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Geriatric Nutritional Risk Index as a Possible Predictor of Decline in Kidney Function in Older People

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This study's preliminary results and abstract were presented at the 42nd Annual Meeting of the Korean Society of Nephrology.

Background: The Geriatric Nutritional Risk Index (GNRI) is associated with morbidity and mortality in older individuals. Our study explored the relationship between GNRI, decline in kidney function, and all-cause mortality in older individuals. **Methods:** This retrospective cohort study analyzed data from participants aged ≥60 years who underwent a general health checkup between 2002 and 2018. The primary exposure was the GNRI, divided into quartiles. The primary and secondary outcomes were a decline in kidney function assessed using the 5-year estimated glomerular filtration rate (eGFR) and all-cause mortality, respectively. **Results:** The analysis included a total of 1,599 participants (median age, 63 years; interquartile range [IQR], 61–67; 54% males). The mean±standard deviation of GNRI was 114±7. Compared with the highest GNRI quartile, the lower GNRI quartiles were associated with steeper 5-year slopes in eGFR, with a fully adjusted beta coefficient and 95% confidence intervals (CIs) of –0.50 (–0.86, –0.14), –0.29 (–0.63, 0.05), and –0.19 (–0.53, 0.14) for the first, second, and third GNRI quartiles, respectively. The median follow-up duration was 7.4 years (IQR, 4.6–12.4). During this period, we identified 108 deaths (7.8 per 1,000 person-years). The first GNRI quartile was associated with all-cause mortality compared to the highest GNRI quartile (hazard ratio of 2.20; 95% CI 1.23, 3.95). **Conclusion:** Nutritional status, as evaluated using the GNRI, was associated with 5-year changes in kidney function and all-cause mortality in older individuals.

Key Words: Older individual, Kidney, Mortality, Nutrition

INTRODUCTION

With the aging of the population, the number of older individuals is gradually increasing. The World Health Organization reported that individuals aged ≥ 60 years account for 12% of the global population; by 2050, this number is expected to rise to nearly 22%.[1] Older adults, compared to younger individuals, have age-specific illnesses, various types of chronic diseases, and the after-effects of these diseases, which can accumulate over time, leading to polypharmacy.[2-4] Malnutrition is common among older individuals.[5,6] Along with the aforementioned health conditions, social and environmental issues, inadequate food intake, and impaired physical function may contribute to the development of malnutrition in this population.[5,6] Malnutrition is associated with poor health outcomes, such as cardiovascular disease and mortality in older adults, and is currently considered a modifiable prognostic factor for these outcomes.[7-11]

In older people, kidney function tends to decline with age, due to complications from acute and chronic diseases, and depending on the medications used. This decline in kidney function may lead to clinical and public health burdens.[12,13] Therefore, kidney function must be monitored in older adults to ensure that they are not at risk for health issues associated with declining kidney function.

The Geriatric Nutritional Risk Index (GNRI) was originally developed as a tool for assessing the nutritional status of hospitalized older individuals. Moreover, it is calculated using serum albumin

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levels and body weight. A low GNRI is associated with an increased risk of morbidity and mortality in hospitalized older patients or patients with various diseases, including end-stage renal disease (ESRD), heart failure, cancer, and traumatic injuries.[14-18]

Studies examining the relationship between nutritional status and kidney function are limited.[11,19] Although studies have reported an association between a lower GNRI and progression to ESRD in patients with chronic kidney disease (CKD), studies showing the relationship between the GNRI and decline in kidney function assessed by estimated glomerular filtration rate (eGFR) changes in older adults are lacking.[11,20] Therefore, this study investigated the association of GNRI with the decline in kidney function and all-cause mortality over time in older individuals.

MATERIALS AND METHODS

Study Participants and Data Collection

This retrospective cohort study used de-identified data from participants who underwent a general health checkup at Samsung Changwon Hospital between January 1, 2002, and December 31, 2018. We included participants aged ≥60 years after excluding those without data on baseline body weight, height, serum albumin, and creatinine levels. Additionally, we excluded participants with a baseline eGFR <15 mL/min/1.73 m^2 or those without a follow-up examination on kidney function within 5 years.

Baseline information on age, sex, comorbidities (diabetes, hypertension, coronary artery disease, and stroke), current smoking status, body weight, height, systolic blood pressure (SBP), diastolic blood pressure (DBP), and laboratory variables, including hemoglobin, serum albumin, total cholesterol, serum glucose, serum creatinine, and albuminuria, was collected from the database. Albuminuria was defined as a urine protein dipstick test reading of ≥1.

