

Original Paper

# Association of Geriatric Nutritional Risk Index with Mortality in Hemodialysis Patients: A Meta-Analysis of Cohort Studies

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## Key Words

Geriatric nutritional risk index • Hemodialysis • Mortality • Cardiovascular disease

## Abstract

**Background/Aims:** Geriatric nutritional risk index (GNRI) was developed as a “nutrition-related” risk index and was reported in different populations as associated with the risk of all-cause and cardiovascular morbidity and mortality. Therefore, GNRI can be used to classify patients according to a risk of complications in relation to conditions associated with protein-energy wasting (PEW). However, not all reports pointed to the prognostic ability of the GNRI. The purpose of this study was to assess the associations of GNRI with mortality in chronic hemodialysis patients. **Methods:** We electronically searched original articles published in peer-reviewed journals from their inception to September 2018 in The PubMed, Embase, and the Cochrane Library databases. The primary outcome was all-cause and cardiovascular mortality. We pooled unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs) using Review Manager 5.3 software. **Results:** A total of 10,739 patients from 19 cohort studies published from 2010 to 2018 were included. A significant negative association was found between the GNRI and all-cause mortality in patients with chronic hemodialysis (OR, 0.90; 95% CI, 0.84-0.97,  $p=0.004$ ) (per unit increase) and (OR, 2.15; 95% CI, 1.88-2.46,  $p<0.00001$ ) (low vs. high GNRI). Moreover, there was also a significant negative association between the GNRI (per unit increase) and cardiovascular events (OR, 0.98; 95% CI, 0.97-1.00,  $p=0.01$ ), as well as cardiovascular mortality (OR, 0.89; 95% CI, 0.80-0.99,  $p=0.03$ ). **Conclusion:** Our findings supported the hypothesis that the low GNRI is associated with an increased risk of all-cause and cardiovascular mortality in chronic hemodialysis patients. Based on our literature review,

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GNRI has been found to be an effective tool for identifying patients with nutrition-related risk of all-cause and cardiovascular disease.

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## Introduction

Malnutrition is very common in patients undergoing maintenance hemodialysis (HD) [1] and is associated with an increased risk of mortality [2, 3]. Regular nutritional assessment is recommended for all dialysis patients to reduce mortality and morbidity [4]. Moreover, protein-energy wasting (PEW) is a form of malnutrition that characterizes by a state of decreased body protein mass and energy fuels as a consequence of catabolic inflammatory responses, occurs frequently in elderly and patients with end-stage organ diseases including ESRD [5]. Among the available methods, the malnutrition inflammation score (MIS) is the most well-validated tool for screening HD patients at nutritional risk compared with other indices [6]. However, the MIS requires a subjective assessment by well-trained examiners to ensure consistent results. Recently, the geriatric nutritional risk index (GNRI) was reported to be a very simple and objective method based on body weight, height and serum albumin levels to assess the nutritional status in a number of pathological conditions [7, 8]. To date, the relationship between the GNRI and mortality in hemodialysis patients has not been thoroughly studied. Some studies have investigated the reliability of the GNRI in assessing malnutrition and predicting overall mortality in chronic HD patients [8-11]. The GNRI has also successfully predicted mortality in both elderly people and chronic HD patients [12]. In other studies, however, GNRI has not been found to be a reliable predictor of all-cause and cardiovascular mortality [13-14]. Because of on this uncertainty we decided to conduct a meta-analysis of cohort and case-control studies to summarize the available evidence regarding the association of the GNRI with mortality in chronic hemodialysis patients.

## Materials and Methods

### *Data sources and search strategy*

We performed a search to identify the studies that examined the associations between GNRI and all-cause mortality and cardiovascular mortality in chronic hemodialysis patients. Literature was identified by searching the PubMed, Embase and Cochrane Library databases. The last updated search was performed in September 2018. The searching terms used were “geriatric nutritional risk index or GNRI”, “all-cause mortality”, “cardiovascular mortality”, and “dialysis or hemodialysis”. The search was carried out without restriction on language but was limited to studies that had been conducted on human subjects.

