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Combined evaluation of geriatric nutritional risk index and modified creatinine index for predicting functional dependence in patients on Hemodialysis

Rong Ni[1], Peng Qian[1], Ci Sun[1], Yusheng Xu[1], Kai Song[1] and Weiwei Li[1*]

Abstract

Background In patients undergoing hemodialysis, functional dependence has increasingly been recognized as a critical factor influencing both quality of life and clinical outcomes. This study evaluates the combined effect of the Geriatric Nutritional Risk Index (GNRI) and Modified Creatinine Index (mCI) on predicting functional dependence in patients undergoing maintenance hemodialysis (MHD).

Methods We conducted a cross-sectional survey at the Second Affiliated Hospital of Soochow University from June to December 2023. The study involved 208 MHD patients whose functional status was assessed using Katz and Lawton-Brod questionnaires. Patients were classified into either a normal functional group or a functional dependence group based on their scores. GNRI and mCI were categorized using cut-off values of 98.0 and 21.63 mg·kg^{-1}·d^{-1}, respectively. Logistic regression analysis was used to evaluate the risk factors and develop predictive models. The accuracy of these models was assessed through receiver operating characteristic (ROC) curves.

Results Functional dependence was observed in 110 patients (52.9%). The functional dependence group exhibited significantly higher age, prevalence of diabetes, and pulse pressure, but lower diastolic blood pressure, serum creatinine, serum albumin, cholesterol, GNRI, and mCI compared to the normal functional group (all $P < 0.05$). Logistic regression highlighted significant differences in the risk of functional dependence among the four groups based on GNRI and mCI thresholds ($P < 0.05$). The area under the curve (AUC) for the combined GNRI and mCI model was 0.708 (95% *CI* 0.638–0.778, $P < 0.001$), indicating superior predictive capability over the individual indices (GNRI alone $AUC = 0.657$, mCI alone $AUC = 0.682$).

Conclusion GNRI and mCI, when used in combination, provide a more effective prediction of functional dependence in MHD patients than when used separately.

Keywords Nutrition assessment, Functional dependence, Geriatric nutritional risk index, Modified creatinine index, Hemodialysis

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Background

Malnutrition is widely recognized as a prevalent issue among patients undergoing maintenance hemodialysis (MHD) and is influenced by numerous factors. Among these, abnormal protein metabolism, specifically the dysfunctional synthesis and degradation of muscle protein, is pivotal in the development of malnutrition in this population. The International Society of Nephrology and Metabolism highlighted this issue in 2008 with the introduction of the concept of protein-energy wasting (PEW). Defined as the inadequate intake of nutrients leading to further depletion and resulting in diminished protein and energy reserves, PEW severely hampers the body's ability to meet metabolic demands, causing significant weight loss, progressive skeletal muscle wasting, and a reduction in subcutaneous fat [1]. Research indicates that PEW affects 28–54% of MHD patients and is linked to deteriorated physical function and increased morbidity and mortality rates [2–4].

Given these challenges, it is imperative to identify simple, objective nutritional assessment tools that can facilitate early detection and timely intervention in MHD patients, potentially reducing hospitalizations and mortality rates. The Geriatric Nutritional Risk Index (GNRI) is one such tool, providing a straightforward evaluation of nutritional status through measurements of body mass index (BMI) and serum albumin levels, which reflect visceral protein stores. In contrast, the Modified Creatinine Index (mCI) gauges somatic skeletal muscle creatinine production based on serum creatinine levels, serving as an indicator of somatic protein status. While both indices are independently associated with an increased risk of mortality and cardiovascular incidents in hemodialysis patients, their individual predictive capacities have limitations [5–7].

Functional dependence refers to the inability of an individual to independently perform basic and instrumental activities of daily living, typically assessed through Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). ADL primarily includes fundamental self-care tasks such as bathing, dressing, and eating, while IADL involves more complex tasks like managing finances, shopping, and meal preparation. In patients undergoing hemodialysis, functional dependence has increasingly been recognized as a critical factor influencing both quality of life and clinical outcomes [8]. Studies have shown that functional dependence in hemodialysis patients is closely associated with poorer clinical outcomes, including increased hospitalization rates, adverse prognosis, and deteriorating psychological health [9].

