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CLINCAL STUDY

Potential role of the geriatric nutritional risk index as a novel risk factor for the development of non-valvular atrial fibrillation in patients with heart failure

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ABSTRACT

PURPOSE: The geriatric nutritional risk index (GNRI) is a simple and objective nutritional assessment tool for elderly patients. Lower GNRI values are associated with a worse prognosis in heart failure with reduced ejection fraction (HFrEF). Our aim is to investigate the relationship between malnutrition and follow-up cardiovascular (CV) events in HFrEF.

METHODS: A retrospective study was performed on 362 patients with HFrEF. The baseline GNRI was calculated at the first visit. The patients were divided into three groups according to the GNRI: >98, no-risk group; 92 to ≤98, low risk group; 82 to <92, moderate-to-high-risk group. The study endpoint was a composite of follow-up CV events, including all-cause mortality, non-valvular atrial fibrillation (NVAF) , need for cardioverter defibrillator (ICD) therapy, HfrEF-related hospitalizations and need for percutaneous coronary interventions (PCIs).

RESULTS: Follow-up data showed that the group with moderate-to-high risk had a significantly higher incidence of NVAF, PCIs and all-cause mortality compared to other groups ($p<0.001$, p: 0.026 and $p<0.001$ respectively). However, hospitalizations and the need for ICD placement were similar as compared between groups ($p>0.05$). Mean GNRI value was 83.3 in NVAF patients and 101.1 in patients without NVAF ($p<0.001$). Kaplan Meier survival analysis showed that patients from the group with moderate-to-high risk had a significantly worse survival rate ($p < 0.001$). In the multivariate Cox regression analysis, the group with moderate-to-high risk (HR=3.872) and ICD implantations (HR=4.045) were associated with increased mortality.

CONCLUSION: The GNRI value may have a potential role for predicting future events, especially NVAF in patients with HfrEF *(Tab. 4, Fig. 2, Ref. 27)*. Text in PDF *www.elis.sk*

KEY WORDS: malnutrition, heart failure, atrial fibrillation.

Introduction

The aging process is believed to be one of the causes of malnutrition, which itself can be the cause of illness as it is related to many health problems. Malnutrition is still underrecognized, resulting mostly in deprived nutritional status, morbidity, prolonged hospitalization, increased health care costs, and reduced quality of life among the elderly population. Thus, the management and prevention steps to overcome the deterioration of health and well-being among the elderly are crucial, and nutritional screening and assessment are important tasks to be carried out (1).

The geriatric nutritional risk index (GNRI) is a simple and well-established nutritional screening tool for elderly patients. GNRI has been validated as a screening tool for malnutrition in elderly patients by using three objective parameters that are routinely measured; body height, weight and serum albumin (2). GNRI was developed in 2005 by Bouillanne et al (3) and it was designed specifically for the elderly to identify and predict the nutrition-related complications.

Malnutrition is also an independent predictor of mortality, with several reports showing a correlation between malnutrition and mortality in patients with cardiovascular disease (CVD) (4). Epidemic studies have used the GNRI to predict outcomes of CVD and showed that the GNRI score was independently associated with cardiovascular (CV) events in patients with chronic heart failure (HF) (5). Several single-center studies found that malnutrition, as assessed by GNRI, was associated with worse prognosis in patients with HF (5–6).

These results indicate that GNRI can be a powerful predictor for clinical outcomes in different diseases and may be widely used in clinical practice. This study investigated the long-term clinical outcomes of a sample of patients with HF from South-Eastern

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Anatolia. We performed a retrospective evaluation of patients with HF and sought the association between GNRI and mortality, non-valvular atrial fibrillation (NVAF), need for cardioverter defibrillator (ICD) therapy, HF-related hospitalizations and need for percutaneous coronary interventions (PCIs).

Methods

Study population

There were 1,838 patients hospitalized for decompensated HF in our coronary care unit between January 1, 2015 and December 31, 2017. Follow-ups were conducted until December 31, 2020. Among these patients, 927 had HF with reduced ejection fraction (EF < 50 %). According to the following inclusion criteria, 362 patients were eligible for final analysis.