### *Selection criteria*

The inclusion criteria were as follows: (1) studies reporting the association of geriatric nutritional risk index with mortality (all-cause or cardiovascular disease related) in patients with chronic hemodialysis, (2) cohort studies, and (3) studies reporting the odds ratio (OR), relative ratio, or hazard ratio (HR) with 95% confidence intervals (95% CIs) or sufficient data to calculate these figures. The exclusion criteria were as follows: (1) studies including non-hemodialysis patients and (2) nonhuman studies. For studies with the same or overlapping data by the same authors, the most suitable studies with the largest number of cases or most recent publication dates were selected.

The exposure of interest was the GNRI. The GNRI was calculated based on the patient's serum albumin and body weight using the equation developed by Bouillanne et al. [15] and modifying the nutritional risk index for elderly patients as reported by Yamada et al. [16] as follows:  $GNRI = (14.89 \times \text{albumin (g/dl)}) + (41.7 \times (\text{body weight/ideal body weight}))$ . The primary outcome of interest was risk estimates of all-cause and cardiovascular events or mortality with the GNRI. The ORs of GNRI from continuous variables or dichotomous variables was calculated separately. The ORs of the GNRI as dichotomous variables was calculated by low vs. high GNRI group. Cardiovascular events were defined as coronary events, including

non-fatal myocardial infarction, unstable angina, and coronary revascularization, hospitalized heart failure, hospitalized ischemic or hemorrhagic stroke, and peripheral vascular disease (PVD) or cerebral-vascular accident. Cardiovascular mortality was defined a demise resulting from coronary heart disease, stroke, sudden death, or complicated peripheral vascular disease.

#### Data extraction

Two investigators (J.X. and M.W.) assessed each study independently and recorded the eligibility, quality, and outcomes. Disagreements were resolved by a third party through consensus. A third investigator (T.H.) provided arbitration in cases of disagreement. We extracted the following study features: first author, publication year, country, number of participants, study design, follow-up time, and outcome of the studies (available unadjusted and adjusted ORs or HRs with their corresponding 95% CIs).

