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Nutritional indicators and implications for human health

Edited by
Luciane Bresciani Salaroli and Juliana Vaz

Coordinated by
Virginia Maria Muniz

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Nutritional indicators and implications for human health

Topic editors
Luciane Bresciani Salaroli — Federal University of Espirito Santo, Brazil
Juliana Vaz — Federal University of Pelotas, Brazil

Topic coordinator
Virginia Maria Muniz — Secretaria de Estado da Saúde do Espírito Santo, Brazil

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EDITED AND REVIEWED BY
Angela M. Zivkovic,
University of California, Davis, United States

*CORRESPONDENCE
Luciane Bresciani Salaroli
lucianebresciani@gmail.com

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Editorial: Nutritional indicators and implications for human health

Virginia Maria Muniz[1,2], Juliana Dos Santos Vaz[3] and Luciane Bresciani Salaroli[2,4]*

[1]State Health Department of Espírito Santo, Vitória, Brazil, [2]Research Group/CNPq in Epidemiology, Health and Nutrition (GEMNUT) of the Federal University of Espírito Santo, Vitória, Brazil, [3]Graduate Program in Nutrition and Foods of the Federal University of Pelotas, Pelotas, Brazil, [4]Graduate Program in Public Health and Graduate Program in Nutrition and Health of the Federal University of Espírito Santo, Vitória, Brazil

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Editorial on the Research Topic
Nutritional indicators and implications for human health

Nutritional assessment aims to investigate nutritional parameters, risk factors and specific deficiencies, in addition to determining nutritional needs and identifying medical, psychosocial and socioeconomic determinants that may influence nutritional support therapy (1, 2). Thus, adequate hospital nutrition management, based on a careful assessment, can contribute to improving the clinical outcomes of individuals and, consequently, the quality of health care (3).

In the community setting, nutritional assessment plays a pivotal role in supporting public health policy managers, contributing to the identification and tackling of epidemic problems, such as obesity—whether resulting from inadequate diets or associated with metabolic disorders—, as well as malnutrition related to food insecurity in low-income regions (4, 5).

Heterogeneous dietary responses among individuals result from a complex interaction among genetic factors, lifestyle, socioeconomic conditions and cultural contexts. These elements highlight the need for more individualized strategies, such as precision nutrition (PN), aiming to optimize health outcomes. Hence, the use of biomarkers of food intake emerges as a promising tool to increase the accuracy of dietary surveys, providing more reliable biological information and contributing to the development of more effective nutritional interventions (6).

In this context, the Research Topic "*Nutritional indicators and implications for human health*" brings together 13 studies that present relevant evidence on the use of nutritional indicators in different approaches, both at the individual and population levels. These studies include analyses based on public and comprehensive databases, field research conducted in high- and low-income regions around the world, as well as literature reviews, which will be highlighted below.

Among the population studies, four used data from the US National Health and Nutrition Examination Survey (NHANES). Liang et al. evaluated the association between the body roundness index (BRI) and osteoarthritis (OA) in adults and identified a positive relationship between BRI and the prevalence of OA in the general population of the

United States of America (USA). Zhang et al. investigating the relationship between new anthropometric indices and the risk of gallstones in US adults, observing a positive association between several anthropometric indicators and the diagnosis of this condition. Yan et al. examined the possible correlation between the intestinal microbiota and the presence of kidney stones among US adults, demonstrating the potential benefits of dietary adjustments based on the dietary index for gut microbiota (DI-GM) in reducing the incidence of kidney stones. Finally, Tan et al. analyzed the associations between nutritional risk, assessed by the Geriatric Nutritional Index (GNRI), and cognitive functions in older adults in the USA, identifying that a lower GNRI was associated with worse performance in several cognitive domains.

Other population-based studies have been conducted in communities with different levels of economic resources and provide relevant evidence for the formulation of public health policies. Liu et al., using data from the Chinese Longitudinal Healthy Longevity Survey (CLHLS), observed that improving dietary behaviors among the elderly can contribute to reducing high Body Mass Index (BMI) values to normal levels; however, the same effect was not observed in cases of low BMI. Zhao et al. applied the AHLC nutritional model (albumin + HDL-cholesterol + lymphocytes + calcium) in a Chinese community population, with good results in the early detection of sarcopenia. Two studies were conducted in communities in Ethiopia. Menber et al. evaluated the performance of the Minimum Dietary Diversity for Women (MDD-W) indicator in predicting the adequacy of micronutrient intake among lactating women in a northeastern region of the country, finding results that diverged from previous studies conducted in other contexts. Zebene et al. investigated the accuracy of mid-upper arm circumference (MUAC) in identifying different forms of thinness among adolescent girls in schools in Addis Ababa, concluding that incorporating this indicator may be especially useful in resource-limited settings.

Three studies are notably addressed in hospital research. Zou et al. analyzed the performance of six nutritional indicators in predicting the prognosis of individuals with COVID-19, identifying the most effective index for this purpose. Díaz-Amaya et al. investigated the relationship between nutritional status, assessed by means of the phase angle, and postoperative complications in pediatric individuals undergoing surgery. The results indicated that the phase angle may be a valuable marker in the prevention of surgical complications in this population. Bae et al. examined variations in the values of the Prognostic Nutrition Index (PNI) in the postoperative period of patients undergoing myocardial revascularization using the off-pump coronary artery bypass (OPCAB) method. The study highlighted the importance of monitoring the PNI in the postoperative period as a tool for screening individuals at higher risk of mortality.

Among the studies presented, two important literature reviews stand out. Lu and Li conducted a systematic review with meta-analysis on the Controlling Nutritional Status (CONUT) score and its application in individuals with hematologic malignancies, demonstrating that CONUT may have predictive value in the prognosis of some of these conditions. Singh et al. developed a review on precision nutrition, an approach that considers multiple individual factors such as age, sex, genetic and epigenetic profile, in addition to pathophysiological conditions to formulate more specific dietary recommendations. This nutritional strategy aims, among other objectives, to favor the enrichment of the desirable microbiota, contributing to the promotion of a healthy diet with potential positive impact, especially for future generations.

Overall, the findings gathered in this Research Topic highlight the relevance of nutritional indicators both in individual clinical assessment, as a tool for planning nutritional support and predicting clinical outcomes, and in qualifying hospital care. Furthermore, they highlight the strategic role of these indicators in public health, especially in addressing nutritional deficiencies in communities with limited economic resources. The studies also reinforce the association between nutritional indicators and various health conditions related to eating habits, lifestyle, and socioeconomic and cultural contexts, pointing to the importance of integrated and contextualized approaches in nutritional care at the population and individual levels.

Author contributions

VM: Writing – review & editing. JV: Writing – review & editing. LS: Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Guillermina Barril,
Princess University Hospital, Spain
Luciana Bicalho Cevolani Pires,
Federal University of Espirito Santo, Brazil
Luciane Bresciani Salaroli,
Federal University of Espirito Santo, Brazil

*CORRESPONDENCE
Qingqing Li
✉ liqingqing@cancerhosp-ln-cmu.com

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The controlling nutritional status score as a predictor of survival in hematological malignancies: a systematic review and meta-analysis

Guimei Lu[1] and Qingqing Li[2]*

[1]Department of Laboratory, Liaoning Cancer Hospital and Institute, Cancer Hospital of China Medical University, Shenyang, China, [2]Department of Endoscopy, Liaoning Cancer Hospital and Institute, Cancer Hospital of China Medical University, Shenyang, China

Objective: The controlling nutritional status score (CONUT) has been widely used for ascertaining the prognosis of various cancers. However, its use in patients with hematological malignancies remains unclear. This review examined evidence on the utility of CONUT as a prognostic marker for patients with hematological malignancies.

Methods: All cohort studies that examined the association between CONUT and outcomes of hematological malignancies and were published on the databases of Embase, Scopus, CENTRAL, Web of Science, and PubMed were searched from the inception of the databases to 30 January 2024. The primary outcome was overall survival (OS), and the secondary outcome was progression-free survival (PFS).

Results: A total of 23 studies were available for review. A meta-analysis of 22 studies showed that high CONUT was significantly associated with poor OS in patients with hematological malignancies (HR: 1.95 95% CI: 1.62, 2.35 I^2 = 89%). The results remained unchanged on sensitivity and subgroup analyses based on study location, sample size, diagnosis, CONUT cutoff, and the Newcastle–Ottawa Scale score. Only six studies reported data on PFS, and the pooled analysis found that high CONUT was a significant marker for poor PFS in patients with hematological malignancies [hazards ratio (HR): 1.64 95% CI: 1.21, 2.20 I^2 = 70%]. These results, too, maintained significance in the sensitivity analysis.

Conclusion: CONUT is an independent predictor of poor OS in patients with hematological malignancies. The results appear to be valid across different cancer types and with different CONUT cutoffs. Scarce data also suggest that CONUT could predict PFS.

KEYWORDS

nutrition, lymphoma, leukemia, survival, recurrence

Introduction

Hematologic malignancies or blood cancers have become increasingly prevalent in the current century. These cancers are lymphatic and myeloid tumors caused by the disturbance of routine hematopoietic function and can be broadly classified into three types, namely, leukemias, myelomas, and lymphomas (1). Their incidence has peaked since the 1990s, with

the global number of cases reaching 1,343,850 in 2019 (2). They account for approximately 10% of all cancer cases diagnosed in the USA, and their prevalence is projected to increase in the upcoming decade (1, 3). By 2030, there will be approximately 4,634,937 new cases of hematological malignancies, leading to significant mortality and disability in the affected individuals (3). Despite advances in chemotherapy and the discovery of newer drugs to manage such malignancies (4), survival remains poor and ranges from just 24 to 86% (5). Acute myeloid leukemia has the poorest 5-year survival rate of 24%, while Hodgkin lymphoma has the highest survival rate of 86% (5). Given the poor survival rate, it is necessary to recognize important prognostic indicators that can be suitably targeted to improve outcomes in such patients.

Malnutrition is highly prevalent among cancer patients across the world. Approximately 70% of all patients hospitalized for malignancies are under-nourished, and this accounts for approximately 20% of all cancer-related deaths (6). Among patients with hematological malignancies, approximately 17–43% are malnourished (7, 8). Indeed, malnutrition is frequently under-studied and under-investigated in clinical practice, despite being an important predictor of adverse outcomes. Malnutrition can reduce the response to anti-cancer therapy, worsen the probability of survival, increase recurrence, and prolong hospital stay (7, 9). One of the major limitations in the identification of malnutrition is the availability of a robust, easy-to-use, and reliable marker. The patient-generated Subjective Global Assessment and the Subjective Global Assessment (SGA) tools have been recommended for nutritional assessment in cancer patients owing to their high specificity and sensitivity compared to other tools. However, these assessments are time-consuming and difficult to complete even by well-trained professionals (10). Therefore, newer easy-to-use and rapid nutritional screening tools have been developed, such as the prognostic nutritional index, geriatric nutritional risk index, Mini-Nutrition Assessment (MNA), Malnutrition Universal Screening Tool (MUST), Nutrition Risk Screening 2002, and the controlling nutritional status score (CONUT) (11). Nevertheless, no single marker has been recognized as the gold standard, and these are dichotomies on the ability of these markers to accurately predict outcomes.

CONUT was first described by de Ulíbarri et al. (12) in 2005 as a rapid nutritional assessment tool for the routine screening of all inpatients. The score gives points for specific ranges of albumin, cholesterol, and total leukocyte counts, which are then combined to obtain the total CONUT score. The patients are then stratified into four levels based on the CONUT score: normal (0–1 points), mild (2–4 points), moderate (5–8 points), and severe (9–12 points), with each level indicating an increased degree of malnourishment. The original authors have noted that CONUT has a specificity and sensitivity of 85 and 92%, respectively, when compared with full nutritional assessment as the gold standard (12). It also has a high agreement with the SGA, which is the recommended tool for nutritional screening in cancer patients (13). Since CONUT is obtained from routinely available blood counts, it provides a rapid, simple, objective, efficient, and reliable assessment of the nutritional status of the patient in clinical practice. The simplicity of CONUT can be gaged when compared with other systematic nutritional indicators such as the SGA, MNA, and MUST, which require complex measurements such as anthropometry, dietary intake change, and weight loss history. The elaborate process in the latter tools is often time-consuming, difficult to complete, and not suitable for busy clinical practice (10).