Inclusion criteria;

- Complete admission and 6-month follow-up data available
- Left ventricle ejection fraction (LVEF) < 50 %
- BNP level > 99 % compared to age-matched controls
- Age over 65 years
- Admission electrocardiography showing sinus rhythm and no history of paroxysmal atrial fibrillation
- Discharge with recovery

Exclusion criteria were as follows;

- Admission with acute coronary syndrome
- LVEF > 50 % (HF with preserved ejection fraction)
- History of cardiac surgery
- Moderate-to-severe valvular heart disease
- History of atrial or ventricular arrhythmias
- Chronic liver disease
- Presence of active infection (as regards to albumin levels)
- Presence of cardiogenic shock at admission

Data collection

Baseline clinical data were collected for each patient. Patient-related information collected at discharge included medical history, laboratory test results, echocardiographic findings, and prescriptions, and the data were recorded into a computer database. Blood tests were performed to determine hemoglobin, sodium, serum creatinine, plasma brain natriuretic peptide (BNP), albumin, total cholesterol, and c reactive protein (CRP) levels. The estimated glomerular filtration rate (eGFR) was calculated using the following formula: eGFR = 194 × serum creatinine −1094× age in years−287 for male patients. The adjusted eGFR value for female patients was calculated using the following formula: eGFR female = eGFR × 0.739 (7). The BMI was calculated as body weight in kilograms divided by the square of the height in meters.

Demographic properties and comorbidities were identified from patients' hospital records and physical examination at the time of presentation. We used standard definitions for risk factors as described in current guidelines. Hypertension (HT) was defined as a systolic blood pressure (SBP) ≥ 140 mm Hg, diastolic blood pressure (DBP) ≥ 90 mm Hg, or current use of antihypertensive medication (8). Diabetes mellitus (DM) was defined as a fasting serum glucose ≥ 126 mg/dL, hemoglobin-A1C ≥ 6.5 %, or the use of blood glucose-lowering agents (9). The standards of the American Society of Echocardiography were used for all measurements. HF was defined as a systolic ejection fraction below 50 % (10). The study was approved by the local ethics committee.

Assessment of nutritional status using the geriatric nutritional risk index

The GNRI was developed by Bouillanne et al (3) as a screening tool for undernutrition in hospital populations. In the present study, the GNRI was calculated from serum albumin and BMI obtained at discharge. We adopted Kinugasa's measurement method as follows; (11)

GNRI = 14.89*serum albumin (g/dL) + 41.7*present body weight /[(height)² (m)²*22] = 14.89*serum albumin (g/dL) + 41:7 * BMI/22. BMI/22 was set to 1 when the patient's BMI/22 was greater than 1.

Grouping of patients

The patients were divided into different risk groups based on their GNRI, according to the classification of Bouillanne et al (3), as follows: GNRI > 98, no-risk group; GNRI 92 to ≤ 98, low nutrition-related risk group; GNRI 82 to < 92, moderate-to-high nutrition-related risk group; GNRI < 82, high nutrition-related risk group. In this study, the patients were divided into 3 groups based on GNRI values because the number of patients with GNRI < 82 was too small to be analyzed: Group I, no-risk group; Group II, low nutrition-related risk group; Group III, moderate-to-high nutrition-related risk group.

Follow-up

The eligible patients were re-evaluated at 6-month intervals. Patients whose detailed data could not be retrieved were excluded from the study (565 patients). Follow-up data were obtained from the hospital or health center registry, clinical notes, or by telephone surveys conducted by two cardiologists. Complete follow-up was achieved only for 362 patients with complete follow-up data, including all-cause mortality, new onset of NVAF, need for ICD therapy, HF-related hospitalizations and need for PCIs. Hospitalization was defined as a hospital stay (≥ 2 days) for HF symptoms, especially dyspnea.

Statistical analyses

All of the statistical analyses were performed using SPSS 23 for Windows (SPSS Inc., Chicago, IL, USA). The distribution of data was evaluated by using Shapiro-Wilk test or Kolmogorov-Smirnov test. Baseline characteristics were presented as mean ± standard deviation or median (quartile deviation), and categorical variables were presented as percentages. For the categorical variable Pearson Chi-Square or Fisher exact test and for continuous variables one-way ANOVA, Kruskal-Wallis test, independent sample t-test or Mann-Whitney test was applied as appropriate. Kaplan-Meier curves were plotted and after checking the assumption of proportional hazard, the log-rank test was used to demonstrate the association between survival and GNRI levels. Factors such as age, sex, chronic diseases, cardiological statements, and geriatric conditions that are accepted as general factors closely

Tab. 1. Baseline and follow-up characteristics for GNRI levels.