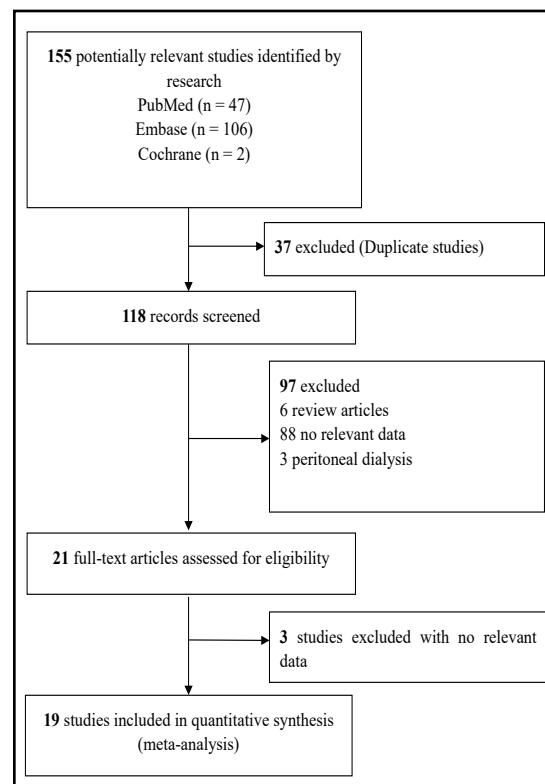
#### Quantitative data synthesis

The Newcastle-Ottawa Scale (NOS) was used in the assessment of the quality of the observational studies (case-control or cohort studies) [17]. There are eight items for cohort studies as follows: (1) representativeness of the exposed cohort, (2) selection of the non-exposed cohort, (3) ascertainment of exposure, (4) demonstration that the outcome of interest was not present at the start of study, (5) comparability of cohorts on the basis of the design or analysis, (6) assessment of outcome, (7) assessment of length of follow-up to allow outcomes to occur, and (8) adequacy of follow-up of cohorts. A judgment of “high”, “unclear” or “low” risk of bias was provided for each domain; a “low” risk of bias was scored 1, and a “high” or “unclear” risk of bias was scored “0”. A quality bar was plotted for each domain to examine the limitations of the studies. Studies of high quality were defined as a score higher than 5 points. Different measures of risk estimates from multiple analyses, such as OR or HR, were extracted from the studies, and the ORs were used as the common measure of association across studies. Unadjusted risk estimates and adjustments were pooled in the meta-analysis. Heterogeneity was evaluated using the Mantel-Haenszel  $\chi^2$  test and the  $I^2$  statistic to assess the degree of inter-study variation.  $I^2$  values of 0 to 24.9%, 25% to 49.9%, 50% to 74.9%, and 75% to 100% were considered as having no, mild, moderate, and significant thresholds for statistical heterogeneity, respectively [18]. We used the random effects model for pooled analysis of adjusted ORs because of anticipated statistical heterogeneity, although the fixed-effects model was also used to ensure the robustness of the model chosen and susceptibility to outliers.

## Results

### Basic information from the included studies

The study selection process is presented in Fig. 1. The literature search yielded 155 potentially relevant records. By screening the titles, we removed 37 duplicate studies. After evaluating the abstract of each study, 97 studies were excluded because they did not meet the inclusion criteria. Subsequently, we carefully read the full text of each of the remaining 21 studies and excluded 3 studies. Finally, 19 cohort studies were included in the meta-analysis. As shown in Table 1, the eligible studies were conducted



**Fig. 1.** Flowchart of selection of studies.

**Table 1.** The basic information of the included studies. Note: NOS: Newcastle-Ottawa Scale

Author	Year	Country	N, total	Age (year)	Follow up time	Retrospective/ prospective	Mortality end point	NOS score
Kobayashi et al [8]	2010	Japan	490	60±12	60 months	prospective	All-cause mortality	7
Park et al [11]	2012	Korea	120	56.2±12.7	120 months	retrospective	All-cause mortality	5
Sirajedine et al [19]	2012	France	46	76±11	18 months	prospective	All-cause mortality	6
Shin et al [20]	2012	Korea	120	56.7±15.9	120 months	prospective	All-cause mortality	5
Beberashvili et al [9]	2013	Israel	75	64.86±11.9	18 months	prospective	All-cause mortality	6
Tsai et al [21]	2014	Taiwan	318	NA	54 months	prospective	All-cause mortality	7
Chen et al [22]	2014	Taiwan	388	59±12	41 months	prospective	All-cause mortality, Cardiovascular event and mortality	7
Sakakibara et al [23]	2014	Japan	785	NA	43 months	prospective	All-cause mortality	7
Jung et al [24]	2014	Korea	120	55.7 ± 12.3	120 months	retrospective	All-cause mortality	7
Panichi et al [10]	2014	Italy	753	65.7±14.1	84 months	prospective	All-cause mortality, Cardiovascular event	7
Takahashi et al [25]	2014	Japan	1568	64±13	63 months	prospective	Cardiovascular mortality	7
Edalat-Nejad et al [26]	2015	Iran	145	60±16	18 months	prospective	All-cause mortality,	6
Komatsu et al [14]	2015	Japan	332	65.4±13.2	36 months	prospective	All-cause mortality, Cardiovascular mortality	7
Zhang et al [27]	2015	China	125	68.6±7.6	60 months	prospective	All-cause mortality, Cardiovascular mortality	6
de Rooij van Zuijdewijn et al [28]	2015	Netherlands	489	63.3±13.8	36 months	prospective	All-cause mortality	7
Beberashvili et al [13]	2016	Israel	352	67.4 ± 13.2	30 months	prospective	All-cause mortality, Cardiovascular event and mortality	7
Tsai et al [29]	2016	Taiwan	104	72	38.5 months	prospective	All-cause mortality	7
Ishii et al [30]	2017	Japan	973	64 ± 12	96 months	retrospective	All-cause mortality, Cardiovascular mortality	7
Matsukuma et al [31]	2018	Japan	3436	NA	48 months	prospective	All-cause mortality	7

from 2010 to 2018 with a total number of 10,739 patients, and the sample size ranged from 46 to 3436. Among the 19 included studies, 16 were from Asia, and 3 were from Europe. Fourteen studies presented risk estimates for associations between the GNRI and all-cause mortality (OR calculated on continuous variables). Five studies reported the relationship between the GNRI and cardiovascular mortality (adjusted OR or HR calculated on continuous variables).