In literature, CONUT has been used for predicting outcomes of colorectal (14), hepatic (15), gastric (16), bladder (17), and breast cancer (18). Furthermore, it has also been recognized as an independent risk factor for poor outcomes in patients with coronary artery disease (19), stroke (20), and hip fracture (21). Given its high validity, several studies have also examined the role of CONUT in predicting prognosis in hematological malignancies, but with variable results. In a previous study, Lu et al. (22) attempted to review the prognostic ability of CONUT for hematological malignancies but could include only six studies. We hereby present a comprehensive and updated review examining the prognostic ability of CONUT in predicting survival after hematological malignancies.

Materials and methods

The reviewers abided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement reporting guidelines while performing and presenting this review (23). Pre-registration was performed on the International Register of Systematic Reviews, PROSPERO (CRD42024506152).

Literature retrieving

Articles were searched in electronic format in the databases of Embase, Scopus, CENTRAL, Web of Science, and PubMed by two reviewers independently. The search included all publications from the inception of the databases to 30 January 2024 and included all articles irrespective of the language. However, the search was restricted to human studies published in either full-text or abstract form.

The search terms used were, "leukemia, lymphoma, myeloma, myelodysplastic, myeloproliferative, CONUT, and controlling nutritional status. We generated search strings by combining these keywords with Boolean operators and used them across all databases (Supplementary Table S1). To supplement the search, we examined Google Scholar as a source for gray literature and also hand-searched references, including original articles and pertinent reviews.

Eligibility criteria and selection of studies

The searched articles were examined against the following PECOS inclusion criteria:

Population (P): Patients with any type of hematological malignancy, regardless of the disease stage and treatment.

Exposure (E): Malnutrition was defined by a high CONUT score. The cutoff for high CONUT was not predefined and varied according to each included study.

Comparison (C): Normal nutrition was defined by a low CONUT score.

Outcomes (O): Overall survival (OS) was the primary outcome, while progression-free survival (PFS) was the secondary outcome. In general, OS is defined as the time from treatment to death due to any reason. PFS is defined as the time from the start of treatment to the first recurrence or disease progression. In the protocol, we had mentioned

recurrence-free survival as the outcome. However, since the included studies reported PFS, recurrence-free survival was substituted by PFS.

Study type (S): Prospective or retrospective cohort studies.

The review excluded studies not on CONUT, studies that did not indicate relevant outcomes, editorials, review articles, and non-peer-reviewed articles. If there was an overlap of the sample between the two articles, we included the one with the largest sample size.

We initially combined the search results of all databases in a single reference manager software (EndNote). Articles were then deduplicated electronically. The two reviewers then carefully read the title and abstract of each study for initial screening. Relevant records were identified and their full-texts were retrieved. Selected studies underwent full-text analysis against the inclusion criteria. Differences between reviewers, if any, were solved by dialog.

Risk of bias and data management

The quality of studies was tested by the Newcastle–Ottawa Scale (NOS) (24). Two reviewers were involved. Studies were judged for the criteria for participant selection, comparability of groups, and validity of results. The number of stars (ranging from 1 to 9) determined the study quality, with a higher number of stars indicating better quality.

Data on study information, patient demographic factors, CONUT cutoff, timing of measurement, percentage classified as malnourished, treatment, outcomes, and follow-up were recorded from the studies by two reviewers. Outcome data were also extracted separately and cross-checked for correctness. Multivariable adjusted ratios on OS and PFS were extracted. If unavailable, they were calculated from raw data. In cases where data were not provided, we attempted to contact the corresponding author once via email.

Statistical analysis

All statistical analyses were performed using "Review Manager" (RevMan, version 5.3). The difference in OS and PFS between high and low CONUT groups was presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Individual ratios from studies underwent logarithmical transformation using the generic inverse variance function of the Review Manager. Data were then combined in the inverse variance random-effect model. Publication bias was judged from funnel plots and the Egger's test. Inter-study heterogeneity was checked by the chi-square-based Q statistics, and I^2 statistics were used for inter-study heterogeneity. A p-value of < 0.10 for Q statistic, and $I^2 > 50\%$ meant substantial heterogeneity.

Sensitivity and subgroup analyses were undertaken for the primary outcome. These analyses were not conducted for PFS due to the low number of studies. For the first analysis, individual studies were removed one at a time, and the HR was checked for significance. The subgroup analysis was performed based on the following variables: study location, sample size, diagnosis, CONUT cutoff, and NOS score.

Results

The PRISMA flowchart is presented in Figure 1. Of the 28 records that were selected for review, 1 could not be retrieved (25). Of the 27 remaining studies, 23 (26–48) were included in the review, and 4 were excluded for various reasons [1 was not on CONUT (49) and 3 did not report the required data (50–52)]. There were no disagreements among the reviewers regarding the inclusion or exclusion of any study. Furthermore, no additional study was identified from the gray literature and bibliography searches.

Data retrieved from studies are demonstrated in Table 1. All studies were from only three countries, namely, Japan (39.1%), China (43.5%), and Turkey (17.4%). All were retrospective cohort studies published between 2019 and 2023. Three studies did not report the mean/median age of patients. In the remaining studies, the age of the patients ranged from 41.6 to 75 years. The included patient populations were affected by myeloid malignancies and multiple myeloma (17.6%), adult T-cell leukemia and lymphoma, (0.9%), myelodysplastic syndromes and acute myeloid leukemia (5.7%), HIV-related lymphoma (2.7%), peripheral T-cell lymphoma (1.8%), Hodgkin lymphoma (5.6%), extranodal NK/T-cell lymphoma (28.2%), indolent non-Hodgkin lymphoma (1.9%), and diffuse large B-cell lymphoma (35.6%). The number of patients in the included studies ranged from 54 to 1,085. CONUT was measured either at diagnosis or at the start of treatment. The CONUT cutoffs used were 2, 3, 3.5, 4, 5, 5.5, and 6. Based on the respective cutoffs, the percentage of patients classified as malnourished ranged from 20.8 to 70.6. The included studies did not routinely report follow-up time. Where data were available, follow-up ranged from 10.5 months to 6.82 years. On quality assessment based on the NOS score, two studies received six stars while three got seven stars. The remaining studies received eight or nine stars, indicating good quality.

Data for meta-analysis on OS were available from all studies. Zhang et al. (39) did not report HR based on a specific CONUT cutoff and used the score as a continuous variable. Hence, their study was not included in the meta-analysis. Using data from 22 studies, we found that high CONUT was significantly associated with poor OS in patients with hematological malignancies (HR: 1.95 95% CI: 1.62, 2.35 $I^2 = 89\%$) (Figure 2). The funnel plot is presented in Figure 3. There was no gross asymmetry noted on the funnel plot, and Egger's test found no publication bias ($p = 0.08$). During the sequential exclusion of studies for the sensitivity analysis, we noted no change in the significance of the results. Multiple subgroup analyses were conducted for OS. Detailed results can be found in Table 2. There was no change in the significance of the results on subgroup analyses based on study location, sample size, diagnosis, CONUT cutoff, and NOS score.

A meta-analysis of PFS is presented in Figure 4. Only six studies reported data on PFS, and the pooled analysis found that high CONUT was a significant marker for poor PFS in patients with hematological malignancies (HR: 1.64 95% CI: 1.21, 2.20 $I^2 = 70\%$). The pooled effect size of PFS remained significant in the sensitivity analysis.

Discussion

The present review accounts for the most updated evidence on the prognostic role of CONUT in patients with hematological malignancies. We combined data from a large number of studies to show that high CONUT was a significant predictor of poor OS. The negative effect of CONUT on OS was persistent, even with various

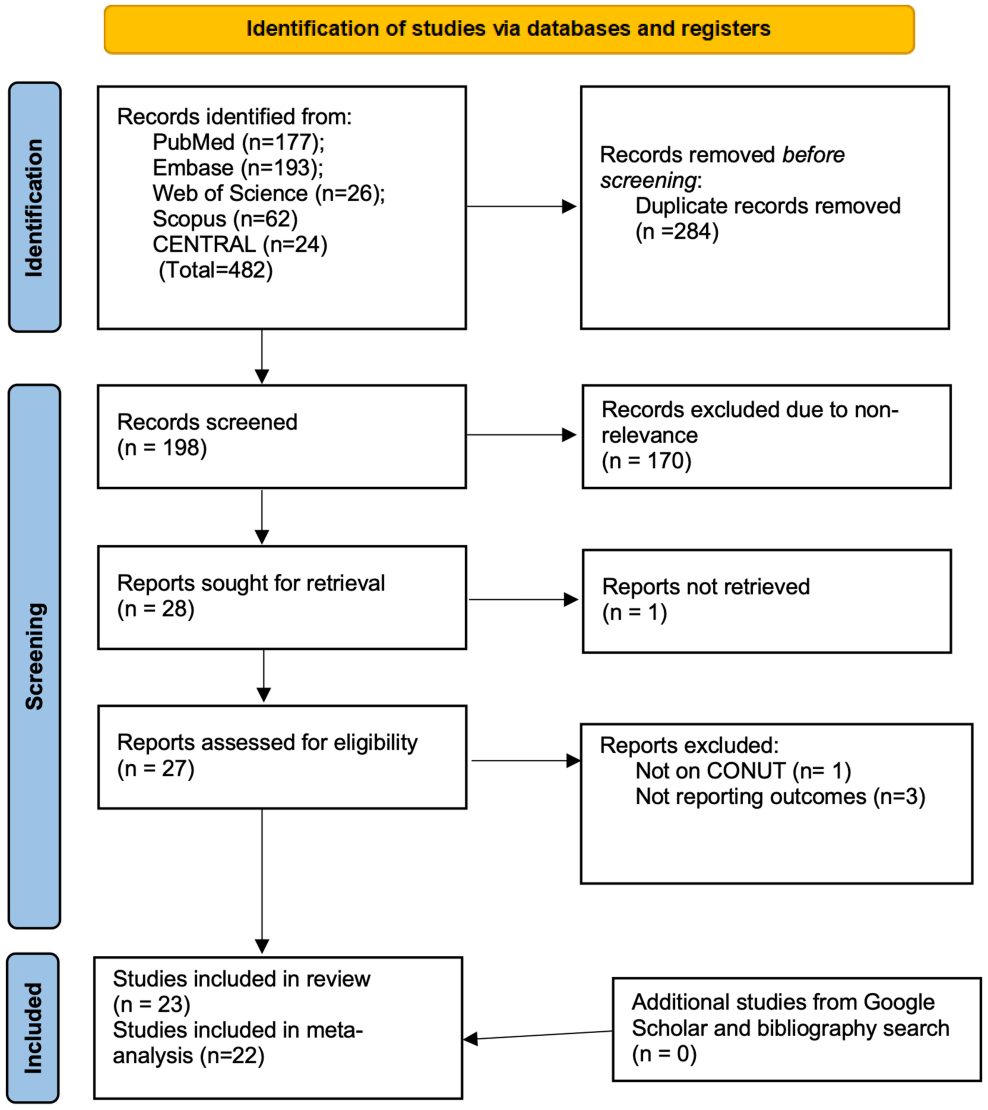

FIGURE 1
Search results of the review.

subgroups and sensitivity analyses. Similarly, the quantitative analysis from a much smaller number of studies also demonstrated that patients with high CONUT have poor PFS.

The validity of CONUT in predicting survival in cancer patients is well-established. Takagi et al. (14) in a meta-analysis of nine studies have found CONUT to be a predictor of OS (HR: 1.97), PFS (HR: 1.68), and cancer-specific survival (HR: 3.64) in colorectal cancer. CONUT has been found to independently predict OS (HR: 1.78), PFS (HR: 1.34), and postoperative complications (HR: 1.85) in hepatocellular cancer patients undergoing surgical intervention (15). Another meta-analysis of five studies has noted that high CONUT is associated with poor OS (HR: 1.78), PFS (1.34), and postoperative complications (HR: 1.85) in gastric cancer patients undergoing gastrectomy (16). The results of our review further expand the validity of CONUT in patients with hematological malignancies. Using a broad search strategy without any limitations of language or publication dates, we were able to retrieve and analyze 23 studies examining the association between CONUT and survival after hematological malignancies. A combined analysis of 22 studies showed that high CONUT led to worse OS, increasing the risk of mortality by 92%. The consistent positive association between CONUT and poor OS among the included studies and the stability of the results on sensitivity analysis lend credibility to CONUT as a rapid prognostic indicator for clinical practice. Nevertheless, the high inter-study heterogeneity is a cause for concern. This can be partially attributed to the variations in the included populations, the variable CONUT cutoffs, and the treatment offered to the included patients. Hematological malignancies include a large group of disorders such as multiple myeloma, lymphomas, leukemias, and myelodysplastic syndromes, and CONUT might have different predictability in different malignancies. However, in the multiple subgroup analyses conducted, CONUT was consistently associated with poor OS in patients with myeloid malignancies, myelodysplastic syndromes, diffuse large B-cell lymphoma, and other lymphomas. Similarly, the location of studies, sample size, and quality of studies also did not affect the significance of the association. While the majority of studies

TABLE 1 Details extracted from included studies.