Variables	Overall (n=362)	No risk (n=206)	Low risk (n=64)	MTH risk (n=92)	p
Age (years)	72 (3.13)	72 (3.5)	72 (3)	70.5 (3.5)	0.691
Sex (male, %)	261 (72.1 %)	149 (72.3 %)	47 (73.4 %)	65 (70.7 %)	0.922
Weight (kg)	80 (7.5)	80 (7.5)	80 (5)	80 (7.5)	0.485
BMI	26.2 (1.5)	27.68 (1.78)	26.20 (1.60)	25 (1.05)	**<0.001***
Systolic blood pressure (mmHg)	120 (12.5)	125 (12.5)	120 (13.75)	120 (12.50)	0.931
Diastolic blood pressure (mmHg)	75 (7.5)	75 (7.5)	75 (7.5)	80 (7.5)	0.991
Heart rate (beat/min)	79.5 (7)	78 (7)	78 (7.5)	78 (7)	0.674
Diabetes mellitus (n, %)	147 (40.6 %)	85 (41.3 %)	24 (37.5 %)	38 (41.3 %)	0.883
Hypertension (n, %)	186 (51.4 %)	101 (49 %)	30 (46.9 %)	55 (59.8 %)	0.171
Smoking (n, %)	139 (38.4 %)	73 (35.4 %)	32 (50 %)	34 (37 %)	0.109
CVO (n, %)	11 (3.0 %)	10 (4.9 %)	0	1 (1.1 %)	0.087
CABG (n, %)	38 (10.5 %)	15 (7.3 %)	9 (14.1 %)	14 (15.2 %)	0.067
PCI history (n, %)	90 (24.9 %)	47 (22.8 %)	17 (26.6 %)	26 (28.3 %)	0.566
HF (n, %)	45 (12.4 %)	23 (11.2 %)	8 (12.5 %)	14 (15.2 %)	0.592
Malignancy (n, %)	8 (2.2 %)	5 (2.4 %)	1 (1.6 %)	2 (2.2 %)	1.000
CKI (n, %)	23 (6.4 %)	11 (5.3 %)	4 (6.3 %)	8 (8.7 %)	0.607
Hemodialysis (n, %)	4 (1.1 %)	1 (0.5 %)	1 (1.6 %)	2 (2.2 %)	0.276
LVEF (%)	40 (3.5)	40 (4.25)	40 (2.75)	40 (5)	0.510
Leukocytes (×10³ /μL)	10.75 (2.30)	11 (2.38)	9.5 (2.05)	10.6 (2.14)	0.693
Hemoglobin (g/dL)	13.50±1.91	13.34±1.90	13.78 2.04	13.48±2.53	0.298
Hematocrit (%)	39.22±5.05	38.85±4.91	39.86±5.50	38.96±5.08	0.324
Platelets (×10³ /μL)	250.5 (70.91)	256 (46)	245 (59)	247 (37.63)	0.687
Fasting plasma glucose (mg/dL)	135.5 (41.5)	134 (42.25)	143 (39.50)	134.5 (42.5)	0.548
Albumin (g/dL)	3.27 (0.35)	3.5 (0.24)	3 (0.25)	2.70 (0.15)	**<0.001***
Urea (mg/ dl)	33 (7.5)	34 (7.5)	32 (9.25)	35 (9)	0.681
Creatinine (mg/dL)	0.80 (0.10)	0.8 (0.10)	0.8 (0.13)	0.8 (0.20)	0.280
eGFR (mL/min)	92 (12)	94 (11)	92 (11.25)	85.5 (14.5)	0.085
Sodium (mEq/L)	138 (2)	138 (1.8)	18 (2)	138 (2)	0.574
Potassium (mEq/L)	4.2 (0.30)	4.2 (0.30)	4.2 (0.23)	4.25	0.480
ALT (IU/L)	22 (6.5)	23 (8)	21 (8.5)	23.5 (6.13)	0.958
AST (IU/L)	30 (12.5)	29 (10.5)	27 (13.5)	33 (12)	0.216
LDL (mg/dL)	133 (20.5)	130 (20)	128 (23.5)	137 (21.5)	0.579
Triglycerides (mg/dL)	153.5 (5.88)	148 (52.25)	142 (55)	163.5 (62.25)	0.788
HDL (mg/dL)	40 (6.5)	39 (6.75)	42 (7.25)	40.5 (6.13)	0.847
Total cholesterol(mg/dL)	193 (29)	190 (26.5)	187 (36)	202 (27.25)	0.711
Direct bilirubin (mg/dL)	0.10 (0.01)	0.10 (0.01)	0.10 (0.03)	0.10 (0.02)	0.215
Indirect bilirubin (mg/dL)	0.50 (0.17)	0.53 (0.17))	0.60 (0.17)	0.48 (0.17)	0.314
BNP (pg/mL)	1060 (962)	850 (996)	1080 (1238)	1200 (757)	0.768
Troponin (ng/mL)	755.5 (1078)	556 (726)	673 (1237)	1066.5 (1376)	0.120
CKMB (U/L)	15.15 (7.21)	14.9 (5.9)	14.4 (7.10)	14.05 (10.76)	0.947
Uric acid (mg/dL)	5.45 (1.05)	5.2 (1.1)	5.3 (1.08)	5.7 (1.22)	**0.032***
INR	1 (0.02)	1.00 (0)	1.00 (0.05)	1.00 (0.05)	0.172
CRP (mg/L)	5.6 (4.40)	5.5 (4.2)	5 (4.975)	5.8 (5.44)	0.682
Follow-up (month)	32.50 (2.5)	33 (2.5)	33 (2.5)	33 (2.5)	0.884
Follow-up ICD (n, %)	69 (19.1 %)	37 (18 %)	14 (21.9 %)	18 (19.6 %)	0.796
Follow-up AF (n, %)	53 (14.6 %)	6 (2.9 %)	5 (7.8 %)	42 (45.7 %)	**0.001***
Hospitalization times	3 (1)	2 (1)	3 (1)	3 (1)	0.225
Follow-up PCI (n, %)	132 (36.5 %)	65 (31.6 %)	23 (35.9 %)	44 (47.8 %)	**0.026***
Mortality (n, %)	44 (12.2 %)	13 (6.3 %)	7 (10.9 %)	24 (26.1 %)	**0.001***
GNRI	98.55 (6)	103.32 (3)	96.14 (1.5)	84.61 (4)	**0.001***