Our study applies the combined GNRI and mCI evaluation framework first established by Yajima [10] et al. to address a critical gap in clinical research both domestically and internationally regarding the combined use of GNRI and mCI for predicting functional dependence in MHD patients. This study aims to bridge this gap by evaluating the efficacy of this combined approach in predicting functional dependence, thereby identifying potential opportunities for intervention that could improve patient quality of life and prognosis.

Methods

Subjects: This cross-sectional study enrolled patients from the Hemodialysis Center of the Second Hospital Affiliated with Soochow University between June and December 2023. Inclusion criteria were: (1) age over 18 years; (2) undergoing regular hemodialysis for more than three months and stable; (3) possessing adequate cognitive function to complete questionnaires; (4) providing voluntary informed consent. Exclusion criteria included: (1) severe infection, autoimmune diseases, hematological disorders, or malignant tumors; (2) corticosteroid or immunosuppressant use within the previous three months; (3) receipt of nutritional support such as serum albumin or amino acid injections within the same timeframe. The study was approved by the Ethics Committee of Soochow University (ethics number SUDA20210827H01).

Data Collection: Patients were selected based on the inclusion and exclusion criteria. Data collected included demographics (age, gender), clinical parameters (height, dry weight, duration of dialysis treatment), socioeconomic status, associated complications, blood pressure, and laboratory results from pre-dialysis samples taken between the long dialysis sessions. Key laboratory measurements included blood urea nitrogen (BUN), serum creatinine (Scr), serum albumin, hemoglobin, C-reactive protein (CRP), cholesterol, triglycerides, serum calcium, serum phosphorus, and the urea clearance index (KT/V).

Calculation and Grouping of GNRI and mCI: GNRI was calculated using the formula from literature [11]: GNRI = 1.489 × serum albumin (g/L) + 41.7 × (BMI (kg/m²)/22, with BMI/22 set as "1" for values ≥ 22 kg/m². Patients were classified into increased or decreased GNRI groups based on a cut-off value of 98.0. The mCI formula was [12]: mCI ($mg \cdot kg^{-1} \cdot d^{-1}$) = 16.21 + 1.12 × (1 if male; 0 if female) − 0.06 × age (years) − 0.08 × KT/V + 0.009 × Scr (μmol/L), with a dichotomous division at 21.63 $mg \cdot kg^{-1} \cdot d^{\wedge -1}$. Patients were then categorized into four groups based on these indices: GNRI and mCI both increased (G1), GNRI increased and mCI decreased (G2), GNRI decreased and mCI increased (G3), GNRI and mCI both decreased (G4).

Assessment of Functional Status: Functional status was assessed using the Dialysis Outcomes and Practice Model Study (DOPPS) [13]. The Katz questionnaire [14] was used to evaluate basic activities of daily living (ADL) such as bathing, dressing, toileting, mobility, bowel and urine control, and eating. Each activity was scored from 0 (dependent) to 2 (independent), with total scores ranging from 0 to 12. The Lawton-Brod questionnaire [15] assessed instrumental activities of daily living (IADL) including tasks like shopping, housework, cooking, and managing finances, with scores also ranging from complete dependence to independence, the total score ranges from 0 to 24. Patients requiring assistance in more than one activity were classified as functionally dependent.

Statistical Analysis: Data were analyzed using SPSS 26.0, GraphPad Prism 9.3, OriginPro 2024b, and R 4.3.3. Normally distributed data were presented as mean ± standard deviation and analyzed using independent t-tests, while non-normally distributed data were presented as medians (P25, P75) and analyzed using the Mann-Whitney U test. Categorical data were analyzed using chi-square tests. Preselection of potential variables based on clinical guidelines and existing literature evidence; Univariate logistic regression screening ($\alpha = 0.05$) for statistically significant variables; Final inclusion in multivariate logistic regression required both clinical relevance and $P < 0.05$; Variance inflation factor (VIF < 5) was applied to control multicollinearity.Logistic regression was used to identify risk factors and develop prediction models, while *ROC* curve analysis assessed the predictive effectiveness of the GNRI and mCI, both individually and combined. A *P*-value < 0.05 was considered statistically significant.