Author, year	Country	Study type	Population	*N*	Male (%)	Median age [IQR] or (range) (years)	CONUT cutoff	Timing of measurement	Mal-nourished (%)	Treatment	Outcomes	Follow-up (months)	NOS score
Araie et al. (26)	Japan	R	Myeloid malignancies	200	50.5	46 [18–67]	5	Before conditioning	28	Allo-HCT	NRM	44.6	8
Ureshino et al. (27)	Japan	R	Adult T-cell leukemia/ lymphoma	54	51.9	NR	5	At diagnosis	35.2	Chemotherapy and Allo-HCT	OS	NR	6
Kamiya et al. (42)	Japan	R	Multiple myeloma	178	29.2	NR	5	NR	47.2	Protease inhibitors and immunomodulatory drugs	OS	NR	9
Matsukawa et al. (44)	Japan	R	DLBCL	615	54.8	69 [20–97]	4	NR	22.9	R-CHOP	OS	NR	8
Nagata et al. (43)	Japan	R	DLBCL	476	54.8	68.5 (27–97)	4	At diagnosis	31.3	R-CHOP	OS, PFS	45	8
Okamoto et al. (38)	Japan	R	Multiple myeloma	64	51.6	66 [41–84]	5	NR	28.1	Protease inhibitors, immunomodulatory drugs, and auto-PBSCT	OS	NR	9
Sakurai and Nakazato (45)	Japan	R	Myelodysplastic syndrome, acute myeloid leukemia	90	66.7	75 (43–93)	5	NR	37.8	Azacitidine	OS	10.5	8
Baysal et al. (48)	Turkey	R	DLBCL	81	51.9	63.5 ± 16.3*	5	NR	37	R-CHOP	OS	NR	8
Cagliyan et al. (29)	Turkey	R	DLBCL	266	50.8	68 (23–91)	2	At diagnosis	45.1	R-CHOP	OS, PFS	51	8
Li et al. (28)	China	R	Multiple myeloma	119	NR	56 [NR]	3.5	At diagnosis	NR	NR	OS	NR	7
Liang et al. (46)	China	R	Multiple myeloma	157	56.1	64 [NR]	3.5	NR	45.2	Chemotherapy	OS	24	8
Zhou et al. (47)	China	R	Multiple myeloma	245	59.2	65 (33–83)	4	NR	NR	Chemotherapy	OS	38	8

(Continued)

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TABLE 1 (Continued)

Author, year	Country	Study type	Population	*N*	Male (%)	Median age [IQR] or (range) (years)	CONUT cutoff	Timing of measurement	Mal-nourished (%)	Treatment	Outcomes	Follow-up (months)	NOS score
Chen et al. (33)	China	R	Myelodysplastic syndrome	121	68.6	65 [59–72]	4	At diagnosis	57.9	NR	OS	NR	7
Liu et al.(31)	China	R	HIV-related lymphoma	149	84.6	53.1 ± 15.1*	6	NR	20.8	Chemotherapy	OS	44	8
Nakamura et al. (32)	Japan	R	Peripheral T-cell lymphoma	99	69.7	67 (16–87)	5	At diagnosis	38.4	Chemotherapy and auto-PBSCT	OS	81.8	8
Qian et al. (30)	China	R	Myelodysplastic syndrome	81	56.8	64 (18–82)	5.5	At diagnosis	39.5	Chemotherapy	OS	13.1	7
Go et al. (37)	China	R	DLBCL	305	57.4	NR	5	Start of treatment	28.2	R-CHOP	OS, PFS	106	8
Gursoy et al. (40)	Turkey	R	Hodgkin lymphoma	307	56.4	41.6 ± 16.3*	3	NR	27.7	Chemotherapy	OS	63.4	6
Kaneda et al. (41)	Japan	R	DLBCL	203	59.1	74 (65–93)	3	At diagnosis	NR	R-CHOP	OS	48	8
Lu et al. (36)	China	R	Extranodal NK/T-cell lymphoma	80	72.5	51.5 [41.5, 60]	5	NR	NR	Chemotherapy and radiotherapy	OS, PFS	NR	8
Tiglioglu et al. (35)	Turkey	R	Indolent non-Hodgkin lymphoma	109	47.7	61.6 ± 12.8*	2	At diagnosis	52.3	Chemotherapy	OS, PFS	NR	8
Wu et al. (34)	China	R	Extranodal NK/T-cell lymphoma	374	65.0	44 (18–79)	2	Seven days prior to treatment	70.6	Chemotherapy and radiotherapy	OS, PFS	82	9
Zhang et al. (39)	China	R	Extranodal NK/T-cell lymphoma	1,085	47.3	47 [35–57]	NR	NR	NR	NR	OS, PFS	62.7	8

Allo-HCT, allogeneic hematopoietic stem cell transplantation; R, retrospective; P, prospective; NOS, Newcastle–Ottawa Scale; CONUT, controlling nutritional status; NRM, non-relapse mortality; DLBCL, diffuse large B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; auto-PBSCT, autologous peripheral blood stem cell transplantation; HIV, human immunodeficiency virus; N, number of participants; IQR, interquartile range.
*Mean ± standard deviation values.

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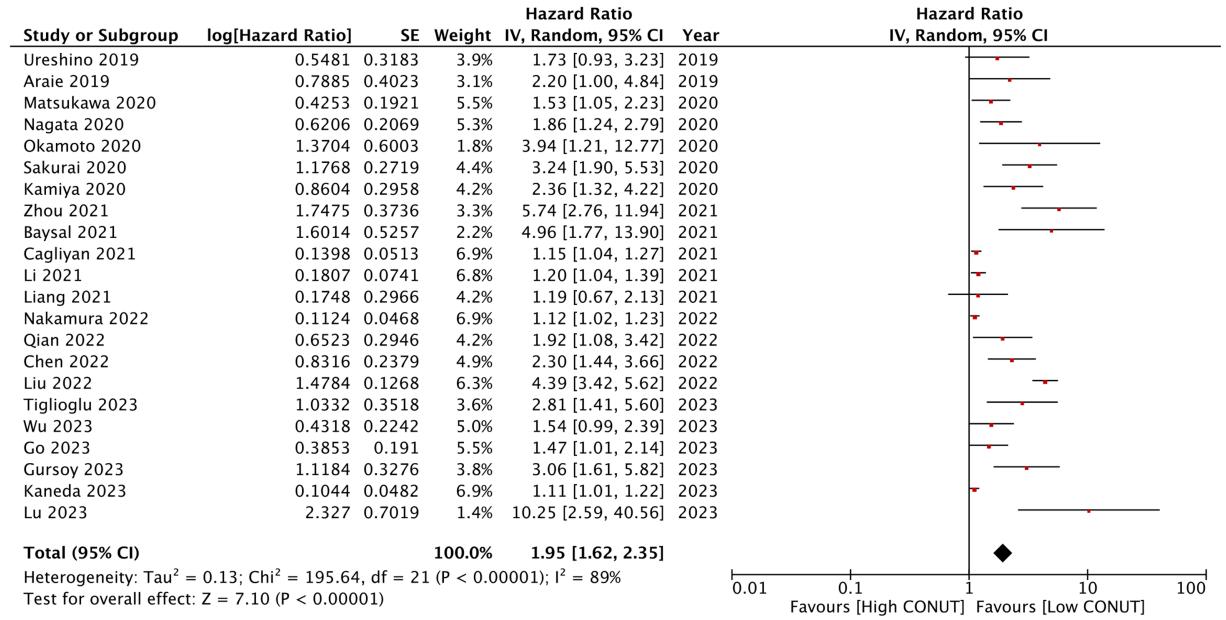

FIGURE 2
The meta-analysis of overall survival between high CONUT and low CONUT.

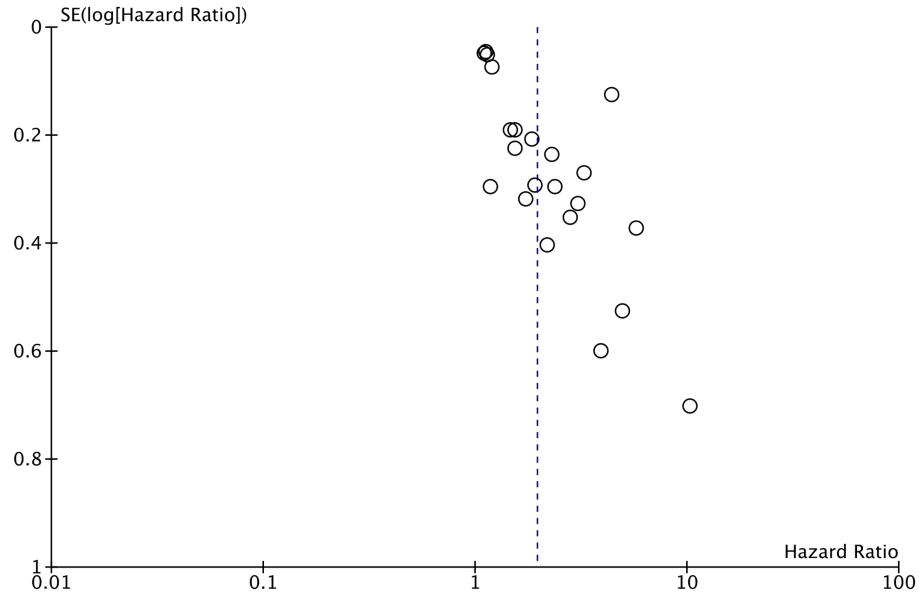

FIGURE 3
A funnel plot for judging publication bias.

reported data on OS, only six reported on PFS. The meta-analysis found that high CONUT was associated with worse PFS in hematological malignancies. Similar to OS, the results were more or less consistent across studies and stable on the sensitivity analysis.

One major inconsistency noted among the included studies was the cutoff of CONUT, which defined malnutrition. As mentioned earlier, CONUT has different levels of malnutrition ranging from mild to severe, but these may not be consistently replicable across all populations. Some studies use the standard cutoffs of CONUT and define malnutrition as those with scores of >5 (moderate–severe CONUT scores), while others use the receiver operator characteristic curve to establish the best cutoff in their population. Such variability has been noted in the earlier meta-analyses (14–16) as well and has been a major hindrance to the applicability of CONUT in clinical practice. In our subgroup analysis based on different CONUT cutoffs, we noted that all cutoffs of CONUT were associated with poor OS. However, the effect size increased with higher cutoffs. The HRs for cutoffs of 2–3.5, 4, and 5–6 were 1.27, 2.27, and 2.56, respectively, indicating that an incremental increase in malnutrition is associated with worse OS.

TABLE 2 Subgroup analysis for overall survival.

Variable	Groups	Studies	Hazard ratio [95% confidence intervals]	I^2
Location	Turkey	4	2.44 [1.15, 5.13]	86
	China	9	2.26 [1.44, 3.56]	92
	Japan	9	1.60 [1.30, 1.97]	78
Diagnosis	Myeloid malignancies	6	2.15 [1.28, 3.62]	81
	Myelodysplastic syndrome and AML	3	2.44 [1.81, 3.30]	0
	DLBCL	6	1.34 [1.13, 1.59]	71
	Other lymphomas	6	2.69 [1.34, 5.41]	96
Sample size	>100	15	1.88 [1.49, 2.36]	91
	<100	7	2.60 [1.49, 4.56]	85
CONUT cutoff	2–3.5	7	1.27 [1.10, 1.47]	66
	4	4	2.27 [1.47, 3.52]	71
	5–6	11	2.56 [1.61, 4.08]	93
NOS score	8–9	17	2.01 [1.61, 2.51]	91
	6–7	5	1.85 [1.25, 2.76]	5

AML, Acute myeloid leukemia; DLBCL, diffuse large B-cell lymphoma.