This study was approved by the Institutional Review Board of Samsung Changwon Hospital (IRB No. SCMC 2022-01-008), which waived the requirement for informed consent from the participants because our study only retrospectively accessed a de-identified dataset based on the health screening cohort of the epidemiological research center at Samsung Changwon Hospital for analysis purposes.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[21]

Exposures and Outcomes

The primary exposure measure in this study was the GNRI, which was divided into quartiles. The primary outcome was a change in kidney function 5 years after baseline, which was assessed using the 5-year slope of eGFR. The secondary outcome was all-cause mortality 5 years after baseline. The GNRI was calculated using the following formula: 14.89 × serum albumin (g/dL) + 41.7 × (actual body weight [kg]) / (ideal body weight [kg]). The ideal body weight was calculated using the following formula: (height [m])^2 × 22 (kg/m^2). The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.[22] A negative slope indicates a decline in eGFR.

Statistical Analyses

Continuous and categorical variables for baseline characteristics were expressed as mean ± standard deviation or median (interquartile range [IQR]) and count (%), respectively. We determined the significance of the trends in the variables across the GNRI quartiles using linear regression analysis or the Wilcoxon-type nonparametric trend test, as appropriate. For the primary outcome variable, the 5-year slope of eGFR was estimated in participants with at least one follow-up eGFR data point measured between follow-up years 2 and 6, in addition to the baseline eGFR, using a linear mixed-effects model with adjustment for baseline eGFR, allowing for a random intercept and slope using an unstructured covariance matrix. We conducted linear regression analyses to assess the association between the categorized GNRI and the 5-year slope of eGFR, using the highest GNRI quartile as the reference. The analyses were hierarchically adjusted for baseline covariates including age, sex, presence of diabetes or hypertension, systolic blood pressure (SBP), diastolic blood pressure (DBP), and levels of serum hemoglobin, total cholesterol, serum glucose, and serum creatinine as follows: (1) unadjusted model; (2) model 1, which included age, sex, presence of diabetes or hypertension, SBP, DBP, and levels of serum hemoglobin, total cholesterol, and serum glucose; and (3) model 2, which included serum creatinine in addition to all variables included in model 1. The association between all-cause mortality and categorized GNRI was estimated using Cox proportional hazards regression models with the aforementioned adjustments. The survival curve was calculated using the Kaplan–Meier method to compare the cumulative incidence of all-cause mortality across the GNRI quartiles. Differences among groups were determined using the log-rank test.

Missing baseline parameters included diabetes, hypertension, coronary artery disease, stroke, smoking status, hemoglobin, total cholesterol, and albuminuria. The frequency of missing data was <0.7% for hemoglobin, total cholesterol, and albuminuria, whereas those for comorbidities and smoking status were <20.0% and 25.6%, respectively. Multiple imputations were performed using a multivariate normal model. The imputation model included all the variables of the fully adjusted model and an outcome variable using

50 imputed datasets. All statistical analyses were performed using STATA version 14.2 (StataCorp LLC, College Station, TX, USA).

RESULTS

Participant Characteristics

Data from 403,677 participants who received a health check-up between 2002 and 2018 were extracted from a de-identified dataset for analysis, and 22,632 participants aged 60 years and older were included in our study cohort. After excluding participants with missing data on baseline body weight, height, serum albumin, and serum creatinine, those with baseline eGFR less than 15 mL/min/1.73 m^2, and those without follow-up serum creatinine data, data from 1,599 participants were finally available for analysis. A flowchart of the cohort construction is shown in Supplementary Fig. S1.

Baseline characteristics of the participants in the GNRI quartiles are discussed in Table 1. The median age of the participants was 63 years (IQR, 61–67), and 54% were male. The mean GNRI scores were 113.7 ± 6.9. The median serum creatinine and eGFR levels were 0.9 mg/dL (IQR, 0.7–1.0) and 81 mL/min/1.73 m^2 (IQR, 72–93), respectively. The group with a higher GNRI was slightly younger, had a higher proportion of patients with diabetes and hypertension, and had a higher SBP and DBP.