Results

1. Basic Characteristics of the Study Population: The study included 208 patients undergoing maintenance hemodialysis (MHD) with an average age of 59.15 ± 14.00 years; 63.5% were male. Comorbidities included diabetes (28.8%), hypertension (89.4%), and cardiovascular disease (22.6%). Notably, 52.9% exhibited functional dependence. Compared to the normal functional group, the functionally dependent group showed significantly higher age (Z =-6.120, $P < 0.001$), proportion of diabetes (χ^2=8.077, $P = 0.004$), and pulse pressure (Z =-3.408, $P < 0.001$), and lower diastolic blood pressure ($t = 3.087$, $P < 0.001$), serum creatinine ($t = 3.599$, $P < 0.001$), serum albumin (Z =-4.680, $P < 0.001$), cholesterol

Table 1 Comparison of clinical data between the normal function group and the functional dependence group

	Normal functional group (*n* = 98)	functional dependence group (*n* = 110)	t/Z/χ2	*P* values
Age (years)	54.00 (44.00,61.00)	67.00 (53.00,76.00)	-6.120	< 0.001
Gender (male/female, n)	63/35	69/41	0.054	0.816
Marriage (yes, n(%))	90 (91.8)	102 (92.7)	0.058	0.810
Economic status (income > expenditure, n, %)	70 (71.4)	72 (65.5)	0.854	0.355
BMI(kg/m^2)	21.95 (20.38, 24.50)	21.95 (20.47, 24.91)	-0.110	0.913
Comorbidities				
Diabetes (n, (%))	19 (19.4)	41 (37.3)	8.077	0.004
Hypertension (n, (%))	87 (88.8)	99 (90)	0.082	0.774
Cardiovascular disease (n, (%))	17 (17.3)	30 (27.3)	2.919	0.088
Systolic blood pressure (mmHg)	145.50(135.00,155.50)	150.00 (139.75, 161.00)	-1.527	0.127
Diastolic blood pressure (mmHg)	81.61 ± 11.96	76.18 ± 13.26	3.087	0.002
Pulse pressure difference (mmHg)	63.50 (51.00, 75.25)	73.00 (62.00, 85.00)	-3.408	< 0.001
Duration of dialysis (months)	37.00 (11.50, 59.00)	33.00 (11.75, 58.25)	-0.293	0.769
Kt/V	1.33 (1.17, 1.56)	1.31 (1.11, 1.53)	-0.812	0.417
Hemoglobin (g/L)	114.41 ± 16.16	111.96 ± 19.45	0.972	0.332
C-reactive protein (mg/L)	5.40 (5.10, 5.70)	5.40 (5.10, 5.70)	-0.141	0.888
Blood urea nitrogen (mmol/l)	23.90 (19.85, 27.45)	22.95 (18.00, 27.35)	-0.951	0.342
Serum creatinine (μmol/L)	996.34 ± 237.13	872.18 ± 256.67	3.599	< 0.001
Serum albumin (g/L)	42.10 (39.85, 43.90)	39.75 (37.65, 42.10)	-4.680	< 0.001
Corrected calcium(mg/dl)	8.87(8.32,9.34)	8.91(8.51,9.46)	-1.051	0.293
Blood phosphorus (mmol/L)	1.97 (1.59, 2.32)	1.79 (1.49, 2.26)	-1.398	0.162
Serum PTH (pg/ml)	280.87(179.90,414.00)	295.55(169.20,429.65)	-0.060	0.952
Cholesterol (mmol/L)	3.78 (3.37, 4.59)	3.61 (2.96, 4.28)	-2.095	0.036
Triglycerides (mmol/L)	1.62 (1.10, 2.54)	1.42 (1.08, 2.03)	-1.720	0.085
GNRI	102.15 (98.52, 105.73)	99.62 (95.69, 102.47)	-3.910	< 0.001
mCI	22.39 (20.89, 23.95)	20.79 (18.62, 22.55)	-4.516	< 0.001

Note: BMI: body mass index; Kt/V: weekly urea clearance index; Serum PTH: Serum parathyroid hormone; Corrected calcium (mg/dL) = Serum calcium (mmol/L) × 4 + 0.32 × (40-Serum albumin (g/L)); GNRI: geriatric nutrition index; mCI: modified creatinine index. Except the data format indicated, the measurement data in accordance with normal distribution were expressed in the form of $\bar{x}$±sd, and the measurement data not in accordance with normal distribution were expressed in the form of M (P25, P75)

