Am J Cardiovasc Dis 2026;16(1):17-29
www.AJCD.us /ISSN:2160-200X/AJCD0169401

Review Article

Geriatric nutritional risk index predicts all-cause mortality in patients with heart failure: an updated systematic review and meta-analysis

Alireza Gholami[1*], Fateme Kazemi[2*], Delaram Nourmohammadi[3*], Reza Behfar[4], Fatemeh Nouroozi[5], Fateme Skandary[4], Nima Zabihi[6], Yeganeh Ghobadi[7], Siamand Abdolghaderi[8], Aida Bakhshi[9,10], Mohammad Hossein Shafieyoun[11], Yaser Khakpour[12], Mahdyieh Naziri[13#], Mohamad Javad Bay[14#]

[1]Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbass, Iran; [2]Student Research Committee, School of Management and Medical Information Sciences, Isfahan University of Medical Sciences, Isfahan, Iran; [3]Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [4]Student Research Committee, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran; [5]Emergency Department of Sayad Shirazi Hospital, Golestan University of Medical Sciences, Gorgan, Iran; [6]Shahid Beheshti University of Medical Sciences, Cardiovascular Research Center, Tehran, Iran; [7]General Practitioner, Mashhad University of Medical Sciences, Mashhad, Iran; [8]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [9]Clinical Research Development Unit, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran; [10]Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [11]Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran; [12]Faculty of Medicine, Guilan University of Medical Sciences, Rasht, Iran; [13]Student Research Committee, School of Medicine, Iran University of Medical Sciences, Tehran, Iran; [14]School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran. [*]Equal contributors and co-first authors. [#]Equal contributors.

Received October 18, 2025; Accepted January 12, 2026; Epub February 15, 2026; Published February 28, 2026

Abstract: Objectives: The role of malnutrition in heart failure (HF) patients is unclear. We assessed the correlation between the Geriatric Nutritional Risk Index (GNRI) and all-cause mortality in HF. Methods: PubMed, Scopus, and Web of Science were searched for observational studies reporting the correlation between GNRI and all-cause mortality in HF patients (up to January 26, 2025). Titles, abstracts, and full texts were screened. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist was used to assess study quality. Data were synthesized via random-effects meta-analysis using the restricted maximum likelihood (REML) method. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Results: Nineteen observational studies with 9,982 subjects were included. A low-risk GNRI group was correlated with raised all-cause mortality in HF patients (hazard ratio (HR) 1.77, 95% CI 1.38-2.16; P < 0.0001). Results were consistent across sensitivity analyses. Heterogeneity was high (I^2 = 99.5%), and meta-regression explained 18.9% of the variance. Egger's test demonstrated possible publication bias (P = 0.0305). The high GNRI subgroup (5 studies, 2,193 patients) had a pooled HR of 3.15 (95% CI 0.93-5.37; P = 0.0055). The CI included 1.0, indicating some uncertainty. Conclusion: GNRI is a reliable nutritional tool predicting all-cause mortality in HF patients. Our study suggests GNRI should be considered for evaluating long-term prognosis in this population.

Keywords: Geriatric nutritional risk index, heart failure, all-cause mortality, malnutrition

Introduction

Heart failure currently represents a global concern, with a prevalence of over 64 million patients [1]. A significant portion of individuals with heart failure are elderly, and this condition is a leading contributor to illness, hospital admissions, and death in older adults [2]. In the United States, total healthcare costs correlated with heart failure are projected to rise from 20.9 billion USD in 2012 to 53.1 billion USD by 2030 [3].

https://doi.org/10.62347/JFZM5494

Malnutrition frequently occurs in individuals with heart failure [4], and various studies have shown that it may be associated with all-cause mortality, an increased risk of cardiovascular events, and hospitalization in these patients, thereby serving as a useful indicator [5, 6]. Furthermore, improving nutritional status at the early stages of the disease and in the management of heart failure can lead to better prognoses [7].

Anthropometric parameters, such as body mass index (BMI) and triceps skinfold thickness, along with biochemical parameters, such as serum albumin and prealbumin, have traditionally served as indices of nutritional status. However, these measures alone cannot provide a comprehensive and precise evaluation of an individual's nutritional condition [8, 9]. Presently, more comprehensive assessments of nutritional status utilize scoring systems including the Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT), and the Geriatric Nutritional Risk Index (GNRI) [10, 11]. Specifically, the GNRI is an objective index calculated using serum albumin concentration and ideal body weight, which makes it practical for use even in busy clinical settings [12]. GNRI has been employed as a predictor of mortality and the length of hospital stay in patients with heart failure [13-15].

Although the association between GNRI and all-cause mortality in heart failure patients has been examined in previous reviews and meta-analyses [16, 17]. Several years have passed since their publication, and numerous new studies on the topic have emerged [18-23]. Therefore, our systematic review aims to re-evaluate the association between GNRI and all-cause mortality in patients with heart failure.

Methods

This study conducted a systematic review and meta-analysis to evaluate the association between the GNRI and all-cause mortality in individuals with heart failure (HF). The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the research protocol was registered in the PROSPERO database (CRD4202-5648496).

Geriatric nutritional risk index

GNRI serves as a straightforward tool for determining the nutritional health of older adults, particularly those with chronic illnesses. It is calculated using a formula that combines serum albumin levels, which reflect protein status, and the ratio of current body weight to ideal body weight, which indicates possible malnutrition or weight loss. Based on the GNRI score, individuals are classified into four risk levels for malnutrition: no risk (≥ 98), low risk (92-97.9), moderate risk (82-91.9), and severe risk (< 82). This tool is widely used in clinical settings to predict outcomes such as recovery, hospitalization, and mortality, and to guide nutritional interventions that enhance the health and quality of life of older adults.

GNRI = (1.489 × serum albumin [g/L]) + (41.7 × current body weight/ideal body weight).

Literature search

To identify relevant articles, we developed an advanced search strategy and applied it to Google Scholar, PubMed/Medline, and Scopus databases. The search focused on key terms related to the GNRI, all-cause mortality, and heart failure, with filters applied to titles and abstracts. The strategy for literature searching was tailored to each database's specific structure, without imposing any restrictions on publication date, type, or language (**Table 1**). To confirm a thorough search, we also reviewed the reference lists of prior systematic reviews and included studies, reducing the risk of missing articles. Two reviewers screened the studies, and any disagreements were resolved through discussion, ensuring an unbiased selection process.