* means statistically significant , GNRI: geriatric nutritional risk index; MTH: moderate-to-high; CVO: cerebrovascular disease; CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention; AF: atrial fibrillation; HF: heart failure; CKI: chronic kidney injury; LVEF: left ventricle ejection fraction; ICD: intracardiac defibrillator; AST: aspartate aminotransferase; ALT: alanine aminotransferase; eGFR: estimated glomerular filtration rate; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; BNP: brain natriuretic peptide; CKMB: kinase isoenzyme; CRP: c-reactive protein; INR: International Normalized Ratio

related to mortality and NVAF in old patients were used as predictors in multivariate Cox regression and binary logistic regression analyses.

Additionally, forward variable selection was applied in both of regression analyses to eliminate statistically non-significant predictors. Furthermore, receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off value of GNRI associated with NVAF (according to be having NVAF or not) and mortality with the Youden J index. In all analyses, a two-sided $p < 0.05$ was considered statistically significant.

Results

Our study included 3-year follow-up data of 362 patients hospitalized for decompensated HF. The patients were classified into different risk groups based on their GNRI, as follows: GNRI > 98, no-risk group; GNRI 92 to ≤ 98, low risk group; GNRI 82 to < 92, moderate-to-high-risk group; no statistically significant difference was found between groups in terms of DM, HT, smoking, chronic kidney injury (CKI), malignancy, history of PCI, coronary bypass graft surgery (CABG) and cerebrovascular disease ($p>0.05$). Also, LVEF were similar as compared between groups. The group with moderate-to-high risk had relatively higher levels of uric acid compared to groups with low or no-risk ($p=0.032$). Other common laboratory values were similar as compared between groups ($p>0.05$). Baseline demographic characteristics, laboratory and follow-up findings of the groups are shown in Table 1.