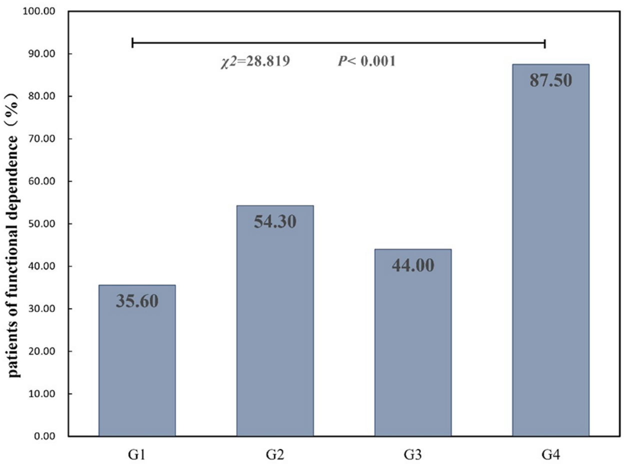

Fig. 1 Comparison of the incidence of functional dependence in subgroups. Note: GNRI: geriatric nutritional risk index; mCI: modified creatinine index; G1 group: GNRI ≥ 98, mCI ≥ 21.64 (*n* = 73); G2 group: GNRI ≥ 98, mCI < 21.64 (*n* = 70); G3 group: GNRI < 98, mCI ≥ 21.64 (*n* = 25); G4 group: GNRI < 98, mCI < 21.64 (*n* = 40)

levels (Z =-2.095, $P = 0.036$), GNRI (Z =-3.910, $P < 0.001$), and mCI (Z =-4.516, $P < 0.001$) (Table 1).

2. Functional Dependence in Subgroups: The incidence of functional dependence varied significantly across groups defined by GNRI and mCI. Group G4 (both indices decreased) exhibited the highest rate at 87.5%, significantly greater than Group G1 (both increased) at 35.6%, G2 (GNRI increased, mCI decreased) at 54.3%, and G3 (GNRI decreased, mCI increased) at 44% ($P < 0.05$) (Fig. 1).
3. Logistic Regression Analysis: In unadjusted analyses, Group G4 was associated with a markedly higher risk of functional dependence compared to G1 (*OR* = 12.654, 95% *CI* 4.417–36.247, $P < 0.001$). This association persisted across progressively adjusted models accounting for age, diabetes, blood pressures, and biochemical parameters, with the fully adjusted model showing an *OR* of 6.493 (95% *CI* 1.214–34.722, $P = 0.029$) (Fig. 2).
4. Correlation Analysis: Pearson correlation analysis showed that the total functional status score negatively correlated with age (r =-0.456, $P < 0.001$)