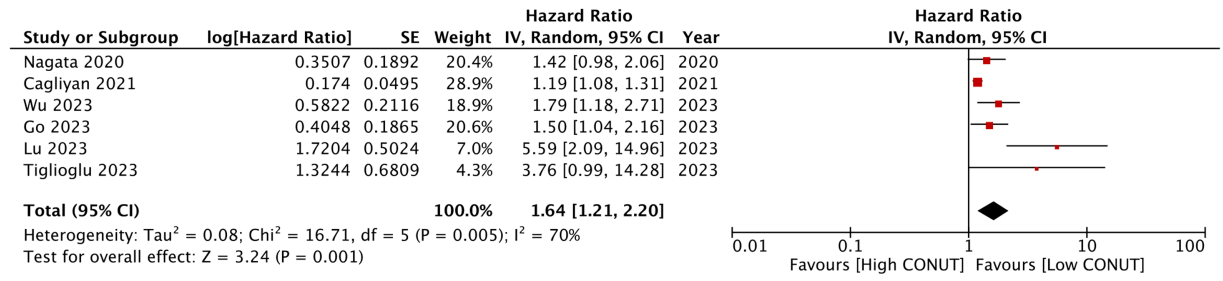

FIGURE 4
The meta-analysis of progression-free survival between high CONUT and low CONUT.

The predictive value of CONUT for survival outcomes can be attributed to its three components. Albumin is an essential marker of the nutritional and immune status of the patient. Malnourished patients also have poor responses to chemotherapy and increased drug-related toxicity, which is an important factor in treating hematological malignancies where chemotherapy is the primary therapeutic modality (53). Furthermore, poor nutrition has been associated with depression, which can be a major hindrance to treatment and therefore worsens survival (54). Albumin is also a marker for the systemic inflammatory response in cancer patients (53). Individually, serum albumin has been shown to be an independent marker of mortality in lymphoma and leukemia patients (55, 56). Second, lymphocytes are the primary component of cell-mediated immunity, as they can control cancer proliferation and metastasis, promote apoptosis, and play an important role in immune surveillance (34). Reduced lymphocyte counts have also been associated with worse clinical features in hematological malignancies (57). Finally, cholesterol plays a major role in maintaining the integrity of cell membranes and immunity, which ensures that immunocompetent cells can attack cancer cells (58). Gao et al. (59) have shown that diffuse large B-cell lymphoma patients with hypocholesterolemia have a worse clinical presentation, such as a high International Prognostic Index score, B symptoms, and advanced stage, as compared to those with normal cholesterol levels. Thus, it can be summarized that all three components of CONUT are associated with cancer survival, and, when combined, they produce a robust easy-to-use marker.

The important strength of the review includes a detailed literature search without any barriers to language or sample size. Our study provides the most comprehensive evidence on the ability of CONUT to predict survival in hematological malignancies. In comparison with the previous review by Lu et al. (22), we added 17 more studies, thereby increasing the statistical power of the meta-analysis. We also undertook sensitivity analyses and detailed subgroup analyses to provide clarity on the topic.

However, several limitations still exist. None of the included studies were prospective, and therefore, they were prone to bias. Another aspect to consider is the high inter-study heterogeneity. Despite detailed subgroup analyses, much heterogeneity persisted in the meta-analysis and could be due to the differences in patient populations, cancer stage, and treatment provided. We were unable

to examine the influence of important moderators such as body mass index, cancer stage, CNS/liver/bone marrow invasion, and bone marrow transplantation on survival outcomes due to a lack of data. Second, there were limited data on PFS and other outcomes, such as treatment response and treatment complications. The latter could not be included in the meta-analysis. Third, all of the data were from only three countries. There was a lack of data in the literature from Western populations, and hence, the results cannot be generalized. At this point, we could not find any concrete reasons for the non-reporting of CONUT from Western countries. Given the ease of use of CONUT, there should not be any reason for not applying CONUT in clinical practice, even in Western populations. We believe that the results of this study may prompt further reporting of data from Western countries and, hence, improve evidence. Fourth, we included myelodysplastic syndromes in the meta-analysis to ensure completeness. Myelodysplastic syndromes frequently lead to acute myeloid leukemia, and they have been considered a type of malignancy by the American Cancer Society. The inclusion of these populations may also have led to heterogeneity in the meta-analysis. Finally, we examined the impact of only pretreatment CONUT scores on OS/PFS. There are no data in the literature on how changes in CONUT scores affect outcomes or how nutritional interventions affect CONUT scores. This could be a topic of research in future studies, and such evidence could help personalize treatment plans, which in turn could improve outcomes in hematological malignancies.

Conclusion

CONUT is an independent predictor of poor OS in patients with hematological malignancies. The results appear to be valid across different cancer types and with different CONUT cutoffs. Scarce data also suggest that CONUT could predict PFS. There is a need for more data from Western populations on the impact of CONUT on other outcomes, such as PFS and treatment response.

Author contributions

GL: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft. QL: Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1402328/full#supplementary-material

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EDITED BY
Hui-Xin Liu,
China Medical University, China

REVIEWED BY
Adianto Nugroho,
Rumah Sakit Umum Pusat Fatmawati, Indonesia
Dimitrios Kehagias,
General University Hospital of Patras, Greece

*CORRESPONDENCE
Huili Wu
✉ wuhuili660912@zzu.edu.cn
Yuanyuan Jiang
✉ jiangyuanyuan@zzu.edu.cn

†These authors have contributed equally to this work and share first authorship

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Associations between novel anthropometric indices and the prevalence of gallstones among 6,848 adults: a cross-sectional study

Jie Zhang[1,2,3†], Depeng Liang[1,2,3†], Lidong Xu[1,2,3], Yanhong Liu[1,2,3], Shan Jiang[1,2,3], Xiaomeng Han[1,2,3], Huili Wu[1,2,3*] and Yuanyuan Jiang[1,2,3*]

[1]Department of Gastroenterology, Zhengzhou Central Hospital Affiliated to Zhengzhou University, Zhengzhou, China, [2]Henan Provincial Medicine Key Laboratory of Colorectal Cancer Diagnosis and Treatment, Zhengzhou, China, [3]Zhengzhou Key Laboratory of Colorectal Cancer Diagnosis, Treatment and Research, Zhengzhou, China

Background: Traditional anthropometric measures, including body mass index (BMI), are insufficient for evaluating gallstone risk. This study investigated the association between novel anthropometric indices and gallstone risk among 6,848 participants from the National Health and Nutrition Examination Survey in the United States.

Methods: Measures calculated included weight (WT), BMI, waist circumference (WC), waist-to-height ratio (WtHR), conicity index (CI), A Body Shape Index (ABSI), Body Roundness Index (BRI), Abdominal Volume Index (AVI), and Weight-adjusted Waist Index (WWI). Logistic regression and smooth curve fitting assessed the relationships between these indices and gallstones, complemented by receiver operating characteristic (ROC) curve analysis to evaluate their discriminative power.

Results: The results indicated significant differences between study groups, with a positive and independent correlation identified between gallstones and all measures except ABSI. Specifically, per 1 SD increase in WC, WT, BMI, WtHR, and AVI was associated with a 57%, 59%, 52%, 53%, and 53% increased risk of gallstones, respectively. Dose-response analysis confirmed a positive correlation between these indices and gallstone risk. ROC analysis highlighted WtHR and BRI as having superior discriminative abilities (AUC = 0.6703). Further, among participants with a BMI < 30 kg/m2, elevated levels of WT, WtHR, CI, BRI, and WWI significantly increased the risk of gallstones ($P < 0.001$). Likewise, elevated BMI heightened the risk at low levels of WT, WC, WtHR, BRI, AVI, and CI ($P < 0.001$).

Conclusion: This study supports the positive association between various anthropometric indicators and gallstones, recommending that newer anthropometric indices be considered more extensively to enhance gallstone prevention and treatment strategies.

KEYWORDS

novel anthropometric indices, gallstones, cross-sectional study, abdominal obesity, NHANES (National Health and Nutrition Examination Survey)

1 Introduction

Gallstones, one of the most prevalent digestive system disorders in the world, cause symptoms including nausea, vomiting, lack of appetite, and discomfort in the abdomen and stomach (1). Gallstones, also known as cholelithiasis, are defined by the buildup of sediments in the gallbladder or common bile duct that are made of mineral or fatty deposits. Additionally, gallstones have been linked to higher rates of occurrence and death from common chronic conditions such as diabetes, hypertension, cardiovascular disease, and gastrointestinal tumors (2–6). Gallstones are estimated to afflict 10–15% of the population in America and other affluent nations and up to 70% of American Indians, according to epidemiologic data (7, 8). In America, gallstones bring about a significant health care burden (9). Numerous risk variables, including race, gender, and age above 40, are linked to the development of gallstones (10, 11). Other risk factors include metabolic syndrome, rapid weight loss, medication use, and a family history of gallstones. Patients are at a significant risk of obesity because of the metabolic alterations brought on by obesity. These changes include abnormalities in the liver and gallbladder, among other metabolic organs, as well as hyperlipidemia, impaired intestinal motility, and increased bile secretion in the liver (12). Type 2 diabetes mellitus, obesity, insulin resistance, and nonalcoholic fatty liver disease (NAFLD) are all regarded as elements of the metabolic syndrome. The most significant risk factor for both gallbladder stones and metabolic syndrome is abdominal fat. It is associated with increased synthesis of cholesterol within the body, excessive bile cholesterol secretion, and a rise in bile-related gallstone-causing components. Studies have shown an obvious correlation between obesity and the development of gallstones, particularly obesity in the abdomen (10). Moreover, for every 5 units increase in body mass index (BMI), the incidence of gallstones has increased 1.63 times (13).

To separate the distribution of body fat, a few novel anthropometric indices (AHIs) have been introduced in the last few decades to measure obesity, particularly central obesity. Anthropometric indices are simple metrics for evaluating nutritional health and rapidly determining illness risk (14). Examples of AHIs include body mass index (BMI), waist circumference (WC), curve index (CI), body roundness index (BRI), abdominal volume index (AVI), weight-adjusted waist index (WWI), and waist-to-height ratio (WtHR). ABSI has been proven to be associated with mortality, diabetes, hypertension, and metabolic syndrome (5, 6). Body fat percentage and visceral fat can be predicted using the body roundness index (BRI) (4). According to Gaoteng Lin's research, there is a correlation between the risk of kidney stones and the innovative AHIs that completely reflect an individual's body shape. These findings can be crucial in determining the risk of kidney stones (KS) (15).

On the other hand, our understanding of how well these indicators predict gallstone risk is somewhat limited. It is still difficult to determine the best anthropometric index for gallstone screening. The purpose of this study is to evaluate and compare the nine anthropometric indices (AVI, CI, WWI, WtHR, BMI, WT, WC, ABSI, BRI, and WtHR) as screening measures for gallstone risk in American adults. The ideal cutoff values for these indices enable medical professionals and health policy makers to estimate the gallstone risk. Subsequently, risk reduction interventions can target high-risk participants, thereby reducing the risk of developing gallstones.

2 Materials and methods

2.1 Study design and participants

This study included baseline data from the cycles of the National Health and Nutrition Examination (NHANES). In order to investigate the prevalence of health, nutrition, and possible risk factors, the National Health and Nutrition Examination Survey (NHANES) conducted a series of interviews and physical examinations on a nationally representative sample of the US population each 2 years. In the study, the data for participants aged over 20 years old who participated in the gallstone questionnaire was extracted from NHANES cycles conducted between 2017 and 2020, and the question was: "Have you ever had gallstones?" Our study received an exemption from the Institutional Review Board as all participants gave written informed permissions in the initial survey and their personal data was completely de-identified. A total of 15,560 individuals completed the questionnaire. The following were the exclusion criteria (Supplementary Figure 1). Ultimately, this study composed 6,848 patients in total, including 720 self-reported gallstone history.