#### Assessment of methodological quality

The NOS quality assessment of the included cohort studies is shown in Fig. 2. The main limitation observed in all the included studies was that there was no description of the derivation of the non-exposed cohort. Two studies performed in Korea showed a low quality (NOS score=5). The remaining 17 studies showed a comparatively high quality (NOS score 6-7). Seven studies showed an adequate follow-up period for the outcome of interest (follow-up time 18 months).

#### Mortality

*Geriatric nutritional risk index and all-cause mortality.* As shown in Table 2, there were nine studies that reported the unadjusted ORs for the association of the GNRI (per unit increase) with all-cause mortality with OR, 0.96; 95% CI, 0.95-0.98,  $p < 0.001$ . As shown in Table 2 and Fig. 3, there were twelve studies that reported the adjusted ORs for the association of the GNRI with all-cause mortality (per unit increase). The results showed a significant association between the GNRI and a decreased risk of all-cause mortality (OR, 0.90; 95% CI, 0.84-0.97,  $p = 0.004$ ). Moreover, there were five studies that reported the unadjusted ORs for the association of the GNRI with all-cause mortality and showed a significant association between the GNRI (low vs. high GNRI) and decreased risk of all-cause mortality (OR, 2.39; 95% CI, 2.09-2.74;  $p < 0.00001$ , Table 2). A total of eight studies reported the adjusted ORs for the association of the GNRI (low vs. high GNRI) with all-cause mortality (OR, 2.15; 95% CI, 1.88-2.46,  $p < 0.00001$ , Fig. 4 and Table 2).

*Geriatric nutritional risk index and cardiovascular morbidity and mortality*

As shown in Table 2 and Fig. 5, three studies reported the adjusted ORs for the association of the GNRI with cardiovascular events (OR calculated on dichotomous variables) and showed a strong association between the GNRI (high vs. low GNRI) and cardiovascular events (OR, 0.98; 95% CI, 0.97-1.00,  $p=0.01$ ). In addition, five studies reported the adjusted ORs for the association of the GNRI with cardiovascular mortality (OR calculated on dichotomous variables) and showed a significant association between the high GNRI and a decreased risk of cardiovascular mortality (OR, 0.89; 95%CI, 0.80-0.99,  $p=0.03$ , Fig. 6 and Table 2).

**Discussion**

In this study, we performed a systematic review of the literature and identified 19 original studies which reported the association between the GNRI and mortality among more than 10, 739 chronic hemodialysis patients. We found that the GNRI is associated with an increasing risk of long-term all-cause mortality in prevalent hemodialysis patients, even after adjusting for age and comorbidity. Moreover, there was also a significant negative association between the GNRI and cardiovascular events, as well as cardiovascular mortality.

GNRI was originally used to predict nutritional assessment and adverse outcomes in the elderly, which was modified and developed by Bouillanne et al. in 2005 [15]. Malnutrition is very common and associated with increased morbidity and mortality in patients with