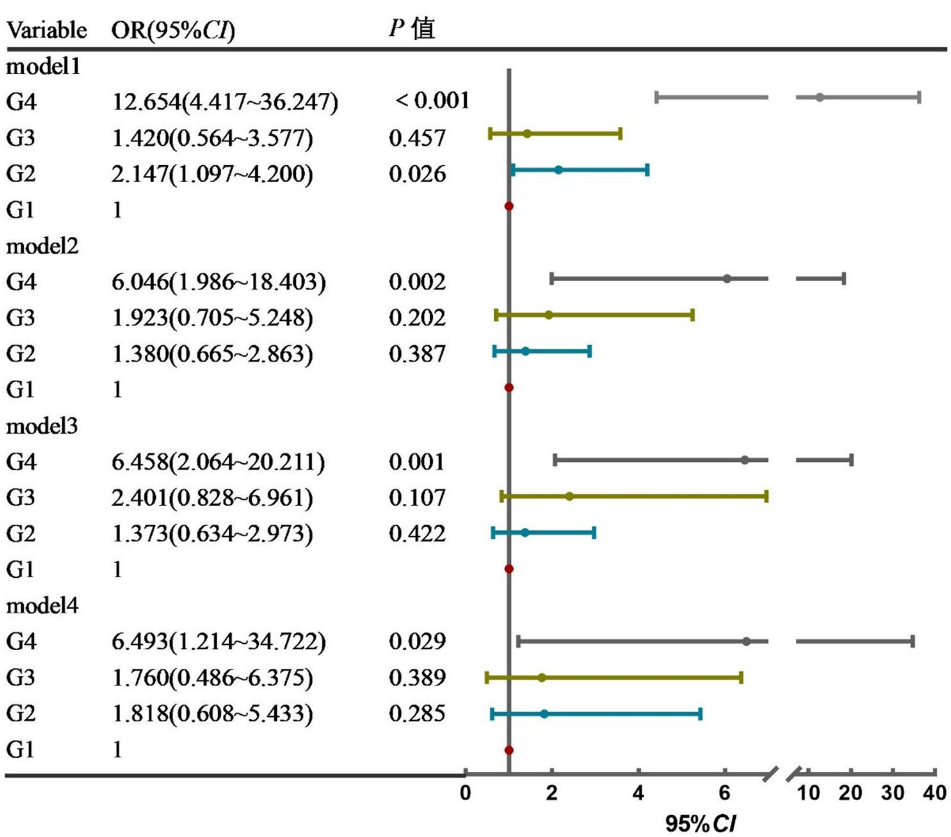

Fig. 2 Comparison of the risk of functional dependence between the subgroups. (Logistic regression analysis). Note: GNRI: geriatric nutritional risk index; mCI: modified creatinine index; Model 1: unadjusted model; Model 2: adjusted for age; Model 3: adjusted for age, diabetes, diastolic blood pressure and pulse pressure; Model 4: adjusted for age, diabetes, diastolic blood pressure, pulse pressure, serum albumin, serum creatinine, an total cholesterol; G1 group: GNRI ≥ 98, mCI ≥ 21.64 (*n* = 73); G2 group: GNRI ≥ 98, mCI < 21.64 (*n* = 70); G3 group: GNRI < 98, mCI ≥ 21.64 (*n* = 25); G4 group: GNRI < 98, mCI < 21.64 (*n* = 40)

and pulse pressure (r =-0.217, $P<0.001$), and positively with diastolic blood pressure ($r=0.374$, $P<0.001$), serum albumin ($r=0.369$, $P<0.001$), serum creatinine ($r=0.274$, $P<0.001$), GNRI ($r=0.245$, $P<0.001$), and mCI ($r=0.347$, $P<0.001$) (Fig. 3).

5. Interactive Effects of Age and BMI: No interaction was found between age and BMI for GNRI ($P>0.05$) or between BMI and mCI ($P>0.05$). However, an interaction was observed between age and mCI affecting the risk of functional dependence ($P=0.021$) (Fig. 4).
6. Predictive Efficacy of GNRI and mCI: *ROC* curve analysis demonstrated that the combination of GNRI and mCI yielded a higher *AUC* of 0.708 (95% *CI* 0.638–0.778, $P<0.05$) for predicting functional dependence, surpassing the AUCs for GNRI alone (0.657, 95% *CI* 0.583–0.731, $P<0.001$) and mCI alone (0.682, 95% *CI* 0.609–0.754, $P<0.001$) (Fig. 5).

Discussion

Epidemiology of Functional Dependence in MHD Patients.

The term "physical function dependence" encompasses the inability to perform personal care and household tasks independently, significantly impacting the quality of life of patients undergoing maintenance hemodialysis (MHD) [8, 9, 16]. Our study reveals that 52.9% of MHD patients experience functional dependence, closely aligning with the 43-81% range reported in the DOPPS study across various demographics. Notably, functional dependence prevalence escalates with age, with those 70 years and older being most affected. This age-related decline in physical function is also pronounced among diabetic patients, where dependence rates soar to 73%, compared to 57% in non-diabetics [13]. The ACTIVE-ADIPOSE study also demonstrate the impact of diabetes on the functional dependence [17]. These findings underscore the compounded impact of chronic illnesses and aging on functional capacities.

Vascular health and functional independence

Vascular health significantly influences functional status. The findings of a prospective, multiethnic cohort study conducted in Northern Manhattan demonstrate that indicators of optimal cardiovascular health are significantly associated with improved functional status. This underscores the critical importance of maintaining ideal cardiovascular health to enhance long-term functional