2.2 Anthropometric index calculation

Expert examiners used established methods and tools at the mobile examination center to measure fundamental anthropometric metrics such as waist circumference, height, and

body weight. Using previously published formulas, compute BMI, ABSI, BRI, AVI, CI, WWI and WtHR. As follows:

$$\begin{aligned}
\text{BMI} &= \text{WT (kg)} / \text{height}^2\text{(m)} \\
\text{ABSI} &= \text{WC (cm)} / [\text{BMI}^{2/3}\text{(kg/m2)} \times \text{height}^{1/2}\text{(m)}] \\
\text{BRI} &= 364.2 - 365.5 \times \{1 - [(\text{WC (cm)} / 2\pi) / \\
&\quad (0.5 \times \text{height(m)})]^2 \}^{0.5} \\
\text{AVI} &= \{2 \times (\text{WC}^2\text{ (cm)}) + 0.7 \times (\text{WC (cm)-Hip(cm)})^2\} / 1000 \\
\text{CI} &= \text{WC(m)} / 0.109/(\text{Weight(kg)} / \text{Height(cm)})^{0.5} \\
\text{WWI} &= \text{WC (cm)} / \text{Weight}^{0.5}\text{(cm/kg}^{0.5}\text{)} \\
\text{WtHR} &= \text{WC (cm)} / \text{Height(cm)}
\end{aligned}$$

2.3 Ascertainment of other covariates

The interview identified age, gender (male/female), and race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and Other Race). Education level is divided into high school graduates or below, partial university graduates, and university graduates or above. Marital status is categorized as Married/Living with a Partner, Divorced/Separated/Widowed, and Never Married. The poverty ratio was categorized as the ratio of monthly family income to poverty levels and categorized into 3 groups: <1.3 (low income), 1.3–3.5 (middle income), > 3.5 (high income), and missing. Physical activities such as walking or cycling, employment, and amusement are all considered sports. It is considered an active activity when a participates in one or more of those activities. It will be regarded as a non-active activity otherwise. Total calorie consumption, total water intake, total carbohydrate intake, total sugar intake, total protein intake, and total fat intake are dietary characteristics. A 2-day average of the intake was used for quantification. Serum was tested for Uric acid (umol/L), serum cholesterol (mg/dl), Sodium (mmol/L), Iron (umol/L), Chloride (mmol/L), Bicarbonate (mmol/L), Potassium (mmol/L). A history of CVD is a previous diagnosis of heart failure, coronary heart disease, angina, heart attack, or stroke. The classification of smoking is as follows: current smoking (smoking $\geq$ 100 cigarettes and current smokers), previous smoking (smoking $\geq$ 100 cigarettes but not currently smoking), never smoking (never smoking or smoking $\leq$ 100 cigarettes). Had 12 or more drinks of alcohol in the previous year? (yes/no). A blood pressure inspector who has completed an approved training program takes the patient's blood pressure. The standardized blood pressure of each participant was determined by averaging the three measurements. Having a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at least 90 mmHg, or being on antihypertensive medication, was the definition of hypertension. One of the following criteria was used to diagnose diabetes mellitus: a) self-reported diabetes; b) fasting blood glucose $\geq$ 126 mg/dl; c) HBA1c level $\geq$ 6.5%; and d) usage of anti-diabetic medications, such as insulin. A cancer history was established based on the self-report of the NHANES medical condition questionnaire.

2.4 Statistical analysis

Because NHANES uses a complex multi-stage probability sampling design method to represent a nationally representative large sample. Therefore, we use linear regression analysis to summarize continuous variables as mean values with standard error (SE). 95% confidence intervals and weighted survey averages are used to describe continuous variables, while categorical variables are described by weighted survey averages and 95% confidence intervals. In the study, all anthropometric variables performed z score conversion as follows: z score = (index-$\text{index}_{\text{mean}}$) / index_{sd} (Supplementary Table 1). Through weighted multivariate logistic regression analysis. In model 1, no adjustments were made. In model 2, adjusted for gender, age, race, and marital status. In model 3, adjusted for all variables and used a smooth curve fitting to analyze the nonlinear relationship between anthropometric indices and the incidence of gallstones. Examine the effects of heterogeneity with a subgroup analysis. Assess the ability to discriminate of several anthropometric indices for gallstone patients by comparing the area under the curve (AUC) and the ROC curve. The DeLong's test is used to evaluate statistical differences between AUCs. Body mass index is classified into two categories based on suggestions set out by the World Health Organization (WHO). A body mass index of > 30 kg/m2 is considered obese. Other anthropometric indicators are bisected based on the best cutoff point in ROC analysis. We further investigated to improve the assessment of gallstone risk by combining BMI with other anthropometric measures. Use Spearman method to perform correlation analysis on two types of anthropometric measurements. Statistical significance was defined as a p-value < 0.05. All the analyses were conducted using R version 4.0.2 (The R Foundation)[1] and Empower software (X&Y Solutions, Inc., Boston, MA, USA)[2].

3 Results

3.1 Baseline characteristics

Table 1 shows the baseline characteristics of NHANES cohort participants with complete information on gallstones and anthropometric indicators. In NHANES from 2017 to 2020, a total of 6848 participants with complete information on gallstones were analyzed after combining anthropometric indicators and covariates. A total of 6128 people (89.49%) had no history of gallstones, while 720 people (10.51%) had a history of gallstones. We found that in the study population, patients with gallstones had almost all higher anthropometric indicators than those without gallstones. It's interesting to note that there was not an apparent difference in ABSI between the two groups. In the gallstone group, the proportion of alcohol consumption and active exercise was lower than in the normal group ($P < 0.05$), and the age of onset, proportion of women, proportion of hypertension, diabetes, cancer, and CVD history were all significantly higher than in the normal group. Interestingly, the total fat intake of non-gallstone patients is higher than that of gallstone patients.

1 http://www.Rproject.org
2 www.empowerstats.com

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TABLE 1 Baseline characteristics of participants, weighted.

	Nonstone formers (*n* = 6128)	Stone formers (*n* = 720)	*P*-value
Age, years	47.22 (45.99, 48.46)	56.76 (55.28, 58.24)	<0.001
Total water intake, gm	2943.43 (2882.26, 3004.59)	2780.28 (2647.26, 2913.31)	0.031
Total energy intake, gm	2112.25 (2083.83, 2140.67)	1926.69 (1858.16, 1995.22)	<0.001
Total protein intake, gm	81.63 (80.18, 83.08)	71.76 (68.69, 74.83)	<0.001
Total carbohydrate intake, gm	238.50 (233.94, 243.05)	225.64 (215.29, 236.00)	0.040
Total Sugar intake, gm	101.18 (97.59, 104.77)	103.14 (96.47, 109.81)	0.630
Total Fat intake, gm	86.78 (85.63, 87.94)	80.69 (76.39, 84.99)	0.009
Serum calcium, mg/dL	9.29 (9.27, 9.32)	9.29 (9.21, 9.36)	0.776
Serum phosphorus, mg/dL	3.58 (3.56, 3.61)	3.59 (3.52, 3.67)	0.780
Creatinine, umol/L	78.06 (77.16, 78.96)	76.26 (73.92, 78.60)	0.141
Serum Cholesterol, mg/dl	187.37 (185.10, 189.63)	188.48 (183.77, 193.20)	0.584
HDL-Cholesterol, mg/dL	53.76 (52.90, 54.62)	52.94 (51.49, 54.38)	0.315
Triglyceride, mg/dL	109.04 (104.51, 113.56)	119.19 (107.97, 130.40)	0.070
LDL-Cholesterol, mg/dL	109.73 (107.38, 112.07)	110.68(105.22, 116.14)	0.721
BMI	29.39 (29.05, 29.73)	32.93 (32.05, 33.82)	<0.001
WT	83.82 (82.73, 84.90)	89.61 (86.77, 92.45)	<0.001
WC	99.96(90.00, 100.93)	108.00(105.79, 110.21)	<0.001
WtHR	0.59 (0.59, 0.60)	0.66 (0.64, 0.67)	<0.001
BRI	5.48 (5.35, 5.61)	7.00 (6.69, 7.31)	<0.001
ABSI	0.08 (0.08, 0.08)	0.08 (0.08, 0.08)	<0.001
AVI	20.63 (20.23, 21.03)	24.07 (23.11, 25.02)	<0.001
WWI	10.98 (10.93, 11.03)	11.49 (11.39, 11.58)	<0.001
CI	1.31 (1.30, 1.31)	1.35 (1.34, 1.36)	<0.001
Uric acid, umol/L	318.35 (314.96, 321.74)	322.47 (312.36, 332.57)	0.444
Serum Sodium, mmol/L	140.47 (139.95, 141.00)	140.25 (139.62, 140.87)	0.054
serum Iron, umol/L	16.05(15.74, 16.36)	14.87(14.28, 15.47)	0.001
serum Chloride, mmol/L,	101.28 (100.99, 101.56)	100.96 (100.59, 101.32)	0.021
serum Bicarbonate, mmol/L	25.58 (25.34, 25.82)	25.56 (25.13, 25.99)	0.927
serum Potassium, mmol/L	4.11 (4.07, 4.15)	4.09 (4.04, 4.13)	0.085
GENDER, *N* (%)			<0.001
male	51.88 (49.99, 53.77)	26.79 (22.82, 31.18)	
female	48.12 (46.23, 50.01)	73.21 (68.82, 77.18)	
PIR, *N* (%)			0.003
<1.3	16.29 (14.77, 17.94)	15.67 (11.72, 20.64)	
1.3–3.5	30.10 (27.36, 32.98)	39.61 (32.30, 47.42)	
≥3.5	43.41 (40.22, 46.66)	36.56 (31.99, 41.39)	
missing	10.20 (8.66, 11.97)	8.16 (5.73, 11.49)	
Race/ethnicity, *N* (%)			0.015
Mexican American	8.28 (6.23, 10.93)	7.25 (5.06, 10.28)	
Other Hispanic	7.26 (5.89, 8.90)	7.21 (4.63, 11.07)	
Non-Hispanic White	64.28 (59.02, 69.22)	70.77 (64.05, 76.70)	
Non-Hispanic Black	10.93 (8.28, 14.31)	6.60 (4.87, 8.87)	
Other Race	9.25 (7.50, 11.35)	8.17 (5.44, 12.09)	
Education levels, *N* (%)			0.109

(Continued)

TABLE 1 (Continued)

	Nonstone formers (*n* = 6128)	Stone formers (*n* = 720)	*P*-value
High school or less	37.03 (33.68, 40.52)	40.06 (35.09, 45.25)	
Some college or associates degree	30.43 (28.36, 32.59)	33.47 (28.25, 39.14)	
College graduate or above	32.53 (28.35, 37.02)	26.47 (20.09, 34.01)	
Marital status, *N* (%)			0.004
Married/Living with Partner	61.97 (59.17, 64.69)	64.27 (58.40, 69.74)	
Widowed/Divorced/Separated	17.89 (16.44, 19.44)	23.11 (18.91, 27.92)	
Never married	20.14 (17.94, 22.54)	12.62 (9.41, 16.71)	
Alcohol, *N* (%)			<0.001
No	37.79 (34.83, 40.85)	52.18 (46.49, 57.82)	
Yes	54.64 (51.60, 57.64)	38.38 (33.63, 43.36)	
Missing	7.57 (6.59, 8.68)	9.44 (6.98, 12.65)	
Physical activity, *N* (%)			<0.001
Inactive	18.21 (16.77, 19.74)	27.74 (23.40, 32.54)	
Active	81.79 (80.26, 83.23)	72.26 (67.46, 76.60)	
Smoking, *N* (%)			0.041
Never	57.16 (55.14, 59.16)	52.24 (45.89, 58.51)	
Former	25.76 (23.84, 27.77)	32.03 (26.69, 37.89)	
Current	17.08 (14.89, 19.52)	15.73 (12.41, 19.74)	
Hypertension, *N* (%)			<0.001
No	62.72 (59.88, 65.48)	43.59 (38.26, 49.07)	
Yes	37.28 (34.52, 40.12)	56.41 (50.93, 61.74)	
Diabetes (%), *N* (%)			<0.001
No	86.30 (85.39, 87.16)	73.29 (68.79, 77.36)	
Yes	13.70 (12.84, 14.61)	26.71 (22.64, 31.21)	
Cancer, *N* (%)			<0.001
No	89.75 (88.79, 90.64)	82.47 (77.30, 86.66)	
Yes	10.25 (9.36, 11.21)	17.53 (13.34, 22.70)	
CVD, *N* (%)			<0.001
No	91.35 (89.53, 92.88)	83.46 (80.08, 86.36)	
Yes	8.65 (7.12, 10.47)	16.54 (13.64, 19.92)	

Data of continuous variables: survey-weighted mean (*95%CI*), *P-value* was by survey-weighted linear regression. Data of categorical variables: survey-weighted percentage (*95%CI*), *P-value* was by survey-weighted Chi-square test. HDL-Cholesterol, High Density Lipoprotein Cholesterol; LDL-Cholesterol, Low Density Lipoproteins Cholesterol; ABSI, A Body Shape Index; BMI, body mass index; CI, conicity index; WC, waist circumference; WT, weight; WtHR, waist-to-height ratio; BRI, body roundness index; AVI, abdominal volume index; WWI, weight-adjusted waist index; PIR, poverty income ratio; CVD, cardiovascular disease.