The follow-up data showed that the group with moderate-to-high risk had a significantly higher incidence of persistent NVAF compared to those with low or no risk ($p<0.001$). Also, the follow-up cases of PCI and mortality were significantly higher among patients from the group with moderate-to-high risk compared to those with low or no risk (p: 0.026 and $p<0.001$ respectively). However, the number of hospitalizations and that of cases in need for ICD placement were similar as compared between groups ($p>0.05$).

Patients developing persitent NVAF (n =53) and those not having NVAF (n=309)

Tab. 2. Baseline and follow-up characteristics for AF or non-AF.

Variables	Non-AF (n=309)	AF (n=53)	p
Age (years)	72 (3.5)	72 (4)	0.528
Sex (male, %)	222 (71.8 %)	39 (73.6 %)	0.869
Weight (kg)	80 (7.5)	81.5 (5)	0.168
BMI	26.2 (1.53)	25 (1.13)	**< 0.001***
Systolic blood pressure (mmHg)	120 (12.5)	125 (14.5)	0.158
Diastolic blood pressure (mmHg)	75 (7.5)	80 (15)	0.292
Heart rate (beat/min)	80 (6.5)	76 (6)	0.068
Diabetes mellitus (n, %)	122 (39.5 %)	25 (47.2 %)	0.364
Hypertension (n, %)	160 (51.8 %)	26 (49.1 %)	0.767
Smoking (n, %)	118 (38.2 %)	21 (39.6 %)	0.879
CVO (n, %)	10 (3.2 %)	1 (1.9 %)	1.000
CABG (n, %)	29 (9.4 %)	9 (17 %)	0.141
PCI history (n, %)	78 (25.2 %)	12 (22.6 %)	0.735
HF (n, %)	36 (11.7 %)	9 (17 %)	0.366
Malignancy (n, %)	7 (2.3 %)	1 (1.9 %)	1.000
CKI (n, %)	19 (6.1 %)	4 (7.5 %)	0.759
Hemodialysis (n, %)	2 (6 %)	2 (3.8 %)	0.104
LVEF (%)	40 (3.5)	40 (5.25)	0.788
Leukocytes (×10³ /μL)	10.8 (2.35)	10.25 (1.75)	0.870
Hemoglobin (g/dL)	13.49± 1.98	13.19 ± 1.39	0.590
Hematocrit (%)	39.23 ± 5.20	37.94 ± 3.95	0.375
Platelets (×10³ /μL)	254 (47)	233.5 (35.38)	0.409
Fasting plasma glucose (mg/dL)	136 (40.13)	134 (46.25)	0.778
Albumin (g/dL)	3.3 (0.30)	2.5 (0.20)	**<0.001**
Urea (mg/ dl)	33 (8.13)	36.5 (8..63)	0.960
Creatinine (mg/dL)	0.8 (0.15)	0.8 (0.15)	0.908
GFR (mL/min)	92 (12)	91.5 (14.63)	0.918
Sodium (mEq/L)	138 (2)	137.5 (2.13)	0.051
Potassium (mEq/L)	4.2 (0.30)	4.2 (0.35)	0.598
ALT (IU/L)	23 (7)	20.5 (7.13)	0.977
AST (IU/L)	29 (11.5)	32 (12.62)	0.603
LDL (mg/dL)	130 (20)	137.5 (22.46)	0.235
Triglycerides (mg/dL)	149 (60.90)	154.5 (50.83)	0.594
HDL (mg/dL)	40 (6.90)	40.5 (6.13)	0.672
Total cholesterol (mg/dL)	190 (27.12)	201 (33.63)	0.493
Direct bilirubin (mg/dL)	0.10 (0.01)	0.10 (0.02)	0.829
Indirect bilirubin (mg/dL)	0.54 (0.17)	0.50 (0.16)	0.809
BNP (pg/mL)	1070 (950)	914 (888)	0.615
Troponin (ng/mL)	610 (871)	1260 (1578)	0.051
CKMB (U/L)	14.4 (6.7)	16.1 (7.8)	0.487
Uric acid (mg/dL)	5.4 (1.05)	5.4 (1.25)	0.944
INR	1 (0)	1 (0.7)	0.469
CRP (mg/L)	5.5 (4.42)	6.6 (5.5)	0.901
Follow-up (month)	33 (2.5)	34 (2)	0.960
Follow-up ICD (n, %)	59 (19.1 %)	10 (18.9 %)	1.000
Hospitalization times	3 (1)	2.5 (1)	0.658
Follow-up PCI (n, %)	111 (35.9 %)	21 (39.6 %)	0.644
Mortality (n, %)	29 (9.4 %)	15 (28.3 %)	**<0.001***
GNRI	100.12 (4.5)	83.31 (4.5)	**<0.001***