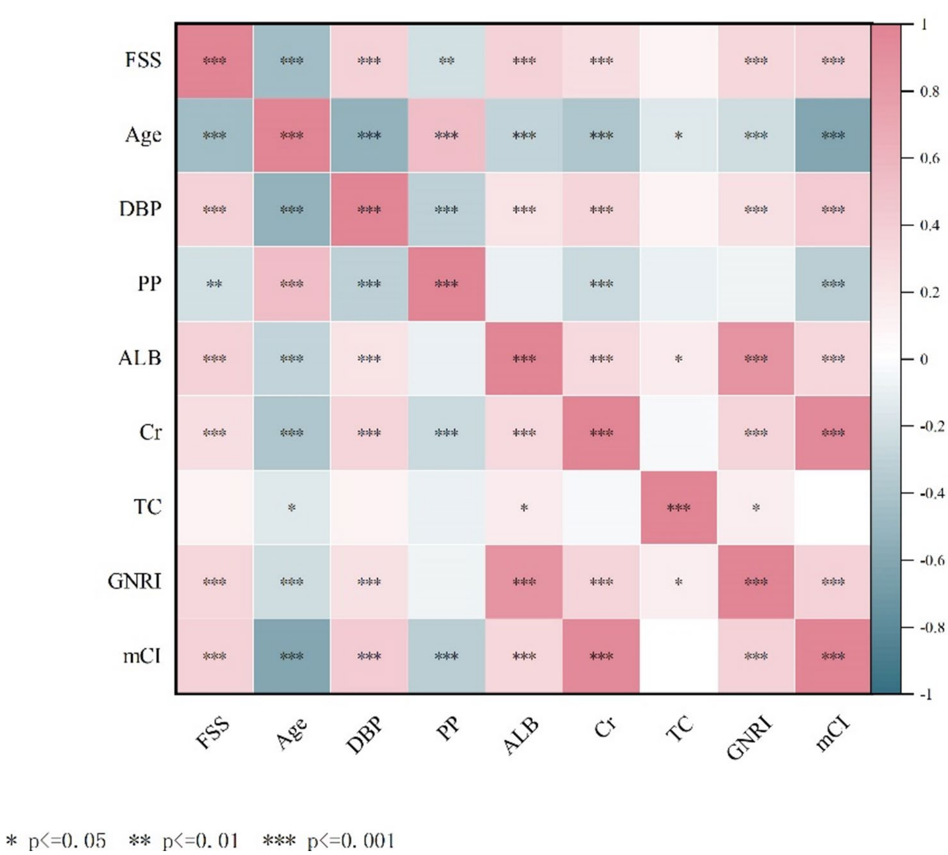

Fig. 3 Correlation analysis between total functional status score and traditional indicators. Note: FSS: functional status score; DBP: diastolic blood pressure; PP: pulse pressure; ALB: albumin; Cr: creatinine; TC: total cholesterol; GNRI: geriatric nutritional risk index; mCI: modified creatinine index