3.2 Associations between nine anthropometric measures and gallstones

Almost all anthropometric indicators are positively correlated with gallstones (Table 2). In model 1, WWI had the highest OR (per 1 SD increment) (OR: 1.90; 95%CI: 1.68–2.16, $P < 0.001$) across all anthropometric indicators. After adjusting for covariates of age, gender, race, marital status, physical activity, smoking, alcohol, hypertension, diabetes, cancer, CVD history, Total water intake, Total carbohydrate intake, Total Fat intake, Total protein intake, WtHR (OR: 1.53; 95%CI: 1.36–1.71; $P < 0.001$), BRI (OR: 1.48; 95%CI: 1.33–1.65; $P < 0.001$), AVI (OR: 1.53; 95%CI: 1.38–1.70; $P < 0.001$), WWI (OR: 1.29; 95%CI: 1.11–1.49; $P < 0.001$), CI (OR: 1.34; 95%CI: 1.17–1.54; $P < 0.001$), WT (OR: 1.59; 95%CI: 1.43–1.75; $P < 0.001$),WC (OR: 1.57; 95%CI: 1.40–1.76; $P < 0.001$)and BMI (OR: 1.52; 95%CI: 1.39–1.67; $P < 0.001$) were still associated with gallstones in model 3. Furthermore, in models 2 and 3, there was no apparent association between the prevalence of gallstones and ABSI. An additive generalized model and smoothed curve fitting were applied to examine the association between gallstones prevalence and anthropometric indicators (Figure 1).

In Figure 2, we found there is a nonlinear association between WWI and CI indicators and gallstone prevalence, while WT, WC, BMI, AVI, WtHR, and BRI are linearly and positively associated with gallstone prevalence. We also carried out subgroup analyses (Supplementary Table 2), stratified by age (<60 and ≥60 years), sex

TABLE 2 Logistic regression analysis of anthropometric indices and gallstones.

	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
WC Z-score	1.56 (1.40, 1.74)	<0.001	1.65 (1.47, 1.86)	<0.001	1.57 (1.40, 1.76)	<0.001
WtHR Z-score	1.79 (1.60, 2.00)	<0.001	1.62 (1.44, 1.82)	<0.001	1.53 (1.36, 1.71)	<0.001
BRI Z-score	1.71 (1.55, 1.89)	<0.001	1.57 (1.42, 1.74)	<0.001	1.48 (1.33, 1.65)	<0.001
ABSI Z-score	1.35 (1.21, 1.50)	<0.001	1.05 (0.93, 1.18)	0.468	0.98 (0.87, 1.10)	0.766
AVI Z-score	1.52 (1.37, 1.67)	<0.001	1.61 (1.44, 1.79)	<0.001	1.53 (1.38, 1.70)	<0.001
WWI Z-score	1.90 (1.68, 2.16)	<0.001	1.42 (1.23, 1.65)	<0.001	1.29 (1.11, 1.49)	<0.001
CI Z-score	1.68 (1.48, 1.91)	<0.001	1.48 (1.28, 1.70)	<0.001	1.34 (1.17, 1.54)	<0.001
WT Z-score	1.27(1.15, 1.41)	<0.001	1.65 (1.48, 1.83)	<0.001	1.59 (1.43, 1.75)	<0.001
BMI Z- score	1.55(1.42, 1.68)	<0.001	1.59 (1.46, 1.74)	<0.001	1.52 (1.39, 1.67)	<0.001

Model 1: unadjusted model. Model 2: gender, age, Race/ethnicity, Marital status. Model 3: gender, age, Race/ethnicity, Marital status, Physical Activity, Alcohol, Smoking, Total water intake, Total carbohydrate intake, Total Fat intake, Total protein intake, Hypertension, Diabetes, Cancer, CVD. ABSI, A Body Shape Index; BMI, body mass index; CI, conicity index; WC, waist circumference; WT, weight; WtHR, waist-to-height ratio; BRI, body roundness index; AVI, abdominal volume index; WWI, weight-adjusted waist index.

(male and female) and BMI (<30 and ≥30 kg/m2). The subjects were divided by age (≥60 and <60 years), gender (male and female), and BMI (≥30 and <30 kg/m2). The results indicate a correlation between anthropometric indicators and gallstones, however, for individuals under 60 years old, females, and those with a BMI < 30 kg/m2, most anthropometric indicators show a stronger correlation with gallstones.

3.3 Discrimination ability of different anthropometric measures

The abilities of several anthropometric indicators to distinguish people with gallstones were assessed using receiver operating characteristic curves (ROC curves) and area under the curve (AUC) (Figure 3). Compared to the other 6 anthropometric indicators, the results show that WtHR and BRI had the best diagnostic abilities (WtHR: AUC = 0.670 95%CI:0.650–0.690; BRI: AUC = 0.670 95%CI: 0.650–0.690). We find WWI, AVI, WC, BMI, CI, and WT all showed favorable AUC values. Furthermore, stratified by BMI (< 30 and ≥ 30 kg/m2), subgroup ROC curve studies were also performed. When comparing participants with a BMI ≥ 30 kg/m2, we discovered that WtHR and BRI had the highest discriminating power. Participants with a BMI < 30 kg/m2 had comparatively higher AUC values for all 7 anthropometric indicators (Supplementary Table 3).

3.4 Combination of BMI and other anthropometric indices

The Spearman method was used to analyze the correlation between several anthropometric indicators. The correlation with BMI was the strongest for BRI (r = 0.921). While CI showed a minimal correlated with BMI (r = 0.503) (Supplementary Table 4). Since BMI is the most commonly used body measure, we evaluated the risk of gallstones in this study by combining BMI with other body measures. As shown in Figure 3, individuals with a BMI < 30 kg/m2 showed positive associations between elevated WT (OR: 2.22; 95%CI: 1.55–3.19; P < 0.001),WC (OR: 1.39; 95%CI: 1.07–1.80; P = 0.014), WtHR (OR: 1.40; 95%CI: 1.01–1.95; P = 0.045),CI (OR: 1.41; 95%CI: 1.07–1.85; P = 0.013), BRI (OR: 1.50; 95%CI: 1.08–2.08; P = 0.014), AVI (OR: 1.84; 95%CI: 1.41–2.40; P < 0.001) and gallstone incidence. However, participants with a BMI < 30 kg/m2 but increased WWI did not show an increased risk of gallstones (P > 0.05). In participants with normal WT, WtHR, CI, BRI and WWI, an elevated BMI also increased the risk of gallstones (all P < 0.05). Gallstone risk significantly increased with higher BMI and other anthropometric indices. The odds ratios (ORs) for WT, WC, WtHR, CI, BRI, AVI, and WWI were 2.58 (95%CI: 2.13–3.14), 2.47 (95%CI: 1.97–3.09), 2.31 (95%CI: 1.91–2.79), 2.45 (95%CI: 1.97–3.06), 2.34 (95%CI: 1.93–2.83), 2.63 (95%CI: 2.14–3.23), and 2.35 (95%CI: 1.86–2.96), respectively. Additionally, participants with a BMI ≥ 30 kg/m2 along with other abnormal anthropometric indicators had the highest risk of gallstones.

3.5 Sensitivity analysis

In sensitivity analysis (Supplementary Table 5), we excluded extreme values with anthropometric measures greater than 99% or less than 1%. The results were consistent with the main analysis results, showing that all 8 anthropometric indicators were positively correlated with the incidence of gallstones. WC (OR: 1.54; 95%CI: 1.33–1.77; P < 0.001), WtHR (OR: 1.50; 95%CI: 1.30–1.72; P < 0.001), BRI (OR: 1.48; 95%CI: 1.29–1.68; P < 0.001), AVI (OR: 1.52; 95%CI: 1.33–1.75; P < 0.001), WWI (OR: 1.30; 95%CI: 1.12–1.52; P < 0.001), CI (OR: 1.30; 95%CI: 1.11–1.52; P < 0.001), WT (OR: 1.59; 95%CI: 1.40–1.82; P < 0.001), and BMI (OR: 1.54; 95%CI: 1.36–1.73; P < 0.001). And we excluded participants with hematological disorders, finding the results to remain reliable (Supplementary Table 6).

4 Discussion

Our research is the first comprehensive examination of the relationship between gallstones and anthropometric indices within a sizable, nationally representative cohort of the American

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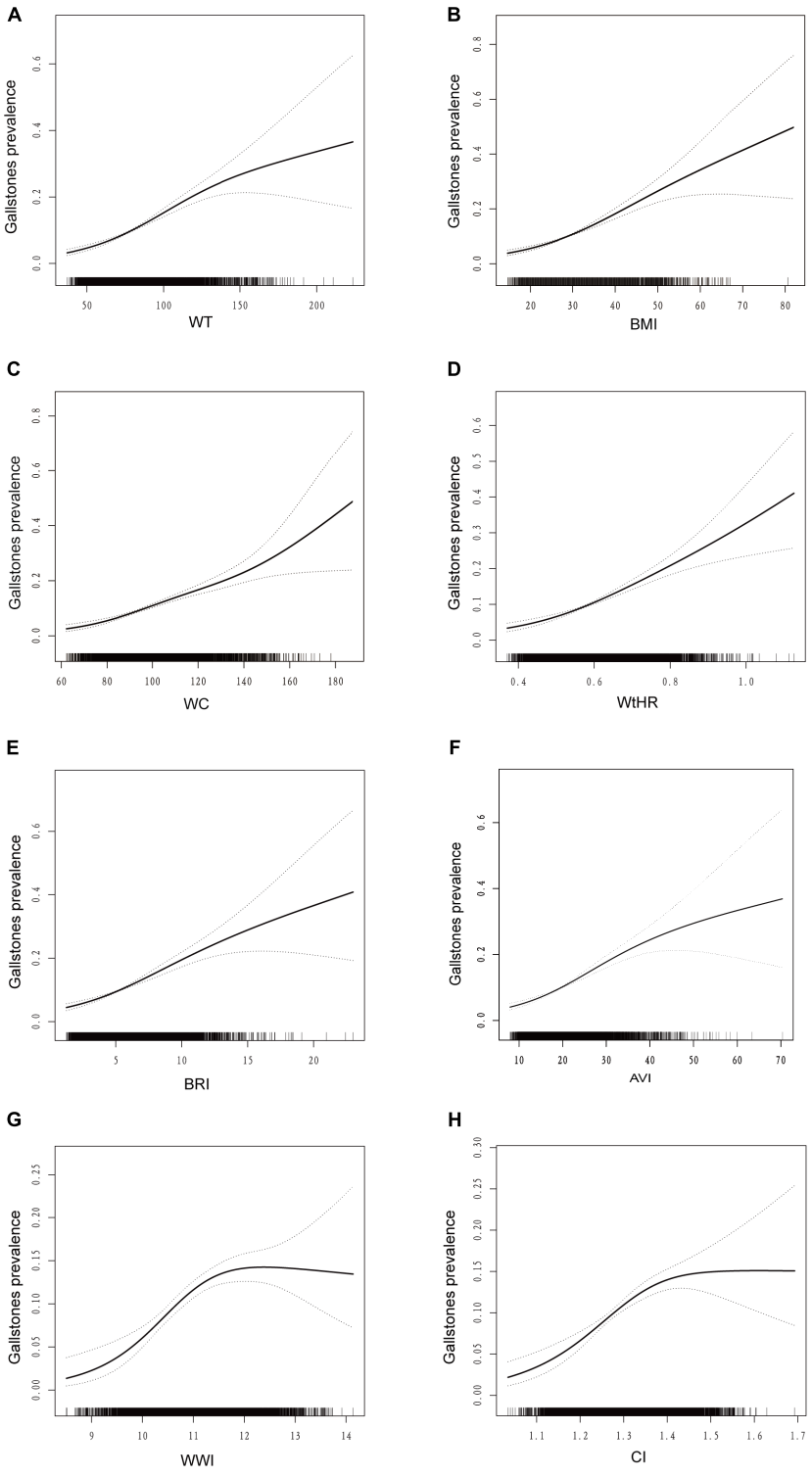
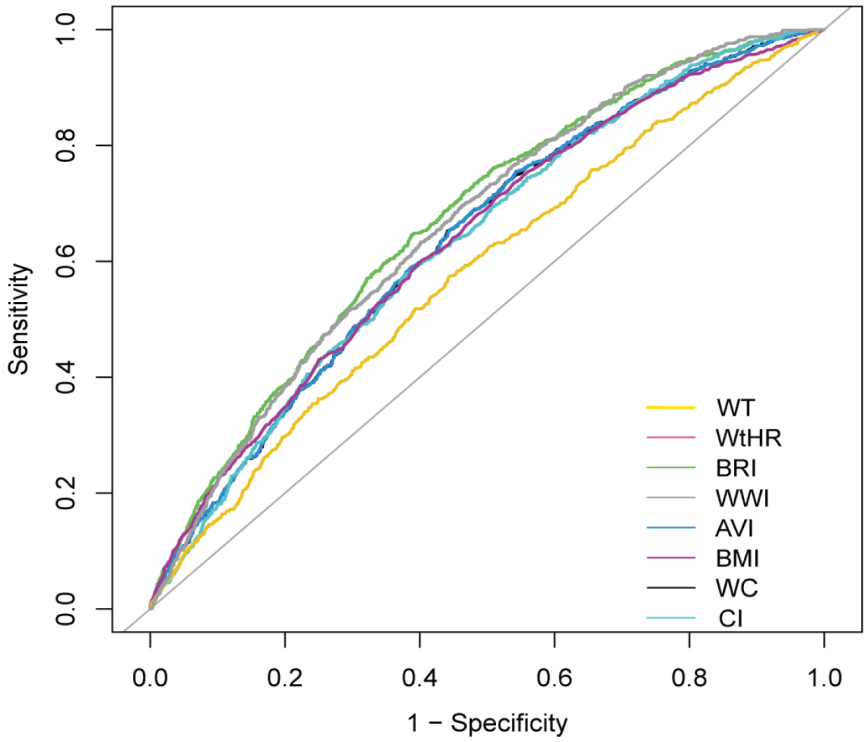