Association between GNRI and the 5-Year Slope of eGFR

The median value of the eGFR slope was −0.44 mL/min/1.73 m^2 (IQR, −1.34 to 1.17) per year. The median values of the actual eGFR changes over 5 years by group were −3.36 (IQR, −7.48 to 1.12), −2.88 (−4.86 to 5.30), −2.65 (−7.46 to 7.67), and −1.91 (−3.67 to 8.42) mL/min/1.73 m^2 for the first, second, third, and fourth quartiles of GNRI, respectively ($p < 0.001$). In the linear regression analyses, the lower GNRI groups were associated with steeper 5-year eGFR slopes, as compared with the highest GNRI group (the reference group). The fully adjusted beta coefficients (β) and 95% confidence intervals (CIs) were −0.50 (−0.86, −0.14), −0.29 (−0.63, 0.05), and −0.19 (−0.53, 0.14) for the first, second, and third quartiles of GNRI, respectively (Fig. 1). Each 10-point decrease in GNRI level was associated with a steeper decline in the 5-year slope of eGFR by 0.26 mL/min/1.73 m^2 per year. The fully adjusted β and 95% CI were −0.26 (−0.45, −0.08).

In subgroup analyses, the association between the GNRI and 5-year eGFR slope was not modified by age, sex, presence of diabetes or hypertension, SBP, DBP, and levels of serum hemoglobin, total cholesterol, and serum creatinine (all for interaction $p > 0.5$).

Table 1. Baseline characteristics of 1,599 participants aged ≥60 years stratified by baseline Geriatric Nutritional Risk Index

	Geriatric Nutritional Risk Index					p-value for trend
	Total	Quartile 1 (81.3–109.1)	Quartile 2 (109.1–113.6)	Quartile 3 (113.6–118.0)	Quartile 4 (118.0–137.2)	
Number of participants	1,599	399	400	400	400	
Age (y)	63 (61–67)	64 (61–68)	64 (61–67)	63 (61–66)	63 (61–66)	0.031
Sex, male (%)	54	55	55	52	55	0.643
Comorbidities (%)						
Diabetes	14.1	11.2	14.0	13.0	18.2	0.022
Hypertension	36.8	24.3	32.7	37.7	52.1	< 0.001
Coronary artery disease	6.0	5.9	4.2	6.2	7.6	0.225
Stroke	2.8	1.3	3.2	3.4	3.4	0.114
Current smoker (%)	9.9	15.8	5.4	7.7	10.8	0.095
SBP (mmHg)	131 ± 18	127 ± 20	129 ± 17	133 ± 16	136 ± 18	< 0.001
DBP (mmHg)	77 ± 11	74 ± 13	76 ± 10	78 ± 10	79 ± 12	< 0.001
Body weight (kg)	63 ± 10	56 ± 8	61 ± 8	64 ± 8	71 ± 9	< 0.001
Height (cm)	161 ± 9	161 ± 8	161 ± 9	161 ± 9	162 ± 9	0.937
Laboratory parameters						
Hemoglobin (g/dL)	14 ± 1	14 ± 1	14 ± 1	14 ± 1	15 ± 1	< 0.001
Serum albumin (g/dL)	4.6 ± 0.3	4.3 ± 0.3	4.5 ± 0.2	4.6 ± 0.2	4.8 ± 0.3	< 0.001
Total cholesterol (mg/dL)	204 ± 40	197 ± 37	204 ± 38	207 ± 40	207 ± 43	< 0.001
Serum glucose (mg/dL)	94 (87–104)	90 (83–99)	93 (87–103)	94 (88–103)	99 (90–111)	< 0.001
Serum creatinine (mg/dL)	0.9 (0.7–1.0)	0.9 (0.7–1.0)	0.9 (0.7–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.1)	< 0.001
Proteinuria (%)	1.2	2.3	0.5	0.8	1.3	0.253

Values are presented as median (interquartile range) or mean±standard deviation.
SBP, systolic blood pressure; DBP, diastolic blood pressure.