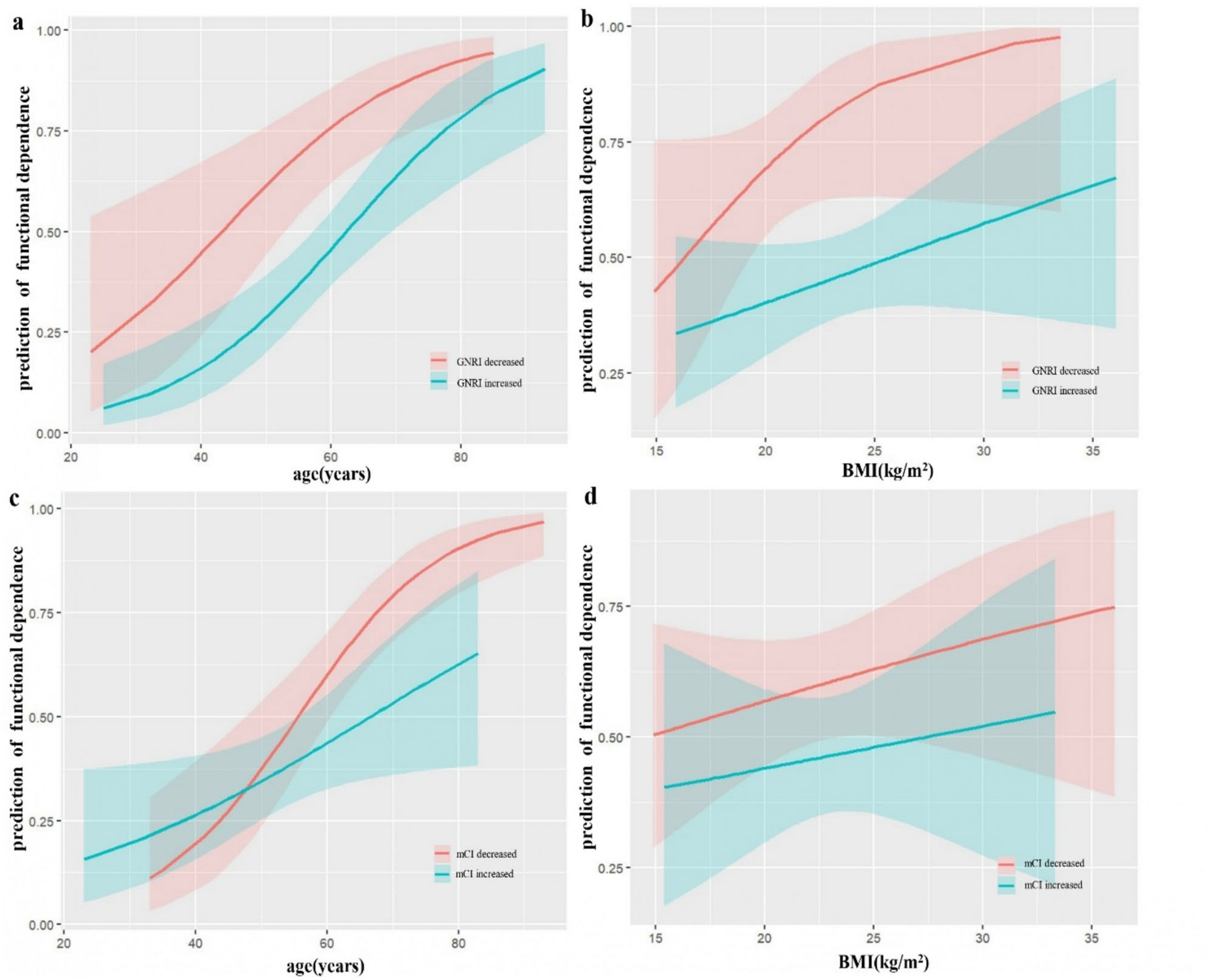

Fig. 4 The interactive effects of age and BMI. Note: BMI: body mass index; GNRI: geriatric nutritional risk index; mCI: modified creatinine index. Interaction of age in GNRI prediction of functional dependence (**a**); Interaction of BMI in GNRI prediction of functional dependence (**b**); Interaction of age in mCI prediction of functional dependence (**c**); Interaction of BMI in mCI prediction of functional dependence (**d**)

status and mitigate the risk of impaired vascular function [18]. In our cohort, functionally dependent patients exhibited increased pulse pressure and decreased diastolic pressure, indicators of arterial stiffness and potential myocardial strain. Although these vascular changes are linked to higher cardiovascular event rates [19, 20], our study's limited sample size of patients with cardiovascular conditions constrains definitive conclusions within the function-dependent group.

Nutritional status and muscle mass

A study conducted on hemodialysis patients in Japan emphasized the significance of body mass index(BMI) and muscle mass in the diagnosis of protein-energy wasting (PEW) and revealed a strong association between a lower BMI threshold and an elevated risk of mortality [21].The linkage between malnutrition, characterized by protein-energy wasting (PEW), and functional dependence is evident in our findings. PEW in MHD patients, marked by weight loss and muscle atrophy, correlates strongly with decreased serum creatinine, serum albumin, and total cholesterol levels—markers of reduced muscle mass and nutritional deficiency. These associations are consistent with those documented in the DOPPS study, affirming the role of nutritional status in maintaining physical independence.

Utility of GNRI and mCI in clinical practice

Our study highlights the GNRI and mCI as pivotal indicators for assessing nutritional and functional status in MHD patients. While GNRI evaluates visceral protein status through BMI and serum albumin levels, mCI assesses somatic protein via serum creatinine. Yamada [22] et al. utilized DOPPS data from Japan to

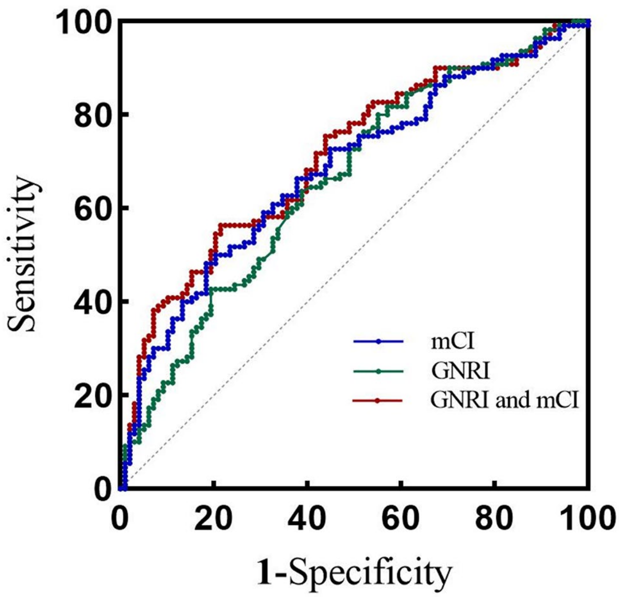

Fig. 5 Predictive Efficacy of GNRI and mCI. Note: GNRI: geriatric nutritional risk index; mCI: modified creatinine index. GNRI and mCI: the combined GNRI and mCI

