant predictors for all-cause mortality, highlighting the significance of low GNRI scores as a promising predictor of mortality risk in hemodialysis patients. Furthermore, a similar association was observed between low GNRI scores and elevated risk of cardiovascular mortality (Tables 4,6).

Historically, serum albumin has been shown as an effective prognostic predictor in hemodialysis patients, findings that align with our results. However, it is crucial to note that hypoalbuminemia can result not only from malnutrition but also

from other factors such as inflammation and sodium or water retention. Therefore, while hypoalbuminemia and low BMI both indicate malnutrition, relying on these markers alone is insufficient for diagnosing malnutrition or accurately predicting prognosis. The GNRI may exhibit a higher predictive value for identifying malnutrition risk and poor prognosis than a single variable, such as serum albumin or BMI (Bouillanne et al, 2005; Jung et al, 2014). Researchers have further demonstrated that incorporating the GNRI with serum albumin and BMI allows for better evaluation of an individual's protein and energy balance, thereby improving the accuracy of malnutrition assessments.

The detrimental influence of age on all-cause and cardiovascular mortality in hemodialysis patients is well-established. The present study analyzed the influence of age, serum cholesterol, and the GNRI using ROC curves, indicating that serum cholesterol had an insignificant influence after adjustments (Figs. 3,4,5). Furthermore, the optimal thresholds for age and GNRI scores for predicting the adverse outcomes were also determined. Kobayashi et al (2010) reported a GNRI cut-off value of 90 for predicting outcomes in patients undergoing maintenance hemodialysis. Patients with GNRI scores of <90 showed more severe chronic inflammation, increased C-reactive protein levels, and a higher risk of mortality compared to those with GNRI scores ≥ 90. These patients also exhibited reduced serum albumin, blood urea nitrogen, and creatinine levels, a finding that is consistent with our study. Similarly, Panichi et al (2014) reported a GNRI score of <92 as an important predictor of all-cause mortality but not cardiovascular mortality in hemodialysis patients. Researchers have revealed that PEW in hemodialysis patients may alter the risk of cardiovascular events, which may occur more frequently in obese patients with high serum cholesterol levels.

In our study, ROC curve analysis for predicting cardiovascular mortality in hemodialysis patients indicated that the GNRI was not a significant predictor (Figs. 6, 7,8). A plausible explanation for this result is the competing risk between overall survival and cardiovascular events in malnourished individuals. Additionally, compared to other studies, the alleviated GNRI cut-off value identified in our study compared to previous investigations may be due to the racial differences, variation in ideal body weight selected, and other mortality-influencing factors such as geographic location, culture, dietary habits, lifestyle, and socioeconomic conditions. Specifically, the ideal body weight used to calculate the GNRI score in our study was based on a BMI of 22.5, a reference standard in the Italian population.

This study has several limitations that should be addressed when interpreting the results. First, the predetermined inclusion criteria limited the study cohort to patients from a single center, introducing potential selection bias and restricting the generalizability of the findings to a broader population of hemodialysis patients. Second, information bias could have influenced the results due to the collection of clinical data from medical records, where inaccuracies or incomplete data might have been included. Although efforts were made to minimize these biases, such as strict adherence to inclusion criteria and rigorous data verification processes, their potential impact on the outcomes cannot be entirely ruled out. Lastly, the study's observational design impedes the establishment of causal relationships, and residual

confounding may persist despite adjustments for known confounders employing multivariate models. Further investigation involving larger, multi-center cohorts and prospective study designs are needed to validate our findings.

In conclusion, after adjusting for confounding factors, a low GNRI score was observed to be closely correlated with an increased risk of all-cause and cardiovascular mortality in hemodialysis patients. These findings underscore the significance of the GNRI as a promising prognostic predictor in this patient cohort.

Conclusion

This study identified age, serum albumin, serum creatinine, and GNRI as significant predictors of all-cause mortality, with GNRI emerging as a strong independent predictor. These findings underscore the significance of nutritional status in assessing patient prognosis. Regular monitoring of GNRI, along with other key variables, could enhance risk stratification and patient management. Further research is recommended to explore the potential benefits of early nutritional interventions in improving outcomes for high-risk populations.

Key Points

- This study identified age, serum albumin, serum creatinine, and GNRI as significant predictors of all-cause mortality.
- GNRI was observed as a strong independent predictor, highlighting the crucial role of nutritional status in assessing patient outcomes.
- Regular monitoring of GNRI could improve patients' risk stratification and clinical management.
- The findings support further investigation into early nutritional interventions to reduce mortality risk in high-risk populations.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding authors upon request.

Author Contributions

YTY, HH and YJY designed the research study. YW, QZ, QC and YH performed the research. XS, JH and JW analyzed the data. YTY wrote the first draft. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the Institutional Review Board of the First Affiliated Hospital of Nanchang University (Approval Number: IIT [2023] Ethical Review No. 401). An informed consent was obtained from each patient. The study design complied with the ethical principles outlined in the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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