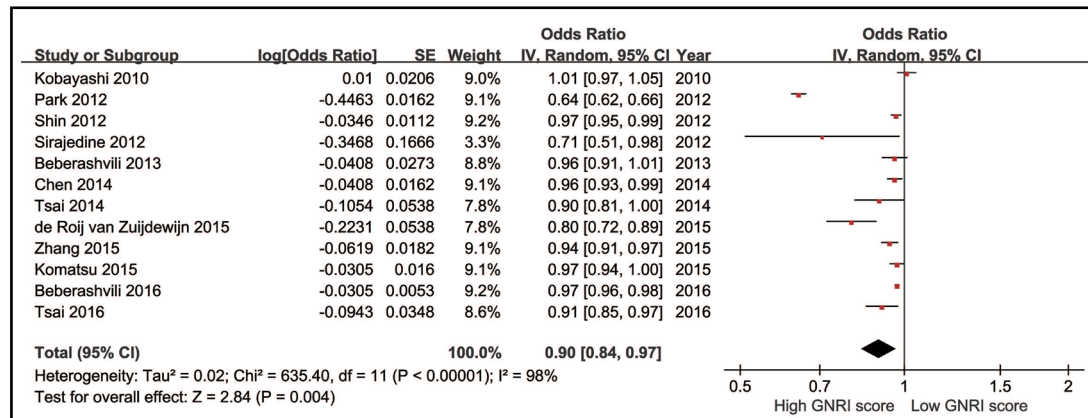
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Beberashvili 2013	+	?	+	+	+	+	-	+
Beberashvili 2016	+	?	+	+	+	+	+	+
Chen 2014	+	?	+	+	+	+	+	+
de Roij van Zuidewijn 2015	+	?	+	+	+	+	+	+
Edalat-Nejad 2015	+	?	+	+	+	+	-	+
Ishii 2017	+	?	+	+	+	+	+	+
Jung 2014	+	?	+	+	+	+	+	+
Kobayashi 2010	+	?	+	+	+	+	+	+
Komatsu 2015	+	?	+	+	+	+	+	+
Matsukuma 2018	+	?	+	+	+	+	+	+
Panichi 2014	+	?	+	+	+	+	+	+
Park 2012	+	?	+	-	-	+	+	+
Sakakibara 2013	+	?	+	+	+	+	+	+
Shin 2012	+	?	+	-	-	+	+	+
Sirajedine 2012	+	?	+	+	+	+	-	+
Takahashi 2014	+	?	+	+	+	+	+	+
Tsai 2014	+	?	+	+	+	+	+	+
Tsai 2016	+	?	+	+	+	+	+	+
Zhang 2015	+	?	+	-	+	+	+	+

**Fig. 2.** Risk of bias summary by NOS quality assessment.

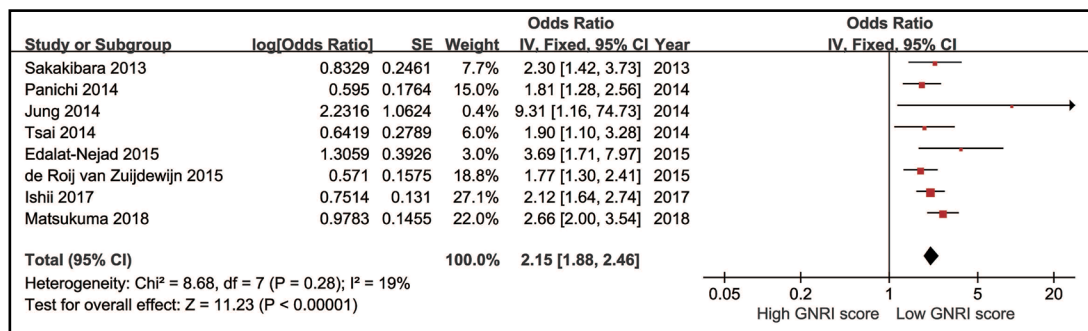


**Table 2.** The association between GNRI and mortality and cardiovascular event. Note: NR: not reported, a: calculated by dichotomous variable