Criteria for selecting studies

For studies to meet the inclusion criteria in this meta-analysis, the following statements should be considered: (1) The study should focus on observational research, ensuring that potential confounding factors from interventions are appropriately addressed. (2) It should investigate the association between the GNRI and all-cause mortality in individuals with heart failure. (3) The study population should comprise geriatric patients diagnosed with heart failure. (4) The GNRI should be reported in

Table 1. Search strategies for PubMed, Scopus and WOS

Search engine	Search strategy	Search date	Search results
PubMed	("heart failure" [tiab] OR "Heart Diseases" [tiab] OR "Cardiac Disorder" [tiab] OR "Cardiac Diseases" [tiab] OR "Cardiac failure" [tiab] OR "Cardiovascular Diseases" [tiab] OR "Congestive Heart Failure" [tiab] OR "Myocardial Failure" [tiab] OR "Heart Decompensation" [tiab] OR "Heart insufficient" [tiab]) AND ("Geriatric Nutritional Risk Index" [tiab] OR "GNRI index" [tiab]) AND (mortality [tiab] OR fatality [tiab] OR death [tiab])	26-1-2025	95
Scopus	(TITLE-ABS-KEY ("Heart failure" OR "Heart Diseases" OR "Cardiac Disorder" OR "Cardiac Diseases" OR "Cardiac failure" OR "Cardiovascular Diseases" OR "Congestive Heart Failure" OR "Myocardial Failure" OR "Heart Decompensation" OR "Heart insufficient")) AND (TITLE-ABS-KEY ("Geriatric Nutritional Risk Index" OR "GNRI index")) AND (TITLE-ABS-KEY ("mortality" OR "fatality" OR "death"))	26-1-2025	239
Web of Science	(TS=("Heart failure" OR "Heart Diseases" OR "Cardiac Disorder" OR "Cardiac Diseases" OR "Cardiac failure" OR "Cardiovascular Diseases" OR "Congestive Heart Failure" OR "Myocardial Failure" OR "Heart Decompensation" OR "Heart insufficient")) AND (AB=("Geriatric Nutritional Risk Index" OR "GNRI index") OR TI=("Geriatric Nutritional Risk Index" OR "GNRI index")) AND AB=(mortality OR fatality OR death)	26-1-2025	259

alignment with the methodological framework of the study. (5) Cut-off GNRI value?

Exclusion criteria

Studies were excluded from the meta-analysis if they met any of the following conditions: (1) Non-observational study design, including randomized controlled trials, interventional studies, reviews, editorials, case reports, or conference abstracts. (2) Did not examine the association between GNRI and all-cause mortality in patients with heart failure. (3) The study population was not limited to geriatric patients, but included a mixed-age population without subgroup analysis for older adults with heart failure. (4) GNRI was not reported, or the method of its calculation was inconsistent with established criteria. (5) GNRI cut-off values were not clearly defined or differed significantly from standard or commonly accepted thresholds without justification. (6) Insufficient data for effect size extraction (e.g., hazard ratios, confidence intervals) or studies with missing key outcome data. (7) Duplicate publications or multiple reports from the same cohort without additional relevant data.

Data extraction and study quality assessment

To extract data from the articles, information on the authors, year of publication, follow-up period for each article, main output, and study design was collected. Information about the participants was also extracted.

To check the eligibility of the articles imported into the study, two screeners reviewed them separately based on their titles and abstracts. After that, among the articles whose inclusion criteria were approved by the two screeners, their full texts were also reviewed by the researchers. The inclusion criteria are as follows:

To evaluate the quality of cross-sectional cohort, case-control, and analytical studies, two screeners independently used the Joanna Briggs Institute (JBI) Critical Appraisal Checklist. A third screener participated in this process to resolve discrepancies.

Statistical analysis

We used STATA 13.1 for all statistical analyses and reported pooled effect estimates as hazard ratios (HRs) or odds ratios (ORs) with 95% confidence intervals (CIs), which were displayed in forest plots for clearer visualization. Heterogeneity was quantified using the I^2 statistic, and a random-effects model was applied when substantial heterogeneity was present ($I^2 > 50\%$). A two-sided P value < 0.05 was considered statistically significant for all tests. To verify the robustness of the pooled esti-

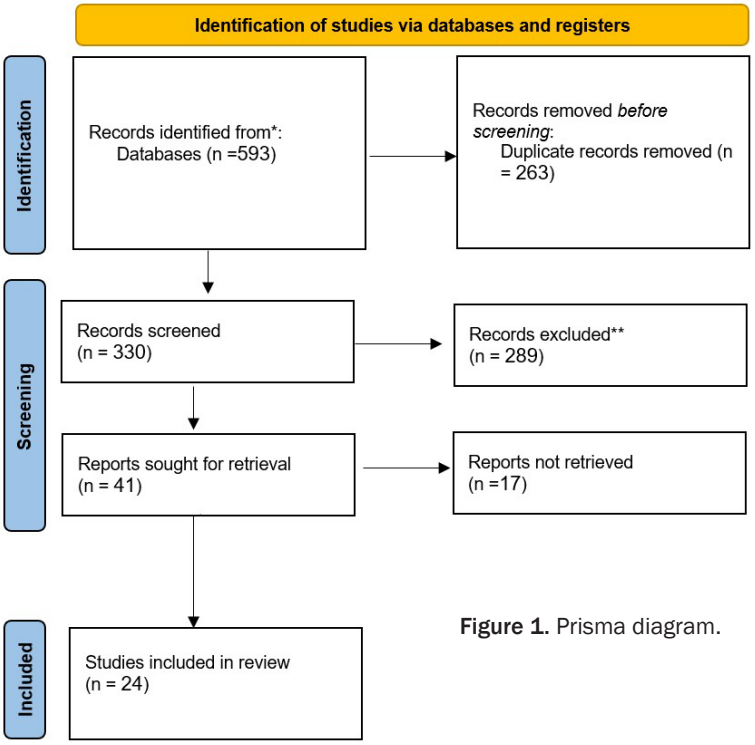

Figure 1. Prisma diagram.

mates, we performed leave-one-out sensitivity analyses. Finally, potential publication bias was evaluated by visual inspection of funnel plot symmetry and Egger's regression test for small-study effects.

Results

The initial database search yielded 593 records. After removing 263 duplicates, 330 unique articles remained for title and abstract screening. Following this screening, 289 studies were excluded based on irrelevance to the research question or failure to meet inclusion criteria. A total of 41 full-text articles were assessed for eligibility. Ultimately, 24 studies met the inclusion criteria and were included in the final systematic review and meta-analysis (**Figure 1**).