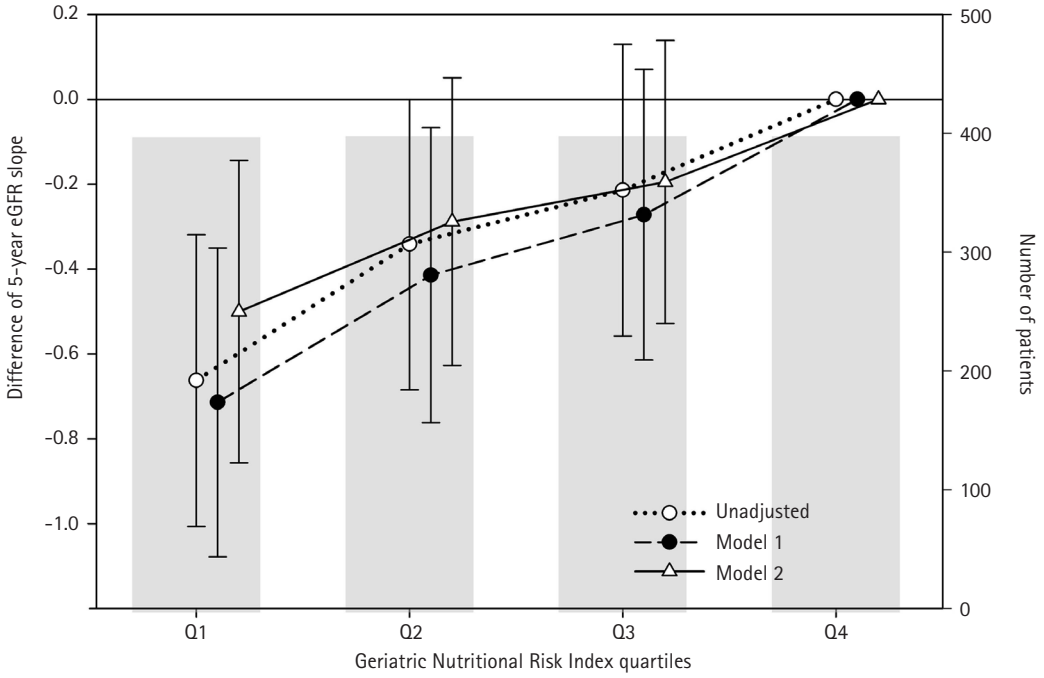

Fig. 1. Association between categorized Geriatric Nutritional Risk Index and 5-year slope of estimated glomerular filtration rate (eGFR). Points and bars represent beta coefficients and 95% confidence intervals, respectively. Model 1 is unadjusted. Model 2 is adjusted for age, sex, diabetes, hypertension, systolic blood pressure, diastolic blood pressure, hemoglobin, total cholesterol, and serum glucose. Model 3 is adjusted for all variables included in model 2 as well as baseline serum creatinine.

Association between GNRI and All-Cause Mortality after 5 Years from Baseline

Among the 1,599 participants, the median follow-up duration was 7.4 years (IQR, 4.6–12.4). During this period, we identified 108 (7.8 per 1,000 person-years) all-cause deaths. The Kaplan–Meier curve for cumulative all-cause mortality stratified by GNRI quartiles is shown in Fig. 2. All-cause mortality significantly increased in the first GNRI quartile (log-rank $p < 0.001$). The Cox regression analyses showed similar results: compared to the highest quartile of GNRI, the fully adjusted hazard ratios and 95% CIs were 2.20 (1.23, 3.95), 0.65 (0.33, 1.27), and 1.06 (0.57, 2.00) for the first, second, and third quartiles of GNRI, respectively (Table 2).

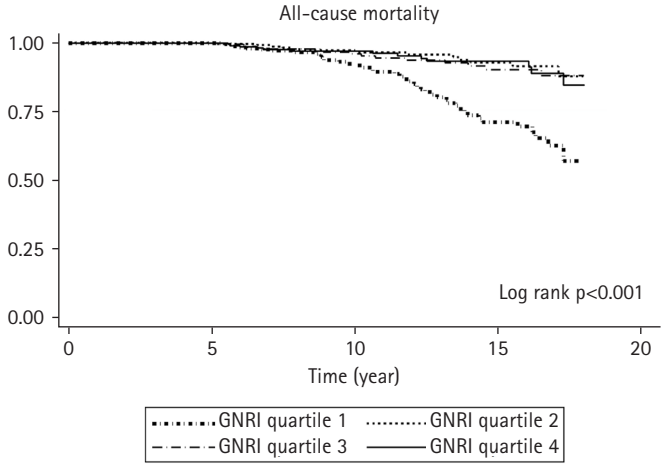

Fig. 2. Kaplan–Meier curve for all-cause mortality according to the Geriatric Nutritional Risk Index (GNRI) (log-rank p<0.001).