* means statistically significant , GNRI: geriatric nutritional risk index; MTH: moderate-to-high; CVO: cerebrovascular disease; CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention; AF: atrial fibrillation; HF: heart failure; CKI: chronic kidney injury; LVEF: left ventricle ejection fraction; ICD: intracardiac defibrillator; AST: aspartate aminotransferase; ALT: alanine aminotransferase; eGFR: estimated glomerular filtration rate; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; BNP: brain natriuretic peptide; CKMB: kinase isoenzyme; CRP: c-reactive protein; INR: International Normalized Ratio

Tab. 3. Cox regression analysis for mortality.

Variable	Hazard ratio	95% Confidence interval of hazard ratio	p
GNRI Levels			<0.001*
Low risk	1.792	0.712–4.499	0.214
MTH risk	3.872	1.971–7.607	<0.001*
ICD			<0.001*
ICD implantation	4.045	2.218–7.317	<0.001*

* means statistically significant; GNRI: geriatric nutritional risk index; MTH: moderate-to-high; ICD: intracardiac defibrillator

Tab. 4. Binomial Logistic Regression according to AF or non-AF.

Variable	β estimates with standard errors	OR	p
GNRI Levels			<0.001*
Low Risk (β_1)	1.038±0.623	2.825	0.096
MTH Risk (β_2)	3.332±0.464	28.000	<0.001*

* means statistically significant, GNRI; Geriatric nutritional risk index, MTH: moderate to high

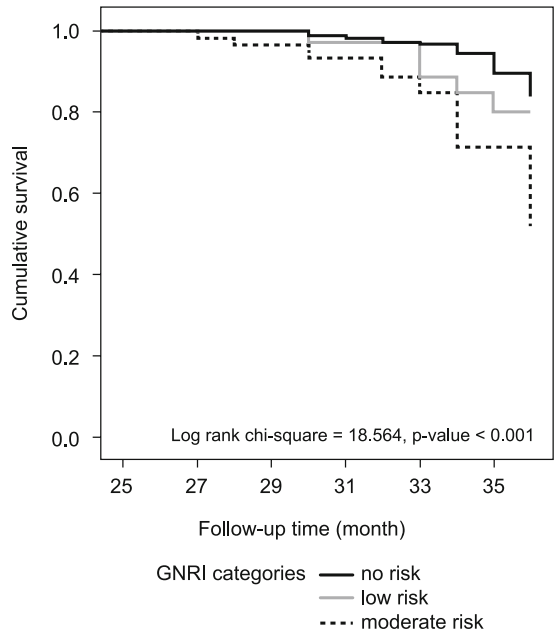

Fig. 1. Kaplan-Meier survival curves according to GNRI.

had similar rates of DM, HT, smoking, CKI, malignancy, and history of PCI and CABG. LVEF were similar as compared between groups ($p > 0.05$). Patients with NVAF had significantly lower albumin and BMI values ($p < 0.001$). Other laboratory values were similar ($p > 0.05$). Mean GNRI value was 83.3 in NVAF patients and 101.1 in patients without NVAF ($p < 0.001$). Patients with follow-up NVAF had significantly higher mortality compared to patients without NVAF ($p < 0.001$). However, the number of hospitalizations, that of cases in need for ICD placement and follow-up cases of PCI were similar as compared between patients with and without NVAF ($p > 0.05$). Baseline demographic