A total of 24 studies were included, primarily cohort studies conducted across various countries, notably Japan, China, the UK, Italy, and the USA. Most studies focused on hospitalized patients with HF, including acute decompensated HF, chronic HF, and HF with preserved or reduced ejection fraction (HFpEF, HFrEF), with patient ages generally ranging from 60 to 90 years. Sample sizes varied widely, from 143 to over 5,000 patients. The GNRI was consistently used across studies, though slight variations in the formula and cut-off values were noted. GNRI was often classified into risk categories - typically with GNRI < 92 or < 98 indicating moderate to severe malnutrition risk. Several studies compared GNRI with other nutritional indices such as CONUT and PNI. Across most cohorts, male patients constituted the majority. In addition to showing the prevalence of malnutrition, many studies highlighted the prognostic value of GNRI in predicting all-cause mortality, hospitalization, and functional outcomes in elderly patients with HF (**Table 2**).

Subgroup analysis: low GNRI

Pooled effect size and forest plot

A total of 19 studies were included in the meta-analysis for the low GNRI subgroup. The pooled HR for all-cause mortality among patients with low GNRI was 1.77 (95% CI: 1.38-2.16, $P < 0.0001$) under a random-effects model using the REML method. This result demonstrates a statistically significant association, suggesting that patients with low nutritional status - as reflected by a low GNRI - face a 77% raised risk of all-cause mortality in comparison to those with higher GNRI scores. The effect size was visually confirmed through the forest plot, in which the overall summary diamond does not cross the line of no effect (HR = 1), indicating a statistically significant pooled effect (**Figure 2**).

Heterogeneity

There was substantial heterogeneity across the included studies ($\tau^2 = 0.67$; $I^2 = 99.53\%$; $H^2 = 214.20$). The Cochran's Q-test was significant ($Q(18) = 734.45$, $P < 0.0001$), confirming that the variability in effect sizes is unlikely to be due to chance alone. This suggests that dif-

Table 2. Summary of Included Studies

First Author	Year of Publication	Country	Study Design	Geriatric Nutritional Risk Index (GNRI) Formula/Definition	Number of Participants	Age (Mean ± SD)	Gender (Male/Female)
Nakamura T	2020	Japan	cohort study	GNRI = 14.89 × serum albumin (g/dL) + 41.7 × BMI/22 Low GNRI group (GNRI < 92) indicating malnutrition risk High GNRI group (GNRI ≥ 92) indicating low or no malnutrition risk|213 consecutive patients	A cohort of 213 patients aged 80 years and older, consecutively admitted for worsening heart failure	87.2 ± 4.9 years	43.7% male 56.3% female
Nakamura T	2018	Japan (Kitasato University Hospital)	cohort study	GNRI = 14.89 × serum albumin (g/dL) + 41.7 × BMI/22 kg/m GNRI used as a nutritional screening tool alongside CONUT and PNI	949 consecutive patients aged ≥ 60 years admitted for cardiovascular disease (CVD), evaluated before discharge for nutritional status including AC, CONUT, GNRI, and PNI	72.3 ± 7.2 years	68.2% male 31.8% female
Narumi T	2013	Japan (Yamagata University School of Medicine)	cohort study	CONUT, PNI, GNRI CONUT: 61% at risk (mild 34%, moderate 20%, severe 7%) PNI: 60% at risk (moderate 30%, severe 30%) GNRI: 69% at risk (mild 25%, moderate 24%, severe 20%)	388 consecutive patients with chronic heart failure	69.6 ± 12.3 years	60% male 40% female
Nishi S	2019	Japan (Ibaraki Prefecture)	cohort study	GNRI calculated at discharge using : Major risk: GNRI < 82 Moderate risk: GNRI 82 to < 92 Low risk: GNRI 92 to < 98 No risk: GNRI ≥ 98 Cut-off for analysis: GNRI = 92 (low GNRI < 92 = moderate/severe risk; high GNRI ≥ 92 = low/no risk)	110 HFpEF patients aged 65 years and older discharged after symptom alleviation from initial 838 HF patients registry; exclusions included dialysis patients and those without GNRI data	78.5 ± 7.2 years	53.6% male 46.4% female
Ono M	2023	Japan (West Tokyo Heart Failure Registry)	Retrospective	Lower GNRI (< 92): moderate or severe nutritional risk Higher GNRI (≥ 92): low or mild nutritional risk	1474 patients with acute decompensated heart failure from 6 centers	76 (65-83)	58.5% male 41.5% female
Ouchi Sh	2017	Japan (Juntendo University Hospital)	cohort study (biomarker study in cardiac ICU)	GNRI calculated on admission using formula: No risk: GNRI > 98 Low risk: GNRI 92 to ≤ 98 Moderate risk: GNRI 82 to < 92 High risk: GNRI < 82	267 consecutive patients with acute decompensated heart failure admitted to cardiac ICU	73 (64-82) years	53.7% male 46.3% female
Pagnesi M	2024	Italy (4 centers)	Retrospective	GNRI calculated as: GNRI = 1.489 × serum albumin (g/L) + 41.7 × (body weight [kg]/ideal body weight) Ideal body weight = 22 × height^2 (m^2) Malnutrition defined as GNRI ≤ 98 Patients stratified into malnutrition (GNRI ≤ 98) and no malnutrition (GNRI > 98) groups	510 consecutive patients with severe heart failure (defined by ≥ 1 'I NEED HELP' high-risk marker); exclusions: missing GNRI data	74 ± 12 years	66.5% male 33.5% female
Sargento L	2017	Italy	cohort study of stable geriatric outpatients with HFrEF	GNRI = 1.489 × serum albumin (g/L) + 41.7 × (current body weight/ideal body weight); ideal weight by Lorentz formula 11.2% at risk of malnutrition (GNRI ≤ 98)	143 heart failure outpatients, aged above 65, with reduced ejection fraction (LVEF < 40%) and stable condition	75.7 ± 6.9	56.3% male 43.7% female
Fan X	2024	China	cohort study, single-center	Men: height (cm) - 100 - ((height - 150)/4) Women: height (cm) - 100 - ((height - 150)/2.5) Patients divided into tertiles: Low GNRI < 96.50 Medium GNRI 96.50-102.45 High GNRI > 102.45	218 elderly HFpEF patients hospitalized at Air Force Medical Centre	Median 85 years (range 77-89)	males (67.4%) females (32.6%)