-Author	All-cause mortality		Cardiovascular mortality		Cardiovascular event	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Kobayashi et al [8]	0.92 (0.89, 0.94)	1.01 (0.97, 1.05)	NR	NR	NR	NR
Park et al [11]	1.00 (0.97, 1.02)	0.64 (0.62, 0.66)	NR	NR	NR	NR
Sirajedine et al [19]	0.92 (0.85, 0.99)	0.71 (0.51, 0.98)	NR	NR	NR	NR
Shin et al [20]	NR	0.97 (0.95, 0.99)	NR	NR	NR	NR
Beberashvili et al [9]	0.99 (0.97, 1.01)	0.96 (0.91, 1.01)	NR	NR	NR	NR
Tsai et al [21]	NR	0.90 (0.81, 1.00)	NR	NR	NR	NR
Chen et al [22]	0.79 (0.51, 1.22)	0.96 (0.93, 0.99)	NR	0.59 (0.34, 1.02)	NR	0.75 (0.50, 1.13)
Sakakibara et al [23]	NR	2.30 (1.42, 3.73) <sup>a</sup>	NR	NR	NR	NR
Jung et al [24]	4.85 (1.38, 17.04) <sup>a</sup>	9.31 (1.16, 74.73) <sup>a</sup>	NR	NR	NR	NR
Panichi et al [10]	0.98 (0.97, 0.99)	1.81 (1.28, 2.56) <sup>a</sup>	NR	NR	NR	0.99 (0.98, 1.00)
Takahashi et al [25]	NR	NR	NR	0.75 (0.71, 0.79)	NR	NR
Edalat-Nejad et al [26]	2.68 (1.35, 5.30) <sup>a</sup>	3.69 (1.71, 7.97) <sup>a</sup>	NR	NR	NR	NR
Komatsu et al [14]	0.94 (0.91, 0.97)	0.97 (0.94, 1.00)	0.97 (0.93, 1.00)	0.98 (0.95, 1.02)	NR	NR
Zhang et al [27]	NR	0.94 (0.91, 0.97)	NR	0.91 (0.86, 0.95)	NR	NR
de Roij van Zuidewijn et al [28]	NR	0.80 (0.72, 0.89)	NR	NR	NR	NR
Beberashvili et al [13]	0.97 (0.96, 0.98)	0.97 (0.96, 0.98)	0.98 (0.96, 0.99)	0.97 (0.95, 0.99)	0.99 (0.97, 1.00)	0.98 (0.97, 0.99)
Tsai et al [29]	0.93 (0.89, 0.97)	0.91 (0.85, 0.97)	NR	NR	NR	NR
Ishii et al [30]	2.47 (1.96, 3.13) <sup>a</sup>	1.90 (1.10, 3.28) <sup>a</sup>	1.83 (1.27, 2.61) <sup>a</sup>	1.57 (1.06, 2.33) <sup>a</sup>	NR	NR
Matsukuma et al [31]	3.23 (2.46, 4.29) <sup>a</sup>	2.66 (2.00, 3.59) <sup>a</sup>				

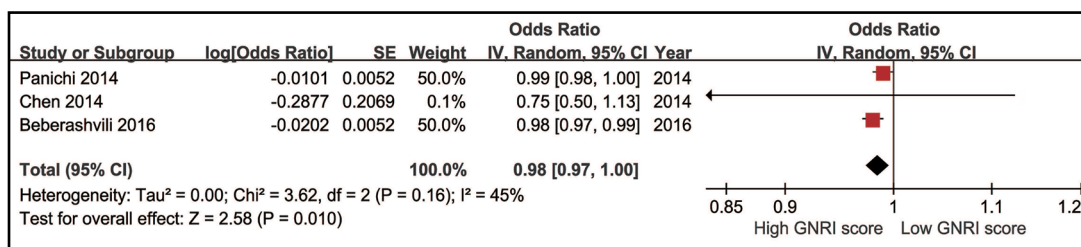


**Fig. 3.** The association between GNRI and all-cause mortality for adjusted ORs (continue variables).

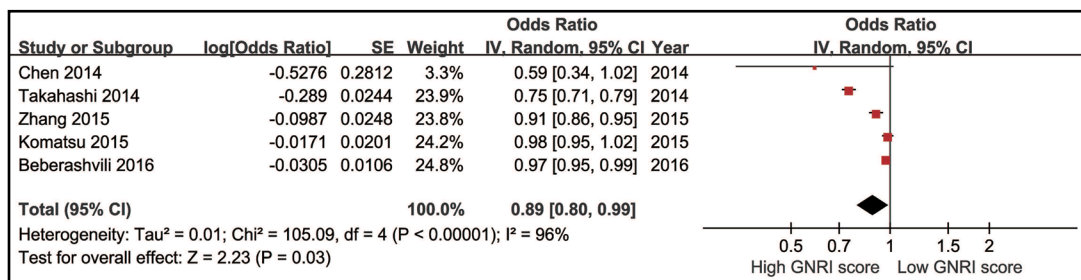


**Fig. 4.** The association between GNRI and all-cause mortality for adjusted ORs (dichotomous variables).

HD treatment. Previous study reported that 31.6% of the HD patients were considered malnourished according to GNRI [33]. Yamada K et al. has used GNRI to nutritional screening for HD patients and shown that GNRI was the simplest and most accurate risk index compared with several other nutritional screening tools [34]. For peritoneal dialysis (PD) patients. Szeto CC et al. found that GNRI is significantly correlated with other nutritional indices [35]. Current evidence showed that GNRI has already been accepted and widely used as a nutrition assessment tool and shown good performance in dialysis patients. Except for