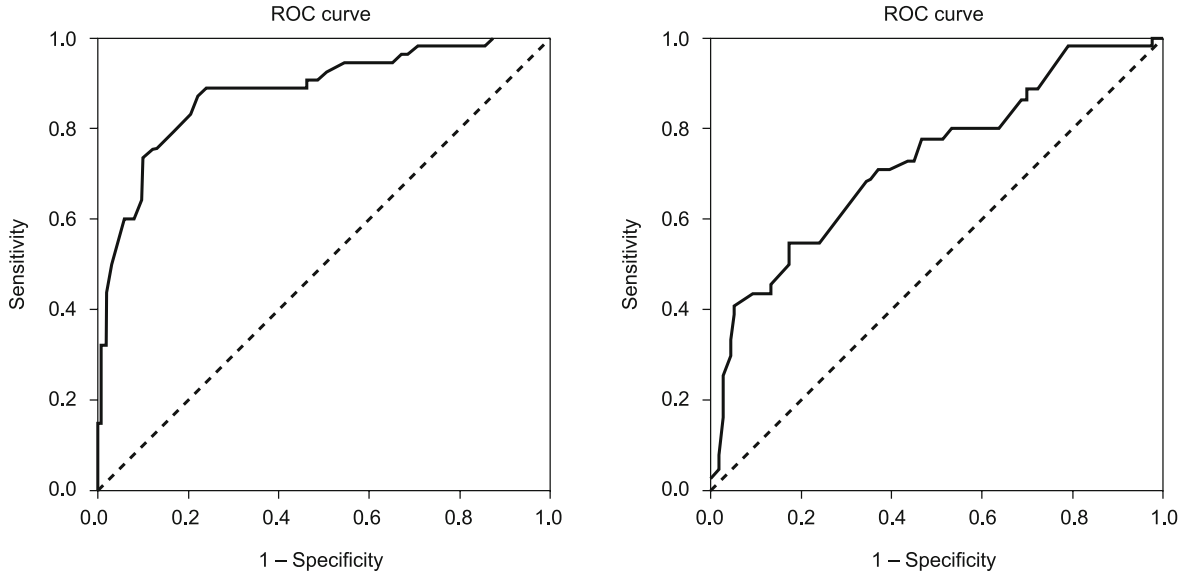

Fig. 2. ROC curve of geriatric nutritional risk index (GNRI) according to non-valvular atrial fibrillation (NVAF) and mortality, from left to right. AUC: area under the curve; ROC: receiver operating characteristic. For AF AUC=0.884, p < 0.001, cut-off value 95.45, 88.7 % sensitivity, 76.4 % specificity. For Mortality AUC = 0.725, p < 0.001, cut-off value 90.68, 54.5 % sensitivity, 82.7 % specificity.

characteristics, laboratory and follow-up findings of the groups are shown in Table 2.

Based on GNRI values, the Kaplan Meier survival analysis showed that patients with moderate-to-high nutritional risk had a significantly worse survival compared to patients without nutritional risk ($p<0.001$) (Fig. 1). In the multivariate Cox regression analysis with forward variable selection, only two variables were associated with increased mortality as follows: moderate-to-high risk (HR=3.872 in Table 3) and the ICD implantation (HR=4.045 in Table 3). The other variables were not found with mortality over the follow-up period.

In Table 4, the effects of GNRI levels, age, sex, chronic diseases, cardiological statements, geriatric conditions on the odds ratio of NVAF were examined by binomial logistic regression analysis with forward variable selection, and only GNRI levels were found as statistically significant. In the analysis, patients with no risk level were set as the reference category. According to Table 4, when a patient has a moderate-to-high GNRI risk, he or she is 28 times more likely to belong to the NVAF group than to the non-NVAF group. For the prediction of NVAF, the cut-off value of 95.45<GNRI has 88.7 % sensitivity and 76.4 % specificity; For the prediction of mortality, the cut-off value of 90.68< GNRI has 54.5 % sensitivity and 82.7 % specificity in the ROC curve analyses. These results are shown in Figure 2.

Discussion

In our study, we reported that GNRI values had a predictive value for the development of persistent NVAF. The prevalence of cardiovascular disorders has increased markedly because of a rapidly ageing society and westernized lifestyle, both of which increase the risk of cardiovascular diseases. The growing prevalence of HF is also an important problem among the elderly because HF is observed predominantly in that particular population. There is a strong association between malnutrition, inflammatory state, and cardiovascular disease, which has been described as 'malnutrition–inflammation complex syndrome (MICS) (2). It has been particularly evaluated in patients with HF and chronic kidney disease, in whom malnutrition has been recognized as a consistent prognostic factor associated with higher mortality (12). Our findings were consistent with prior studies related to higher GNRI values and increased mortality (4, 6, 12). Thus, malnutrition should be considered as an important predictor of mortality in HF patients.