Chen W	2023	USA	Retrospective cohort study	GNRI = [1.489 × serum albumin (g/L)] + [41.7 × (body weight (kg)/ideal body weight (kg))]; ideal body weight calculated by Lorentz equations; ratio set to 1 if body weight > ideal weight	5627 ill elderly patients with heart failure admitted to the intensive care unit for at least 48 hours	70.85 ± 13.27 years	59.2% male 40.8% female
Hirose S	2021	Japan	cohort (FRAGILE-HF study)	GLIM criteria vs. Geriatric Nutritional Risk Index (GNRI) GLIM: 42.4% malnourished GNRI (< 92): 46.5% malnourished Moderate agreement between GLIM and GNRI (Cohen's kappa = 0.46)	890 hospitalized HF patients aged ≥ 65 years, ambulatory at discharge	82 (GLIM malnourished), 79 (GLIM well-nourished)	57% male 43% female
Honda Y	2016	Japan	cohort study	Ideal body weight calculated using Lorentz formula GNRI cutoffs: Major risk: < 82 Moderate risk: 82 to < 92 Low risk: 92 to < 98 No risk: ≥ 98 Cutoff for study: 92	490 consecutive patients aged 65 years and older hospitalized with acute heart failure (AHF)	79 years ± 7	58% male in the low GNRI group, and 59% male in the high GNRI group
Minamisawa M	2019	Americas (USA, Canada, Brazil, Argentina)	Transactional	Categories: Absent risk: GNRI ≥ 98 Low risk: GNRI 92- < 98 Moderate/severe risk: GNRI < 92	1,677 HFpEF patients (adequate GNRI data, age ≥ 45, LVEF ≥ 45%)	64.1 to 79.5 years	59% males 51% females
Miura M	2023	Japan	cohort study	GNRI assessed at discharge GNRI was an independent predictor of both primary (HR 0.957; P < 0.001) and secondary outcomes (HR 0.963; P = 0.002) GNRI predicted outcomes better than physical function (SPPB) and activities of daily living (BI)	839 hospitalized elderly HF patients (> 65 years), median follow-up 228 days	84.0 (78.0-89.0)	48% male 52% female
Takahashi H	2014	Japan	cohort study	Ideal body weight = height^2 (m^2) × 22 (BMI method) Patients divided into quartiles Q1: < 84.9 Q2: 85.0-91.1 Q3: 91.2-97.2 Q4: > 97.3	1,568 ESRD patients starting hemodialysis between 1998-2009; median follow-up 10 years	64 ± 13 years	67% male 33% female
Sze S	2017	UK	cohort study of hospitalized HF patients with LVSD	Ideal weight: Men: height (cm) - 100 - [(height - 150)/4] Women: height (cm) - 100 - [(height - 150)/2.5] GNRI ≤ 98 classified as malnourished	265 patients hospitalized with HF and LVEF < 40%	80 ± 7	61.9% male 38.1% female
Wada H	2017	Japan	cohort study of CAD patients undergoing first PC	Ideal body weight calculated using BMI of 22 kg/m^2 (height^2 × 22) Patients divided into tertiles: < 98 98 to 104	2,853 CAD patients undergoing first PCI between 2000 and 2011	65.9 ± 10 years	82.1% male 17.9% female
Yoshihisa A	2017	Japan	cohort study of hospitalized HF patients	PNI: 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mm^3) GNRI: 14.89 × serum albumin (g/dL) + 41.7 × (body weight/ideal body weight) Based on serum albumin, total cholesterol, and lymphocyte count; scores 0-12	1307 hospitalized HF patients	66.5 years (mean)	792 males (60.5%), 515 females (39.5%)

Sze SH	2018	UK	cohort of outpatients with suspected HF	Ideal weight = 22 × height^2 (m^2) GNRI > 98 normal; 92-98 mild; 82-91 moderate; < 82 severe malnutrition Based on serum albumin, cholesterol, lymphocytes; scores 0-12 PNI: 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mm^3) PNI > 38 normal; 35-38 moderate; < 35 severe malnutrition	4,021 patients referred with suspected HF; 3,386 confirmed HF (35% HFrEF, 65% HFnEF)	75 (67-81) years	61% male 39% female
Sze SH	2018	UK	cohort of ambulatory CHF patients	deal body weight = 22 × height^2 (m^2) GNRI > 98 normal; 92-98 mild; 82-91 moderate; < 82 severe malnutrition	952 confirmed CHF patients	75 (67-81) years	69% male 31% female
Yasumura K	2020	Japan	Retrospective	BMI = weight (kg)/height (m)^2 GNRI < 92 defined as malnutrition	203 patients hospitalized with ADHF	81 ± 9 years	62% male 38% female
UEMURA U	2020	Japan	cohort study of acute HF patients with overweight/obesity (BMI ≥ 25 kg/m^2)	based on serum albumin, total cholesterol, lymphocyte count; scores 0-12; ≥ 2 indicates undernutrition GNRI1: 14.89 × serum albumin (g/dL) + 41.7 × 1 (body weight/ideal body weight ratio set to 1) GNRI2: 14.89 × serum albumin (g/dL) + 41.7 × (body weight/ideal body weight) Ideal body weight = 22 × height^2 (m^2) Undernutrition defined by CONUT ≥ 2, GNRI < 98	170 acute HF patients with BMI ≥ 25 kg/m^2	67 ± 15 years	59.4% male 40.6% female
Sze SH	2018	UK	cohort of ambulatory CHF patient	Simple tools: CONUT score, GNRI, PNI Multidimensional tools: MUST, MNA-SF, SGA Laboratory tests: serum cholesterol, albumin, lymphocyte count	467 ambulatory CHF patients, 67% male, median NT-proBNP 1156 ng/L	76 (21-98) years	67% male 33% female
Shi T	2023	China	cohort of hospitalized HF patients	Advanced Lung Cancer Inflammation Index (ALI): ALI = BMI × Albumin/NLR Geriatric Nutritional Risk Index (GNRI): GNRI = 14.89 × Albumin (g/dL) + 41.7 × BMI/22 Patients divided into 4 groups by median ALI and GNRI values	1123 hospitalized HF patients	66.8 ± 12.6 years	61.7% male 38.3% female
Sun T	2023	China	cohort of ischemic heart failure (IHF) patients undergoing PCI	GNRI = 14.89 × serum albumin (g/dL) + 41.7 × (actual BMI/ideal BMI) Ideal BMI set to 22 kg/m^2 Patients divided into quartiles based on GNRI values	1745 IHF patients undergoing PCI	60.2 ± 10.9 years	83.2% male 16.8% female
Tohyama M	2023	Japan	cohort study	Hemoglobin-Geriatric Nutritional Risk Index (H-GNRI): combines GNRI and hemoglobin levels H-GNRI Risk Groups: Low risk (score 2): 6.9% Intermediate risk (score 1): 27.0% High risk (score 0): 66.1%	3532 hospitalized HF patients ≥ 65 years	65-74 (13%), 75-89 (58%), ≥ 90 (29%)	49.3% male 50.7% female
Zhanga S	2024	USA	cohort study using MIMIC-IV database of ICU patients with acute heart failure (AHF)	GNRI, CONUT, PNI GNRI = 14.89 × serum albumin (g/dL) + 41.7 × (actual body weight/ideal body weight) Ideal body weight = 22 × (height in meters)^2 If actual body weight > ideal body weight, ratio is set to 1	1310 critically ill AHF patients, age ≥ 65 years	78.7 (72.3-85.0) years	54.7% male 45.3% female