FIGURE 1
Dose–response relationship analysis between anthropometric measures and gallstones. The area between the upper and lower dashed lines is represented as the 95% CI. Each point shows the magnitude of the anthropometric measures and is connected to form a continuous line. GAM regression was adjusted for gender, age, race/ethnicity, marital status, physical activity, alcohol, smoking, total water intake, total carbohydrate intake, total fat intake, total protein intake, hypertension, diabetes, cancer, CVD. **(A)** association between WT and the risk of gallstones; **(B)** association between BMI and the risk of gallstones; **(C)** association between WC and the risk of gallstones; **(D)** association between WtHR and the risk of gallstones; **(E)** association between BRI and the risk of gallstones; **(F)** association between AVI and the risk of gallstones; **(G)** association between WWI and the risk of gallstones; **(H)** association between CI and the risk of gallstones. BMI, body mass index; CI, conicity index; WC, waist circumference; WT, weight; WtHR, waist-to-height ratio; BRI, body roundness index; AVI, abdominal volume index; WWI, weight-adjusted waist index.



Anthropometric Measures	Best threshold	Specificity	Sensitivity	ROC area(AUC)	P for difference in AUC
WtHR	0.6217	0.6124	0.6458	0.6703(0.650,0.690)	reference
BRI	5.9281	0.6124	0.6458	0.6703(0.650,0.690)	1.000
AVI	18.9479	0.4574	0.7556	0.6373(0.617,0.658)	<0.001
CI	1.3412	0.6206	0.5778	0.6335(0.613,0.654)	<0.001
BMI	30.1500	0.5976	0.6014	0.6373(0.616,0.658)	<0.001
WT	82.9500	0.5550	0.5750	0.5805(0.559,0.603)	<0.001
WWI	11.1495	0.5379	0.6958	0.6625(0.643,0.682)	0.299
WC	101.4500	0.5586	0.6528	0.6370(0.617, 0.658)	<0.001

Sensitivity and specificity were calculated using the best thresholds.

FIGURE 2
ROC curves of anthropometric measures for discriminating gallstone. ROC, receiver operating characteristic; AUC, area under the curve; BMI, body mass index; CI, conicity index; WC, waist circumference; WT, weight; WtHR, waist-to-height ratio; BRI, body roundness index; AVI, abdominal volume index; WWI, weight-adjusted waist index.

population. This study, based on two cycles (2017–2020) of the NHANES database, investigated eight anthropometric indices (WtHR, BRI, AVI, WWI, CI, WC, BMI, and WT). In the fully adjusted model, these indices showed a positive correlation with the risk of gallstones. Of these, BRI demonstrated the most significant discriminating power. Additionally, WtHR, with its simpler computation, offers discriminative capacity comparable to BRI.

Metabolic syndrome (MetS) and gallstone disease share common risk factors, including insulin resistance and central obesity (16, 17). Studies identify obesity as a distinct risk factor for gallstones. Although metabolic surgery has emerged as an effective tool for sustainable weight loss and glycemic control, gallstone formation before and after bariatric surgery will continue to concern clinicians (18). A recent study by Khalid O. Alyahyawi et al. found a causal relationship between gallstone disease, total bilirubin levels, and BMI (19). According to many studies, an increase in BMI is an independent risk factor for the occurrence of gallstones (20, 21). The chance of gallstone development increases by 1.63 times for every 5 percentage point increase in BMI (13). Interestingly, we also found that this association is more pronounced in women than in men (22). Obese individuals, regardless of metabolic health, are more likely to have gallstones than healthier counterparts, suggesting that obesity can independently accelerate gallstone formation. Interestingly, the total fat intake of the gallstone group was lower than that of the non-gallstone group, which may be related to the higher proportion of women in the gallstone group and their generally older age. The results of Wei et al.'s study are consistent with those of this study (23). Previous studies have shown that the increased risk of gallstones is associated with high intake of energy, total fat, saturated fatty acids, and monounsaturated fatty acids (24). However, in Tsai et al.'s study, excessive intake of unsaturated fats may reduce the risk of male gallstones (25). Mendelian randomization studies have shown that unsaturated fatty acids reduce the risk of cholecystitis and gallstones (26). Meanwhile,

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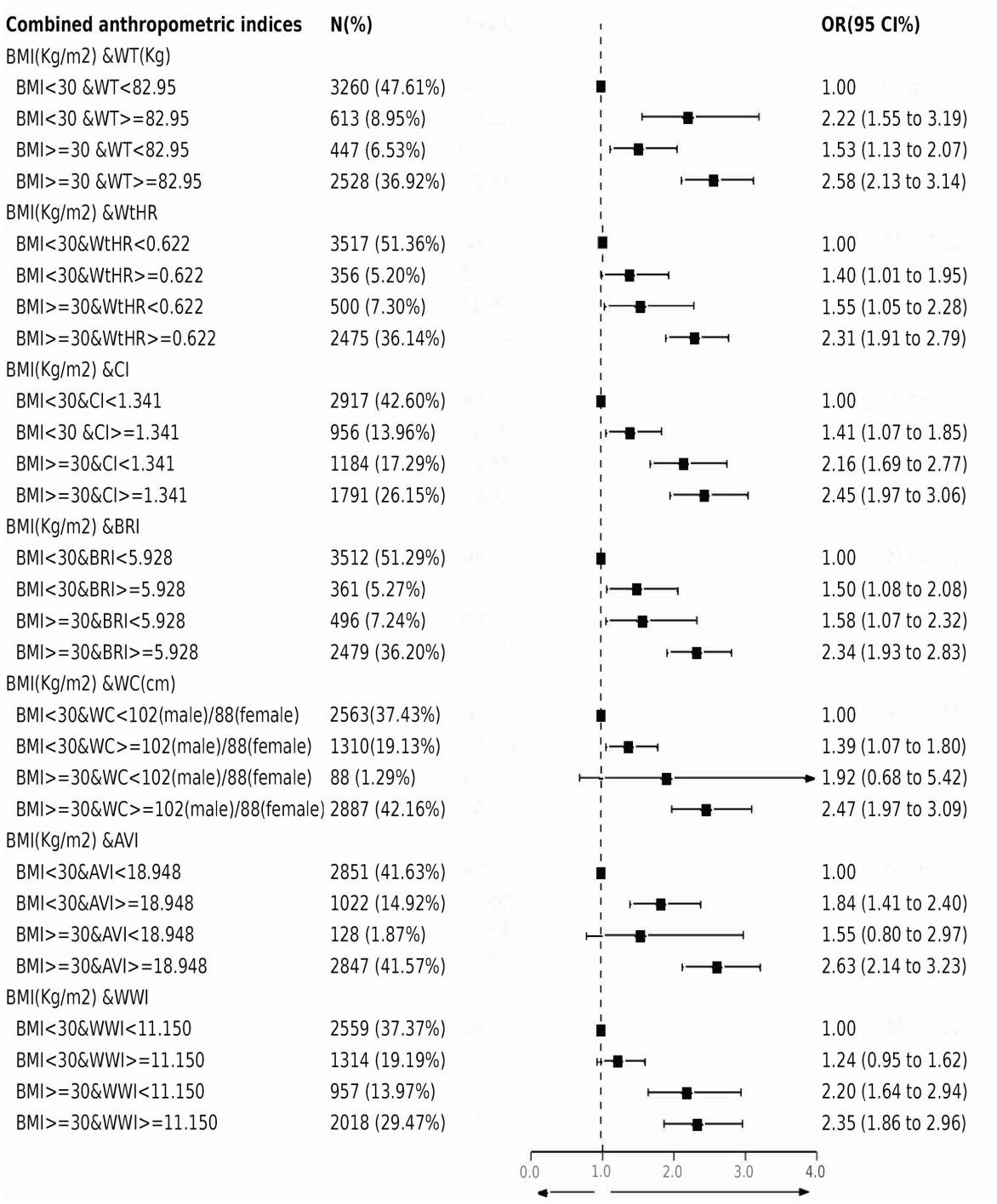

FIGURE 3
Association between gallstones and combined anthropometric indices. Multivariable logistic regression was conducted after adjusting for confounding factors of gender, age, race/ethnicity, marital status, physical activity, alcohol, smoking, total water intake, total carbohydrate intake, total fat intake, total protein intake, hypertension, diabetes, cancer, CVD.

obese individuals have a higher risk of cholesterol stone formation compared to normal weight individuals in terms of gallbladder peristalsis (27). These findings highlight that whether a patient has metabolic syndrome or not, they can still benefit from maintaining a normal weight to prevent gallstones (28). Increased hepatic bile secretion, inadequate bile acid secretion, and increased liver absorption and use of cholesterol are all linked to hyperinsulinemia. Additional research has demonstrated an independent association between gallstones, type 2 diabetes, and insulin resistance. Higher insulin levels observed in gallstone patients suggest that insulin resistance is a significant risk factor for the formation of gallstones (29). According to research by Méndez Sánchez et al., individuals with gallstones had insulin levels that were 26.2% higher (OR: 2.3; 95%CI 1.14–4.66, $p = 0.03$) than those in the control group (30).

Currently, most research uses BMI and weight as the primary indicators of obesity. However, in young, muscular individuals, what may appear as obesity could actually be the result of increased muscle mass (31). Additionally, BMI may not accurately quantify obesity in older adults due to the decrease in muscle mass (32). However, weight and BMI cannot accurately reflect the distribution of body fat (33, 34). To examine various obesity patterns more precisely, several novel anthropometric techniques have been introduced recently. These techniques are specifically designed to differentiate between central obesity and the emergence of chronic illnesses.

Research shows that ABSI is an independent predictor of all-cause mortality rates (35). There is a significant correlation between visceral fat, cardiovascular disease, and ABSI. Visceral fat, which may be used to indicate arterial stiffness in T2DM patients, showed a significant correlation with ABSI in a cross-sectional study of individuals with the disease (36). According to a systematic study, ABSI was more accurate in predicting all-cause mortality than both body mass index (BMI) and waist circumference (WC), though it was less accurate in predicting chronic illnesses. Like BMI and WC, excessive central obesity is linked to an increased risk of chronic illnesses. However, unlike these measures, ABSI does not differentiate between fat and lean mass. Due to its high degree of clustering around the mean and low variation, ABSI's predictability may be limited. While ABSI outperforms BMI and WC in predicting all-cause mortality, it is less effective in predicting chronic illnesses (37). This study also found no correlation between ABSI and gallstones after adjusting for confounding factors.