Another important finding of our study is that the group with moderate-to-high GNRI had also a relatively increased risk of follow-up PCI compared to those with no or low-risk. Several large cohort studies, in which risk indicators have been explored have shown that malnutrition, rather than obesity, was associated with an increased risk of mortality and recurrent interventions in patients with coronary artery disease (13). In another study; Masatoshi et al. (14) demonstrated that lower GNRI values are associated with a higher incidence of CV events in patients with HF with preserved EF (HFpEF). GNRI could allow clinicians to identify HFpEF patients at elevated risk for future CV events and those who may benefit from nutritional support (14). The importance of nutritional status within cardiovascular pathology has been well studied in HF (2, 15). Currently, advanced HF units try to incorporate nutritionists into their teams in order to assess and improve the nutritional status of patients since it has been seen that the improvement in the nutritional status is associated with an improvement in the prognosis of those patients (16). Our findings also support the notion that malnutrition is a risk factor for repeated interventions in patients with HF.

The most important finding of our study was that patients developing NVAF during the follow-up had significantly lower GNRI values. GNRI values are predictive of the development of persistent NVAF, namely when the patient has a moderate-to-high GNRI risk, he or she is 28 times more likely to belong to the NVAF group than to the non-NVAF group. There are no studies in AF patients assessing the impact of nutritional status on clinical outcomes. In this sense, there are only studies that analyzed the relationship between the body mass index (BMI) and clinical events of patients with AF (17–18). Thus, an association between obesity and a more favorable cardiovascular prognosis (so-called 'obesity paradox') has been reported in patients with AF, where being overweight or obese was associated with a lower risk of cardiovascular death or all-cause mortality (19). However, no study has analyzed the prognostic impact of nutritional status beyond BMI.

One recent study provides relevant clinical information on a topic scarcely studied to date, i.e., on the impact of nutritional status on patients with AF. In this study, they report the following main findings: (i) almost half of patients with AF, aged>80 years have some degree of malnutrition; (ii) malnutrition in patients with AF is independently associated with an increased risk of death, ischemic stroke, and major bleeding (20). Our study investigating the risk of developing NVAF in elder HF patients with low GNRI is one of the first researches in this area. Malnutrition is not infrequent in HF patients while iron, magnesium, and calcium imbalances and vitamin D deficiency are known to increase the risk of AF (21–23). These electrolyte imbalances are one of the probable mechanisms to explain the increase in the risk of NVAF in patients with low GNRI.

Also, malnutrition has been associated with a decline in general functional status and high hospitalization and readmission rates (24). A cohort study has shown that GNRI has the ability to predict the length of stay and in-hospital weight loss, whereby the elderly who were detected as having a nutritional risk by GNRI on admission had the tendency to a prolonged hospital stay and weight loss during hospitalization. On top of that, it is less time-consuming as well as an easy tool to be used where minimum participation is needed to aid the clinical healthcare personnel, especially the dietitians, to diagnose someone with malnutrition. These are some of the added points as to why GNRI is accepted to be used as a tool for assessing the nutritional status of hospitalized elderly (25). However, the ratio of cardiovascular disease-related hospitalizations in these studies was only 21.6 %, and many hospitalizations were due to malignancies and other comorbidities. In our study, we did not find any significant association between GNRI values and hospitalizations. This could be explained by the fact that we only included HF-related hospitalizations, and also the number of patients included in our study was smaller compared to other studies. In our study, only two variables were associated with increased mortality; GNRI/moderate-to-high risk and the need for ICD implantation. In patients with heart failure, the need for ICD implantation is associated with increased mortality (26). It is noteworthy that in patients with HF, the moderate-to-high risk/GNRI score is also a predictor of mortality.

The GNRI score is indicative of malnutrition and has been used as a risk index in multiple diseases such as uremia, sepsis, HF, and coronary heart disease. Persons with a GNRI score of 98 or lower are considered at risk of malnutrition and have more severe inflammation and worse outcomes (6, 27). Currently, there is no unique GNRI cut-off value to predict the malnutrition and mortality, while the best cut-off value of GNRI might be different for different ethnic populations. Although the cut-off value or value predictive of GNRI is not always the same, there is a tendency of lower values being associated with greater risk. Further studies are needed to find out the best cut-off value of GNRI for mortality and morbidity prediction.

Conclusion

In summary, our findings have suggested that the GNRI value represents a strong predictor for all-cause mortality and new onset of persistent non-valvular AF in HF patients.

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