**Fig. 5.** The association between GNRI and cardiovascular event for adjusted ORs (continue variables).



**Fig. 6.** The association between GNRI and cardiovascular mortality for adjusted ORs (continue variables).

nutrition screening for malnutrition by GNRI, Kobayashi et al. demonstrated that GNRI also can be used as a significant predictor for mortality in patients on HD patients [36]. Their results have been further confirmed by subsequent studies, especially from Asian chronic HD patients [8, 11, 21]. Besides that, studies from Italy, Netherlands and French also got similar conclusion [10, 28, 37]. Recently, a prospective cohort study with a total of 3436 Japanese HD participants included, Matsukuma et al. demonstrated that lower GNRI levels are an independent risk factor for infection-related mortality and all-cause mortality in patients undergoing HD [32]. Another large number study from Japan also found that low to medium GNRI was associated with all-cause mortality. Moreover, they also found that low-middle GNRI have the highest mortality rate (HR 4.28, 95%CI 2.66 to 6.88) if patients with low phosphorus level [38]. The association between GNRI and mortality has been further validated from PD and nondialysis CKD patients [39, 40]. Based on all the available studies, our meta-analysis further confirmed the results that high GNRI score can decrease the risk of all-cause mortality, while low GNRI was associated with high mortality for dialysis patients.

Albumin and body mass index (BMI) are the basic parameters for calculating GNRI. Previous study has demonstrated that both hypoalbuminemia and low body weight can reflect malnutrition and low BMI could also be an important indicator of PEW. BMI is associated with mortality among HD patients has been have revealed by previous study [32]. And recent studies demonstrated that significant associations of body weight and height, either separately were associated with all-cause morbidity and mortality [33]. Both of albumin and BMI have strong and consistent outcome-predictability of mortality. In a Japan study showed that GNRI is superior to predicting CVD mortality than using albumin and BMI alone [25]. Thus, GNRI combined with albumin and BMI could have critical value in predicting a patient's nutrition status and mortality prognosis.

Chronic inflammation persists in dialysis patients may causally tie underweight to increased mortality through malnutrition [41]. And HD patients with lower GNRI score exhibited reduced hemoglobin and albumin as well as reduced body weight [42]. Study also indicates that patients with low GNRI were associated with poor response to erythropoietin treatment [30]. In addition, lower GNRI were correlated with lower lean mass index (LMI), especially for female patients [43]. Inflammation, anemia and LMI that all contribute to malnutrition. Thus, GNRI is used for nutrition status evaluation and nutrition-related complications prediction. Low GNRI means malnutrition while good nutritional status

is a strong indicator of survival preponderance, so we speculate that GNRI can predicate mortality in HD patients which is mainly malnutrition related.

Recent epidemic studies have used the GNRI to predict outcomes of cardiovascular disease (CVD) [44] and showed that GNRI score were independently associated with cardiovascular events in chronic heart failure patients [45]. Moreover, GNRI has been demonstrated its association with cardiovascular mortality in newly institutionalised elderly [46]. Nowadays, the association has been investigated in HD patients that GNRI can accurately predict cardiovascular mortality [47]. But Chen HY et al. found that GNRI combined with fetuin A showed a significant interaction in the prediction of cardiovascular events but not for all-cause or cardiovascular mortality [22]. Inflammation has a potential contribution to CVD. A study showed that CRP, one of the inflammation markers, is associated with cardiovascular mortality. Moreover, the author further analyzed the cutoff value of CRP and nutrition status index and showed that both GNRI under 91.2 and CRP over 1.9 mg/L independently predicted mortality due to CVD, respectively. Furthermore, the combination of these variables increases their predictive values for the risk of mortality due to CVD and all-cause mortality in HD patients [31]. Lee et al. revealed that a worsening or stationary GNRI was independently associated with higher risk for major adverse cardiac and cerebrovascular events (MACCEs) in PD patients by multivariate cox analysis [48]. And reduced GNRI was also significantly associated with mortality and cardiovascular events in CKD patients not on dialysis treatment [40]. Our results have strengthened the above conclusion. We concluded that GNRI is associated with cardiovascular events as well as mortality. The reason may due to the poor nutritional status. Prior investigations have shown the close association between aortic calcification and cardiovascular mortality, study found that GNRI is an independent risk factor for the progression of aortic calcification [49]. Previous study reported that malnutrition is closely linked to carotid intima-media atherosclerosis in ESRD patients. From the above, we hypothesize that increased cardiovascular mortality caused by low GNRI is malnutrition related, but the exactly mechanism is not well known and further studies are needed to unveil the issue.