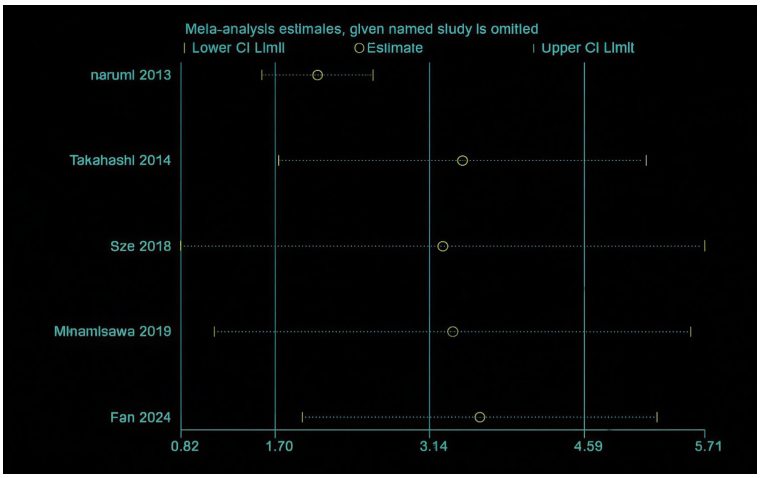

Figure 2. Forrest plot of all-cause mortality among patients with low GNRI.

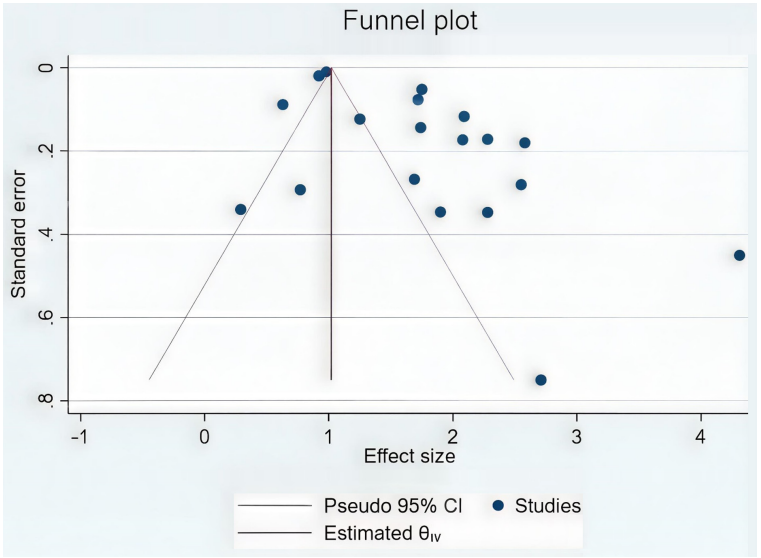

Figure 3. Funnel plot of all-cause mortality among patients with low GNRI.

ferences in study characteristics or populations may have impacted the observed outcomes.

Sensitivity analysis

To assess the impact of each study on the overall pooled HR, a leave-one-out sensitivity analysis was performed. Across all iterations, the pooled effect size remained consistent and statistically significant, ranging from 1.74 to 1.86. None of the excluded studies caused a meaningful shift in the direction or magnitude of the overall effect, indicating strong robustness of the main result. This is visually represented in the influence plot, where all confidence intervals overlap closely, and none cross the line of no effect.

Meta-regression

Meta-regression analysis revealed that approximately 18.92% of the heterogeneity could be explained by study-level moderators (R^2 = 18.92%). The slope coefficient for the standard error was significant (β = 2.53, P = 0.0305), suggesting that study precision variability contributed to the observed heterogeneity.

Funnel plot and publication bias

Visual inspection of the funnel plot revealed mild asymmetry, with a slight skew toward one side of the vertical line, suggesting potential publication bias (**Figure 3**). This was statistically supported by Egger's regression test, which demonstrated evidence of small-study effects (z = 2.16, P = 0.0305). While publication bias cannot be ruled out, the large number of included studies and the stability of sensitivity results lend credibility to the overall finding.

Subgroup analysis: high GNRI

Pooled effect size and forest plot

For the high GNRI subgroup, five studies were included. The pooled HR for all-cause mortality was 3.15 (95% CI: 0.93-5.37, P = 0.0055) under a random-effects REML model. Although the point estimate suggests a protective trend for patients with higher GNRI (implying reduced mortality), the confidence interval includes 1, indicating that the result is not statistically significant at the 95% level, despite a significant z-test (z = 2.78). This discrepancy may reflect high variability in effect sizes. The forest plot showed wide confidence intervals for several studies and considerable variability in individual study effects, contributing to uncertainty in the pooled estimate (**Figure 4**).

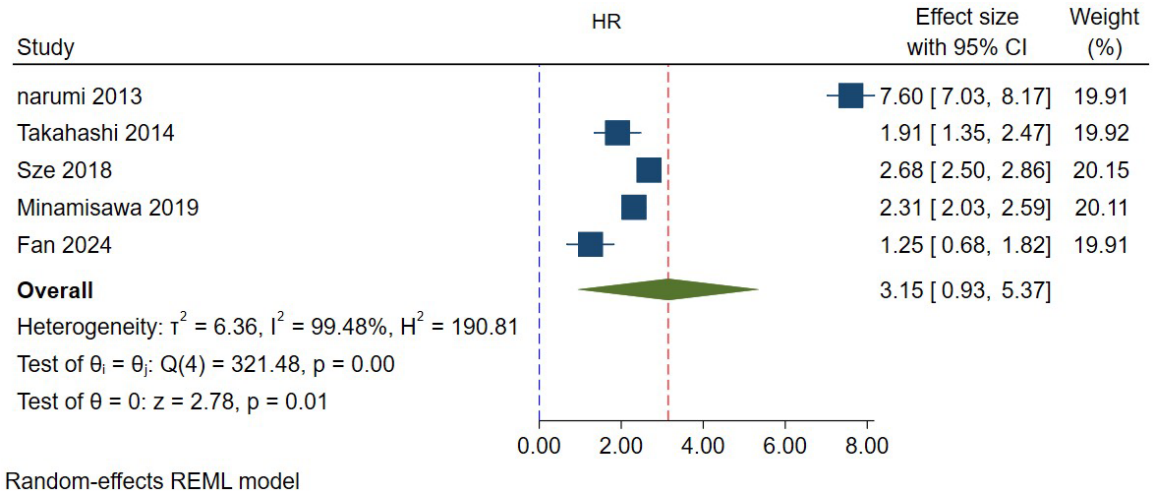

Figure 4. Forrest plot of all-cause mortality among patients with high GNRI.