DISCUSSION

We conducted this study to investigate the association between GNRI, changes in kidney function over time, and all-cause mortality in older adults. Our findings indicated that individuals with lower GNRI values experienced a more rapid 5-year decline in eGFR. However, this significant association was observed only in the first GNRI quartile after adjusting for baseline kidney function. In addition, we observed that the first GNRI quartile was associated with an increased risk of all-cause mortality.

Previous research on the relationship between the GNRI and clinical outcomes has primarily focused on hospitalized older individuals or patients with various illnesses. Few studies have examined the relationship between GNRI and kidney function, particularly as assessed by eGFR changes, in older adults. While studies have suggested a relationship between a low GNRI and an increased risk of progression to ESRD in patients with CKD,[11,20] other studies, such as that by Kiuchi et al.,[23] did not find such an association. We observed that a lower GNRI was associated with a

Table 2. Unadjusted and adjusted hazard ratios for all-cause mortality according to the categorized Geriatric Nutritional Risk Index

	Unadjusted		Model 1		Model 2	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Quartile 1	2.75 (1.61, 4.73)	< 0.001	2.24 (1.25, 3.98)	0.006	2.20 (1.22, 3.95)	0.008
Quartile 2	0.86 (0.45, 1.66)	0.655	0.65 (0.33, 1.28)	0.216	0.65 (0.33, 1.27)	0.209
Quartile 3	1.13 (0.60, 2.10)	0.706	1.07 (0.57, 2.00)	0.838	1.06 (0.57, 2.00)	0.851
Quartile 4	Reference		Reference		Reference	

Model 1 is adjusted for age, sex, diabetes, hypertension, systolic blood pressure, diastolic blood pressure, hemoglobin, total cholesterol, and serum glucose. Model 2 is adjusted for all variables included in model 2 as well as baseline serum creatinine.
HR, hazard ratio; CI, confidence interval.

steeper decline in kidney function in older individuals, which is consistent with the findings of previous studies. However, our study is distinct in that it specifically focused on changes in kidney function as assessed by eGFR. We observed that individuals with lower GNRI values experienced a more rapid decline in kidney function than those with higher GNRI values, despite having fewer traditional risk factors for CKD, such as diabetes and hypertension. Our findings indicate that the nutritional status assessed by the GNRI may be a valuable tool for predicting the decline in kidney function in older individuals, regardless of other comorbidities.

The mechanisms driving the relationship between GNRI and kidney function are currently unclear. However, inflammation is one potential cause. The GNRI is calculated using albumin and body weight as its main components, both of which are associated with malnutrition and inflammation.[24,25] Low-grade inflammation is observed in many older individuals and can contribute to kidney fibrosis.[25-27] Therefore, inflammation may link low GNRI to a decline in kidney function in older individuals.

We observed a significant association between a low GNRI and all-cause mortality only in the first quartile among the GNRI quartiles. This may be because our study population consisted of relatively healthy older individuals who underwent regular health checkups and had higher GNRI levels than those in previous studies.[11] Additionally, the number of all-cause deaths in our cohort was relatively small (6.8%). As a result, our study may not have had sufficient power to detect a more gradual relationship between the GNRI and all-cause mortality.

Our study has several limitations. First, as our study was observational in nature, confounding factors may remain unaccounted for even after adjustment. We did not consider the participants' dietary intake, health behaviors, and socioeconomic status, all of which are associated with nutritional status.[28,29] These factors may affect kidney function.[30,31] Second, while we used multiple imputations to address missing data and adjusted for blood pressure and serum glucose, a significant amount of information was missing regarding comorbidities, such as diabetes and hypertension, in our population. This may have introduced bias into our data analysis. Finally, our results may not be generalizable to older individuals, as only 14% of the participants were > 70 years of age. In addition, changes in medical standards during the long-term follow-up period may have affected the health status and outcomes of our population.

In conclusion, our study suggests that a lower GNRI is associated with a steeper decline in eGFR over 5 years and a higher risk of all-cause mortality in older individuals. Therefore, the assessment of nutritional status using the GNRI as a modifiable risk factor should be considered a predictor of kidney function decline in older individuals. However, these findings require validation in larger populations of older individuals, and future studies are needed to determine whether improving nutritional status can prevent kidney function decline in these populations.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization, YJL; Data curation, YJL, NGK; Investigation and Methodology, YJL, NGK; Writing–original draft, SMY, NGK, YJL; Writing–review & editing, YJL.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0215.

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