demonstrate that both GNRI and mCI serve as reliable indicators of nutritional status, independently predicting the risk of mortality in hemodialysis patients. These metrics, although independently significant, when combined, provide a comprehensive overview of a patient's health status. Fujioka [23] et al. supports our findings, suggesting that the integration of GNRI and mCI enhances risk stratification for mortality among hemodialysis patients.

Implications for patient management

The categorization of patients into G1 to G4 groups based on GNRI and mCI scores proved instrumental in identifying those at highest risk for functional dependence. Notably, patients in the G4 group, characterized by low GNRI and mCI, were at a significantly elevated risk, suggesting that both high nutritional status and muscle mass are crucial for functional independence. This stratification allows for targeted interventions that could improve outcomes for high-risk patients.

Future directions and study limitations

Although this study provides valuable data and insights into the factors affecting functional dependence in hemodialysis patients, several limitations remain.

First, the sample selection may introduce some bias. As we included patients from specific treatment center, the findings may not fully represent hemodialysis patients in other regions or clinical settings. Future studies should include a more diverse patient population to improve the external validity and generalizability of the results.

Second, this study employs a cross-sectional design, which limits our ability to draw causal inferences. While we observed an association between the GNRI and mCI in predicting adverse clinical outcomes related to functional dependence, the lack of long-term follow-up data prevents dynamic observation of functional dependence over time. Therefore, longitudinal studies are needed to further validate these findings.

Another limitation concerns the handling of extreme cases in the sample. Although we included only stable, regularly dialyzed patients and excluded or adjusted for those with severe edema or extreme BMI values, this may not have fully eliminated the potential confounding effects of these patients. Patients with extreme edema or nutritional states could uniquely influence dialysis treatment and functional dependence assessments. Future research should explore how to better handle such patient groups.

In conclusion, while this study offers insights into the combined use of GNRI and MCI in predicting functional dependence in hemodialysis patients, it has notable limitations. Future research should address these limitations and adopt more comprehensive and refined study designs to further validate these findings.

Conclusions

The Geriatric Nutritional Risk Index (GNRI) and Modified Creatinine Index (mCI) prove to be effective, easily accessible tools for assessing the nutritional status of patients undergoing maintenance hemodialysis (MHD). Our findings underscore their utility, demonstrating that when used in combination, GNRI and mCI provide a significantly enhanced predictive capability for identifying the risk of physical functional dependence in this patient population, surpassing the predictive accuracy of using either index alone.

This study, however, is not without its limitations. The small sample size and the cross-sectional nature of the study design limit the generalizability of the results. Additionally, the absence of external validation for our predictive model may affect the reliability of applying these findings in broader clinical settings. To build on the insights gained from this research, future studies should focus on larger, multi-center trials to confirm and extend these findings. Such studies should aim to incorporate longitudinal designs and seek external validation of the prediction models to ensure their accuracy and applicability across various clinical environments.

By enhancing our understanding and implementation of GNRI and mCI, healthcare providers can better identify MHD patients at high risk of functional dependence, potentially leading to targeted interventions that can significantly improve patient outcomes.

Abbreviations

GNRI	Geriatric nutritional risk index
mCI	Modified creatinine index
MHD	Maintenance hemodialysis
ROC	Receiver operating characteristic
PEW	Protein-energy wasting
BMI	Body mass index
ADL	Activities of daily living
IADL	Instrumental activities of daily living
Kt/V	Weekly urea clearance index
Serum PTH	Serum parathyroid hormone

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Author contributions
Rong Ni contributed to the study design, data acquisition, data analysis, and manuscript writing. Peng Qian, Ci Sun, Yusheng Xu, Kai Song contributed to the data analysis. Weiwei Li contributed to the study design, commentary, and revision of the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of Soochow University. All the patients consented to participate in the study and signed the written informed consent.

Consent for publication
The authors consented to publish the manuscript.

Competing interests
The authors declare no competing interests.

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