Heterogeneity

There was substantial heterogeneity among the included studies (τ^2 = 6.36; I^2 = 99.48%; H^2 = 190.81). The test for heterogeneity was highly significant (Q(4) = 321.48, P < 0.0001), suggesting substantial inconsistency in the findings and warranting caution in interpreting the pooled HR.

Sensitivity analysis

The leave-one-out analysis showed some variability in the pooled HR across studies, ranging from 2.10 to 3.61. Although all estimates continued to show a directionally similar trend (i.e., reduced mortality with high GNRI), in some iterations the confidence intervals were wider or approached null. Notably, omitting the Narumi 2013 study resulted in the most significant drop in effect size, suggesting that this study had a moderately strong influence on the overall estimate.

Meta-regression

Meta-regression analysis did not identify any statistically remarkable moderators. The slope for the standard error was non-significant (P = 0.674), and the model accounted for none of the between-study variance (R^2 = 0.00%). This implies that the observed heterogeneity cannot be explained solely by differences in study precision or sampling error.

Funnel plot and publication bias

The funnel plot for the high GNRI subgroup showed reasonable symmetry, and Egger's test did not demonstrate evidence of small-study effects (z = 0.42, P = 0.6744). Therefore, there is no significant indication of publication bias in this subgroup. Given the small number of studies (n = 5), however, the power to detect such bias is limited.

Discussion

The findings of the present study indicated GNRI as a contributing factor to the elevated risk of all-cause mortality in individuals with HF. For more precise analysis, the patients of the enrolled studies were classified into two groups, high GNRI and low GNRI. The meta-analysis conducted on the groups revealed that low GNRI significantly influenced the risk for all-cause mortality of patients with HF.

Low GNRI

Patients with low GNRI had a significantly raised risk of all-cause mortality, indicating that malnutrition, as measured by GNRI, is a robust predictor of adverse outcomes in HF patients. Multiple included studies reported consistent findings. For example, Pagnesi et al. [24] identified malnutrition, as assessed by GNRI, as an independent predictor of higher all-cause mortality in heart failure patients, indicating that GNRI-based nutritional assessment can effectively identify those at elevated risk. Fan et al. [25], on the other hand, did not observe GNRI to be an independent risk factor for all-cause mortality and instead highlighted low PNI as an independent predictor. In another study, Ono et

al. [18] reported that lower discharge GNRI (d-GNRI), rather than admission GNRI (a-GNRI), was an independent predictor of mortality in acute decompensated heart failure.

Several mechanisms may explain the correlation between low GNRI and poor outcomes in HF patients. BMI has long been utilized as an assessment parameter of nutrition. Nevertheless, it is only a measure of body size and may not represent the actual nutritional condition [26]. It has been shown that BMI and serum albumin levels can be influenced by fluid status. An elevated extracellular fluid volume reduces serum albumin levels while increasing BMI. Given such a counteracting impact, the GNRI would minimize the influence of fluid status since it is a combined index of BMI and albumin [27].

Malnutrition is described as an imbalance between the body's requirements and energy intake, which has shown a close relation to the diseases of the cardiovascular system [20]. Malnutrition may contribute to the progression of HF as a component of a vicious cycle related to inflammation, cachexia, and autonomic dysfunction [28, 29].

Chronic diseases, including HF, are characterized by increased muscle catabolism, elevated cytokine production, and loss of appetite, leading to lower albumin levels. Aging is also a factor in the reduction of albumin metabolic reserve in an individual, and these factors render the nutritional status of elderly patients with chronic illnesses highly susceptible to minor or acute stresses [30]. Decline in albumin level can result in myocardial and pulmonary edema, oxidative stress, diuretic resistance, fluid retention, and an enhanced inflammatory response, which all lead to HF progression [31].

With a focus on the potential role of inflammation in HFpEF pathogenesis, recent insights suggest that systemic microvascular endothelial inflammation, correlated with concomitant conditions, may play a key role in myocardial fibrosis, increased oxidative stress, and alterations in signaling pathways in cardiomyocytes [32]. These changes stimulate remodeling and dysfunction of cardiomyocytes and microvascular endothelial cells in skeletal and cardiac muscle [32]. Meanwhile, the GNRI, which was developed for screening nutritional status, is also used to assess inflammatory status in elderly patients and shows a notable correlation with inflammatory biomarkers [33]. Recent research has demonstrated a correlation between natriuretic peptides and malnutrition [34-37]. A significant association has also been detected between natriuretic peptides and nutritional scores, such as GNRI, in decompensated HF patients [27]. The correlation between high levels of natriuretic peptides and malnutrition is likely explained by their role as markers of congestion, leading to intestinal edema, inflammation, and malabsorption [38]. Increased levels of natriuretic peptides, including BNP and NT-proBNP, have a robust association with poor prognosis in patients with heart failure. Higher amounts of these markers are correlated with elevated cardiovascular and all-cause mortality and the rate of hospitalization [39, 40]. Malnutrition in HF patients is more closely related to increased right-sided volume overload than to systolic dysfunction of LV [41-43]. Cardiac cachexia,a systemic wasting process involving every compartment of the body, including fat, skeletal muscle, and bone [38], results from haemodynamic changes in HF [42], and provokes neurohumoral responses which have, in turn, been involved in gastrointestinal and liver function [41], anorexia, negative energy balance, systemic inflammation and catabolic processes, and loss of skeletal muscle, fat and lean mass [44, 45]. However, these reactions and systemic inflammation are associated with heart muscle damage and cardiac overload [46]. Cachexia has been identified as an independent predictor of increased all-cause mortality in heart failure patients, with a notably high prevalence reported in one study [47].

High GNRI

While patients with higher GNRI showed a trend toward lower all-cause mortality, our meta-analysis did not find a statistically significant association.