With respect to GNRI cutoff value. Bouillanne et al. determined 4 GNRI cutoff values to indicate the risk of malnutrition, GNRI <82, major nutrition-related risk; GNRI 82 to <92, moderate nutrition-related risk; GNRI 92 to 98, low nutrition related risk; GNRI >98, no risk. And they thought that a GNRI score of under 82 indicates malnutrition for hospitalized elder patients [15]. However, the GNRI cutoff was slightly different among previously studies [10, 15, 25, 27]. Zhang et al. showed that GNRI under 98, the risk of all-cause mortality will increase [27]. But two studies showed the risk increased only when GNRI under 92 [10, 25]. Table 3 listed the different GNRI cutoffs which indicates for malnutrition and mortality. In addition to predict value of GNRI for morality. Studies also showed that GNRI was correlated with walking ability and suggested that a GNRI of 87 might be the target for maintaining walking ability [50]. Currently, there is no unique GNRI cutoff to predict the malnutrition and mortality. And the best cutoff value of GNRI might be different for different ethnic populations. Although the cutoff value or predict value of GNRI is not always the same, there is a trend that the value is lower, the risk is greater. Further studies are needed to find out that best cutoff value of GNRI for morality prediction.

**Table 3.** Association between different GNRI cutoffs with malnutrition and mortality

Author	GNRI cutoff	Nutrition status and Outcome	Population and Patients
Bouillanne et al [15]	<82	Malnutrition	Caucasian hospitalized elder patients
	82 to <92	Moderate nutrition-related risk	
	92 to 98	Low nutrition related risk	
	>98	No risk	
Panichi et al [10]	< 92	Malnutrition and increase overall mortality	Caucasian hemodialysis patients
Takahashi et al [25]	<92	Malnutrition and increase cardiovascular mortality	Japanese hemodialysis patients
Zhang et al [27]	<98	Malnutrition and increase all-cause mortality	Chinese hemodialysis patients
Park et al [11]	<90	Malnutrition and increase mortality	Korean hemodialysis patients
Ishii et al [31]	<91.2	Malnutrition and increase overall mortality	Japanese hemodialysis patients



For nondialysis CKD patients, a study showed that a low GNRI was independently associated with progression to dialysis and may be useful in predicting the risk of adverse renal outcomes in patients with CKD stages 3-5 [51]. In addition, study has shown that GNRI is a favorable predictor of muscle function in renal transplant recipients [52]. Besides, GNRI was now considered as a novel prognostic factor for cancer patients [53, 54]. These results indicate that GNRI can be a powerful predictor for clinical outcome in different diseases and may be widely used in clinical practice.

However, there are some limitations that should be considered. The follow-up time of the included studies varied from 18 months to 120 months, which may cause heterogeneity. The cutoff value of GNRI was not the same when calculating the ORs for GNRI and all-cause mortality (dichotomous variables). In addition, the factors that have been adjusted in each study are also not the same. Finally, there are limited studies on the association of GNRI and cardiovascular mortality and cardiovascular events. Therefore, the evidence is not strong enough and more studies are needed.

### Conclusion

In summary, our findings have suggested that the GNRI value represents a strong predictor for all-cause and cardiovascular mortality in HD patients. And we recommended that GNRI should not be just for nutritional status assessment but also can be used as a good prognosis marker for HD patients.

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### Disclosure Statement

The authors declare that there are no conflicts of interest.

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