Limitation and future directions

The main limitation of this meta-analysis is that it included only observational studies, which increases the likelihood of residual confounding and limits the ability to make definite causal

connections between GNRI and all-cause mortality, particularly among HF patients. In addition to this limitation, the degree of between-study heterogeneity, the diverse categories of GNRI cutoffs, potential publication bias in low GNRI subpopulations, and the substantial representation of hospital-based elderly Asian subjects in the total sample likely limit the generalisability of these findings. Future research should therefore examine large, prospective, multicenter cohorts, in which standardised definitions of GNRI have been applied, across a broad range of HF populations and phenotypes, and conduct interventional or patient-level investigations to ascertain if GNRI-guided dietary management will produce meaningful improvement in clinical outcomes and refined risk stratification for patients with heart failure.

Conclusion

Our updated meta-analysis indicated a remarkable relationship between low GNRI and elevated risk for all-cause mortality in patients with heart failure. The findings highlight the important role of nutritional status assessment as a prognostic factor in patient outcomes and also suggest GNRI as a helpful non-invasive tool for risk stratification. Despite significant heterogeneity, the consistent effect seen in the sensitivity analysis remains reliable. Although higher GNRI values showed a protective trend in these patients, the estimate was not statistically significant, possibly because of the small number of studies and high between-study variability. All things considered, these results emphasize the crucial role of routine nutritional evaluation in the management and prognosis of heart failure patients.

Disclosure of conflict of interest

None.

Address correspondence to: Mahdyieh Naziri, Iran University of Medical Sciences, Hemmat Highway, Next to Milad Tower, Tehran, Iran. Tel: +98-021-86701; E-mail: nazirimahdyieh@yahoo.com; Mohamad Javad Bay, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran. Tel: +98-021-23871; E-mail: mhmdjwadbay@gmail.com

References

[1] Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018; 392: 1789-1858.

[2] Butrous H and Hummel SL. Heart failure in older adults. Can J Cardiol 2016; 32: 1140-1147.

[3] Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, Ikonomidis JS, Khavjou O, Konstam MA, Maddox TM, Nichol G, Pham M, Piña IL and Trogdon JG. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013; 6: 606-619.

[4] Kinugawa S and Fukushima A. Malnutrition in heart failure: important but undervalued issue. JACC Heart Fail 2018; 6: 487-488.

[5] Minamisawa M, Seidelmann SB, Claggett B, Hegde SM, Shah AM, Desai AS, Lewis EF, Shah SJ, Sweitzer NK, Fang JC, Anand IS, O'Meara E, Rouleau JL, Pitt B and Solomon SD. Impact of malnutrition using geriatric nutritional risk index in heart failure with preserved ejection fraction. JACC Heart Fail 2019; 7: 664-675.

[6] Nakamura T, Matsumoto M, Haraguchi Y, Ishida T and Momomura SI. Prognostic impact of malnutrition assessed using geriatric nutritional risk index in patients aged ≥ 80 years with heart failure. Eur J Cardiovasc Nurs 2020; 19: 172-177.

[7] Tsuchihashi-Makaya M and Kinugawa S. Nutrition as a new treatment target in chronic heart failure. Circ J 2013; 77: 604-605.

[8] Fuhrman MP, Charney P and Mueller CM. Hepatic proteins and nutrition assessment. J Am Diet Assoc 2004; 104: 1258-1264.

[9] Jeejeebhoy KN. Nutritional assessment. Nutrition 2000; 16: 585-590.

[10] Yamana I, Takeno S, Shimaoka H, Yamashita K, Yamada T, Shiwaku H, Hashimoto T, Yamashita Y and Hasegawa S. Geriatric nutritional risk index as a prognostic factor in patients with esophageal squamous cell carcinoma-retrospective cohort study. Int J Surg 2018; 56: 44-48.

[11] Kanemasa Y, Shimoyama T, Sasaki Y, Hishima T and Omuro Y. Geriatric nutritional risk index as a prognostic factor in patients with diffuse large B cell lymphoma. Ann Hematol 2018; 97: 999-1007.

[12] Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, Benazeth S, Cynober L and Aussel C. Geriatric nutritional risk index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr 2005; 82: 777-783.

[13] Liang L, Zhao X, Huang L, Tian P, Huang B, Feng J, Zhou P, Wang J, Zhang J and Zhang Y. Prevalence and prognostic importance of mal-

nutrition, as assessed by four different scoring systems, in elder patients with heart failure. Nutr Metab Cardiovasc Dis 2023; 33: 978-986.
[14] Dong CH, Chen SY, Zeng HI, Yang B and Pan J. Geriatric nutritional risk index predicts all-cause mortality in patients with heart failure: a systematic review and meta-analysis. Clinics (Sao Paulo) 2021; 76: e2258.
[15] Hirose S, Miyazaki S, Yatsu S, Sato A, Ishiwata S, Matsumoto H, Shitara J, Murata A, Kato T and Suda S. Impact of the geriatric nutritional risk index on in-hospital mortality and length of hospitalization in patients with acute decompensated heart failure with preserved or reduced ejection fraction. J Clin Med 2020; 9: 1169.
[16] Hao X, Li D and Zhang N. Geriatric nutritional risk index as a predictor for mortality: a meta-analysis of observational studies. Nutr Res 2019; 71: 8-20.
[17] Li H, Cen K, Sun W and Feng B. Prognostic value of geriatric nutritional risk index in elderly patients with heart failure: a meta-analysis. Aging Clin Exp Res 2021; 33: 1477-1486.
[18] Ono M, Mizuno A, Kohsaka S, Shiraishi Y, Kohno T, Nagatomo Y, Goda A, Nakano S, Komiyama N and Yoshikawa T. Geriatric nutritional risk index at hospital admission or discharge in patients with acute decompensated heart failure. J Clin Med 2023; 12: 1891.
[19] Tohyama M, Shirai Y, Shimizu M, Kato Y, Kokura Y and Momosaki R. Predictive value of the hemoglobin-geriatric nutritional risk index in patients with heart failure. Nutrients 2023; 15: 4789.
[20] Sun T, Ma M, Huang X, Zhang B, Chen Z, Zhao Z and Zhou Y. Prognostic impacts of geriatric nutritional risk index in patients with ischemic heart failure after percutaneous coronary intervention. Clin Nutr 2023; 42: 1260-1267.
[21] Balun A, Akgümüş A, Çetin ZG and Demirtaş B. The prognostic value of geriatric nutritional risk index in evaluating rehospitalization and one-year mortality in patients with heart failure. Cureus 2023; 15: e44460.
[22] Chen W, Chen M and Qiao X. Interaction of lactate/albumin and geriatric nutritional risk index on the all-cause mortality of elderly patients with critically ill heart failure: a cohort study. Clin Cardiol 2023; 46: 745-756.
[23] Zhang S, Chen N, Huang Z, Yan N, Ma L and Gao X. Geriatric nutritional risk index is associated with the occurrence of acute kidney injury in critically ill patients with acute heart failure. Ren Fail 2024; 46: 2349122.
[24] Pagnesi M, Serafini L, Chiarito M, Stolfo D, Baldetti L, Inciardi RM, Tomasoni D, Adamo M, Lombardi CM, Sammartino AM, Loiacono F, Maccallini M, Villaschi A, Gasparini G, Montella M, Contessi S, Cocianni D, Perotto M, Barone G, Anker SD, Merlo M, Cappelletti AM, Sinagra G, Pini D and Metra M. Impact of malnutrition in patients with severe heart failure. Eur J Heart Fail 2024; 26: 1585-1593.
[25] Fan X, He Q, Zhang K, Lan X, Li Y and Zhang H. Comparison of the value of four objective nutritional indices in assessing the long-term prognosis of elderly patients with heart failure with preserved ejection fraction. Rev Cardiovasc Med 2024; 25: 201.
[26] Uemura Y, Shibata R, Masuda A, Katsumi Y, Takemoto K, Koyasu M, Ishikawa S, Mitsuda T, Murohara T and Watarai M. Utility of the nutritional screening in predicting adverse outcome of patients with overweight/obesity and acute heart failure. J Card Fail 2020; 26: 566-573.
[27] Suzuki N, Kida K, Suzuki K, Harada T and Akashi YJ. Assessment of transthyretin combined with mini nutritional assessment on admission provides useful prognostic information in patients with acute decompensated heart failure. Int Heart J 2015; 56: 226-233.
[28] Sze S, Pellicori P, Zhang J and Clark AL. Malnutrition, congestion and mortality in ambulatory patients with heart failure. Heart 2019; 105: 297-306.
[29] Kalantar-Zadeh K, Anker SD, Horwich TB and Fonarow GC. Nutritional and anti-inflammatory interventions in chronic heart failure. Am J Cardiol 2008; 101: 89E-103E.
[30] Beberashvili I, Azar A, Sinuani I, Shapiro G, Feldman L, Sandbank J, Stav K and Efrati S. Geriatric nutritional risk index, muscle function, quality of life and clinical outcome in hemodialysis patients. Clin Nutr 2016; 35: 1522-1529.
[31] Liu M, Chan CP, Yan BP, Zhang Q, Lam YY, Li RJ, Sanderson JE, Coats AJ, Sun JP, Yip GW and Yu CM. Albumin levels predict survival in patients with heart failure and preserved ejection fraction. Eur J Heart Fail 2012; 14: 39-44.
[32] Redfield MM. Heart failure with preserved ejection fraction. N Engl J Med 2016; 375: 1868-1877.
[33] Gärtner S, Kraft M, Krüger J, Vogt LJ, Fiene M, Mayerle J, Aghdassi AA, Steveling A, Völzke H, Baumeister SE, Lerch MM and Simon P. Geriatric nutritional risk index correlates with length of hospital stay and inflammatory markers in older inpatients. Clin Nutr 2017; 36: 1048-1053.
[34] Booth J, Pinney J and Davenport A. N-terminal proBNP--marker of cardiac dysfunction, fluid overload, or malnutrition in hemodialysis patients? Clin J Am Soc Nephrol 2010; 5: 1036-1040.
[35] Bednarek-Skublewska A, Zaluska W and Ksiazek A. The relationship between serum level

of N-terminal pro-B-type natriuretic peptide and nutritional status, and inflammation in chronic hemodialysis patients. Clin Nephrol 2010; 73: 14-20.
[36] Nakayama Y, Yamada Y, Ishii S, Hitaka M, Yamazaki K, Masai M, Joki N, Sakai K and Ohashi Y. Association between intra- and extracellular water ratio imbalance and natriuretic peptides in patients undergoing hemodialysis. Nutrients 2023; 15: 1274.
[37] Ducros J, Larifla L, Merault H, Galantine V, Bassien-Capsa V and Foucan L. N-terminal Pro-B-type natriuretic peptide and malnutrition in patients on hemodialysis. Int J Nephrol 2020; 2020: 9528014.
[38] Rahman A, Jafry S, Jeejeebhoy K, Nagpal AD, Pisani B and Agarwala R. Malnutrition and cachexia in heart failure. JPEN J Parenter Enteral Nutr 2016; 40: 475-486.
[39] Santaguida PL, Don-Wauchope AC, Oremus M, McKelvie R, Ali U, Hill SA, Balion C, Booth RA, Brown JA, Bustamam A, Sohel N and Raina P. BNP and NT-proBNP as prognostic markers in persons with acute decompensated heart failure: a systematic review. Heart Fail Rev 2014; 19: 453-470.
[40] Nguyen DV, Nguyen SV, Pham AL, Nguyen BT and Hoang SV. Prognostic value of NT-proBNP in the new era of heart failure treatment. PLoS One 2024; 19: e0309948.
[41] Valentova M, von Haehling S, Bauditz J, Doehner W, Ebner N, Bekfani T, Elsner S, Sliziuk V, Scherbakov N, Murín J, Anker SD and Sandek A. Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. Eur Heart J 2016; 37: 1684-1691.
[42] Carr JG, Stevenson LW, Walden JA and Heber D. Prevalence and hemodynamic correlates of malnutrition in severe congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol 1989; 63: 709-713.
[43] Melenovsky V, Kotrc M, Borlaug BA, Marek T, Kovar J, Malek I and Kautzner J. Relationships between right ventricular function, body composition, and prognosis in advanced heart failure. J Am Coll Cardiol 2013; 62: 1660-1670.
[44] Anker SD and Coats AJ. Cardiac cachexia: a syndrome with impaired survival and immune and neuroendocrine activation. Chest 1999; 115: 836-847.
[45] Poehlman ET, Scheffers J, Gottlieb SS, Fisher ML and Vaitekevicius P. Increased resting metabolic rate in patients with congestive heart failure. Ann Intern Med 1994; 121: 860-862.
[46] Saunders JT, Nambi V, de Lemos JA, Chambless LE, Virani SS, Boerwinkle E, Hoogeveen RC, Liu X, Astor BC, Mosley TH, Folsom AR, Heiss G, Coresh J and Ballantyne CM. Cardiac troponin T measured by a highly sensitive assay predicts coronary heart disease, heart failure, and mortality in the atherosclerosis risk in communities study. Circulation 2011; 123: 1367-1376.
[47] Prokopidis K, Irlik K, Hendel M, Piaśnik J, Lip GYH and Nabrdalik K. Prognostic impact and prevalence of cachexia in patients with heart failure: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle 2024; 15: 2536-2543.