The World Health Organization (WHO) suggests measuring the circumference of the abdomen at the point where the top edge of the ilium and the lower edge of the ribs meet to determine the precise measurement technique for the WtHR. According to a meta-analysis, WtHR is a better predictor of diabetes, hypertension, and cardiovascular diseases than WC and BMI (38). In a study conducted in China, elevated BMI, WC, and WtHR were identified as independent risk factors for newly diagnosed gallstones (20). The model used to determine the Body Roundness Index (BRI) is based on a theoretically derived constant. Comparisons of BRI with conventional measures such as BMI, weight, or height have shown improved predictions of body fat percentage and visceral fat index (39). Additionally, elevated BRI levels have been independently associated with T2DM episodes, according to prior research. BRI is also directly linked to organ damage caused by hypertension, including left ventricular hypertrophy, microalbuminuria, arterial stiffness, and lower limb atherosclerosis (40). Moreover, CI has been used to diagnose T2DM and hypertension. According to Mantzoros et al., CI was not only a predictor of hypertension risk but also correlated with lipid profiles and fasting blood insulin levels (41). Research also indicates a link between the AVI and several conditions, including metabolic syndrome, diabetes, nonalcoholic fatty liver disease, hypertension, and declining renal function (42–45). However, the relationships between the BRI, CI, and AVI with the risk of gallstones remain unclear. The WWI is a new obesity assessment metric that normalizes WC to body weight, offering a simpler and more rational approach than BMI alone (46). Previous studies have shown that WWI is positively correlated with mortality rates of hypertension, diabetes, and cardiovascular disease (47, 48). In a study conducted in the United States, a higher WWI was also found to be positively correlated with the incidence of gallstones (49). This aligns with the outcomes that WWI demonstrated in our study. Our analysis shows that WtHR and BRI have a more significant impact on the incidence of gallstones compared to other central obesity markers. Based on the ROC curve analysis, WtHR and BRI also exhibited superior diagnostic capacity relative to other anthropometric measurements, offering a reliable forecast for gallstone risk. The study has several advantages and implications. Firstly, it is based on a substantial sample size that provides robust statistical power. Secondly, we utilized smooth curve fitting to illustrate the varying incidence rates of obesity levels and the nonlinear relationships between gallstones and different measurement techniques. Thirdly, anthropometric indicators proved more effective than conventional measurements in screening for gallstone risk, highlighting a strong link between abdominal obesity and gallstones. Anthropometric markers present a simple, non-invasive method for gallstone risk screening, which is beneficial from a public health perspective. However, the study also faces significant limitations. The primary limitation of our study is that the NHANES data on gallstones, derived from patient questionnaire surveys without conducting imaging studies, which may have bias. Secondly, as a cross-sectional study, it cannot establish causal relationships. Therefore, it is imperative for a well-designed prospective study to further investigate the impact of novel anthropometric indices on the incidence of gallstone, and for our observations to be validated. Thirdly, the absence of data on fat content and distribution precludes a direct evaluation of the relationship between body measurements and body or visceral fat. Fourthly, since the NHANES study focuses on the non-institutionalized U.S. population, the results may not be generalizable to other populations.

5 Conclusion

In this cross-sectional study, anthropometric indices including WT, WC, BMI, WtHR, BRI, AVI, WWI, and CI, were found to have a significant positive association with gallstones. Specifically, WT (per 1 SD increment) exhibited the strongest association with gallstones, while WtHR and BRI demonstrated superior discriminatory power for detecting gallstone risk. Assessing the risk of gallstones with BMI alone is insufficient. Greater consideration should be given to recently established anthropometric indicators to enhance gallstone prevention and treatment.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in this article/Supplementary material.

Ethics statement

The studies involving humans were approved by the NCHS Research Ethics Review Committee reviewed and approved the NHANES study protocol. The studies were conducted

in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

JZ: Writing – review and editing, Writing – original draft, Methodology, Conceptualization. DL: Writing – review and editing, Writing – original draft, Methodology, Conceptualization. LX: Writing – review and editing, Supervision, Methodology, Conceptualization. YL: Writing – original draft, Formal analysis, Data curation, Conceptualization. SJ: Writing – original draft, Formal analysis, Data curation, Conceptualization. XH: Writing – original draft, Formal analysis, Data curation, Conceptualization. HW: Writing – review and editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization. YJ: Writing – review and editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1428488/full#supplementary-material

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EDITED BY
Reza Rastmanesh,
American Physical Society, United States

REVIEWED BY
Kelli George,
West Virginia University, United States
Irene Martínez-García,
University of Castilla La Mancha, Spain

*CORRESPONDENCE
Li Zhang
✉ 390026566@qq.com

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A study on the reasonable dietary trajectory of elderly people in the community and its correlation with body mass index

Mengya Liu, Yuqing Chang, Wenjing Guo, Siyi Zhao, Meng Zhang, Xiaoyan Ma, Xiaomei Ji, Youran Liu and Li Zhang*

Bengbu Medical University School of Nursing Bengbu, Bengbu, China

Objective: To explore the reasonable dietary trajectory of elderly people in the community and to test the correlation between different dietary trajectories and body mass index (BMI) of the elderly people in the community to provide a reference for these individuals to formulate scientific interventions and cultivate healthy living habits.

Methods: The data of The Chinese Longitudinal Healthy Longevity Survey (CLHLS) from 2011 to 2018 were used to evaluate the dietary status of elderly people in the community according to their diet, and body mass index was calculated according to height and weight. The latent variable growth mixed (LGMM) model was used to analyze the development trajectory of diet in elderly people, and the multivariate logistic regression model was used to test the relationship between different dietary development trajectories and BMI changes as well as to test the correlation between different dietary trajectories and BMI of the elderly people in the community.

Results: The LGMM fit four dietary trajectories of elderly individuals: the continuous reasonable diet group (37.81%), the dietary behavior decline group (28.84%), the continuous unreasonable diet group (20.16%), and the dietary behavior improvement group (13.19%). The results showed that factors including male sex, rural setting, being spouseless, nonformal education status, not being wealthy, living alone, and having tooth loss were more likely to be classified as the "persistently unreasonable diet group" ($p < 0.05$). The logistic regression results showed that the "continuous reasonable diet group" and the "dietary behavior improvement group" were significantly correlated with the development of obesity to a normal BMI.

Conclusion: The dietary behavior of the elderly was significantly correlated with BMI value, and improving the reasonable dietary behavior of the elderly could reduce the high BMI to the normal range, but could not restore the low BMI to the normal range, indicating that reasonable dietary behavior is an important measure to prevent and improve overweight or obesity in the elderly. There is significant heterogeneity in the dietary behavior of the elderly, and community medical staff should identify the risk factors of various dietary behaviors of other groups as soon as possible, and provide corresponding intervention strategies to help them change their poor dietary behaviors and improve their nutritional status.

KEYWORDS

reasonable diet, body mass index, older adults, aging, China

1 Introduction

According to the National Bureau of Statistics, by the end of 2022, there were approximately 210 million elderly people aged 65 years and above in China, accounting for 14.9% of the total population; this result demonstrates that China has become a deep aging society (1). The greatest challenge posed by the aging population is the severe and complex health problems of elderly people. According to the Report on Nutrition and Health of the Elderly in China, there is a twofold burden of malnutrition and overnutrition among elderly people in China (2). With age, the functions of various body systems gradually decline; moreover, nutritional knowledge is lacking, and insufficient intake of energy, protein and other nutrients leads to an imbalance in the body's needs and intake, thus increasing the risk of malnutrition. According to previous studies, 48.4% of elderly individuals in China have poor nutritional status, and the overall prevalence of anemia among elderly individuals can reach 10.6% (3). Furthermore, due to rapid socioeconomic development, the quality of life of elderly people has improved, and some elderly people exhibit excessive fat, sugar or salt intake and perform less physical labor, thus resulting in an obvious trend toward overnutrition and an increase in the number of overweight and obese individuals. According to the Fifth National Physical Fitness Monitoring Bulletin, the overweight and obesity rates of elderly people in China are 41.7 and 16.7%, respectively (4).

A reasonable diet is the cornerstone of ensuring the health of elderly people, and it is closely related to the maintenance of physical function and quality of life. In 2022, the Chinese Nutrition Society released the Dietary Guidelines for the Elderly (2022), which includes two parts: the general elderly population, aged 65–79 years, and the elderly population, aged 80 years and above (5). In general, older people have a lower need for energy with age, but their need for important nutrients (such as protein) increases. However, due to the decline of sensory functions such as taste, the choice of food gradually solidifies with age, thus resulting in a single variety of food being consumed. The guidelines suggest that for the general elderly population, it is necessary to ensure that there is a variety of food, maintain a good appetite and appropriate weight, and prevent nutritional deficiencies (5). Elderly people often have limited food intake for various reasons, and their demand for energy and nutrients increases. The guidelines suggest that for elderly people, it is necessary to ensure food diversity; moreover, they should eat more fish, poultry, eggs, milk and beans, as well as undergo regular nutritional screenings and receive timely nutritional supplementations (5). These guidelines can help elderly people to better adapt to changes in physical function, and a reasonable diet plays an important role in preventing and delaying the occurrence and development of disease, thus prolonging a healthy lifespan, improving quality of life, and promoting healthy aging.

According to the Report on Nutrition and Health of the Elderly in China, unbalanced dietary intake is the main reason for the dual burden of malnutrition and overnutrition among elderly people (2). Body mass index (BMI) is one of the most commonly used indicators in clinical practice to assess malnutrition or overnutrition in a population; additionally, BMI can not only determine the level of obesity in individuals but can also be used to preliminarily screen people who may be at risk of malnutrition. BMI is the standard for defining the degree of obesity and thinness of individuals, as well as whether they are healthy (6); furthermore, the range of BMI for normal adults is 18.5 kg/m^2–23.9 kg/m^2 (7). In 1997, the World Health Organization (WHO) first recognized obesity as a disease and used body mass index (BMI) as a common measure of overweight/obesity (8). Overweight or obesity is an important manifestation of overnutrition in the elderly population, and there is no doubt that BMI is used to measure overnutrition in the elderly population internationally; moreover, being overweight or obese represent key risk factors for other disorders, such as cardiovascular disease, diabetes, stroke, and certain cancers, which seriously damage their physical and mental health (9). A low BMI is classified as a state of underweight, and Wang et al. (10) used a low BMI to investigate the incidence and trend of malnutrition among elderly individuals in China. Most foreign scholars have conducted clinical studies on the direct representation of low BMI as an indicator of malnutrition and found that it can predict a variety of adverse outcomes, such as frailty and death, thus confirming the clinical value of this indicator (11–13).

The elderly population is a unique group; specifically, there is considerable heterogeneity in this group, and their dietary behavior tends to show different trends due to the multifaceted effects of environmental and other social factors. Previous studies have focused on cross-sectional discussions on the impact of dietary patterns on a disease, ignoring changes in dietary behavior or structure throughout the life course. The BMI range of the elderly population is different from that of the young and middle-aged population, and the appropriate BMI range for the general elderly is 20.0 kg/m^2–26.9 kg/m^2 in the Dietary Guidelines for the Elderly, and "Appropriate range of body mass index and body weight management guidelines for Chinese oldest old" (13) clearly pointed out that the appropriate weight management target for the elderly is 22.0 kg/m^2–26.9 kg/m^2 to prevent the occurrence of adverse health outcomes and reduce or delay the occurrence of related diseases and their complications. Whether the BMI standard proposed in the guidelines is related to the reasonable dietary behavior of the elderly, that is, whether the change of reasonable diet can make the BMI of the elderly normal, and how the change between the two is a question that we need to explore. In order to solve the above problems, this study tested the data from the tracking survey of the influencing factors of the elderly health in China, used the latent variable growth mixed model (LGMM) to explore the dietary development trajectory of the elderly in the community, depicted the development trajectory curve of each subgroup, analyzed the influencing factors of different dietary trajectories of the elderly, and explored the longitudinal association between each trajectory group and BMI, so as to provide a reference for the elderly in the community to formulate scientific personalized interventions and cultivate healthy living habits.

2 Materials and methods

2.1 Research subjects

The Chinese Longitudinal Healthy Longevity Survey CLHLS is a longitudinal survey of elderly people organized by the Center for Healthy Aging and Development Research of Peking University/National Academy of Development, and it encompasses 23 provinces, municipalities and autonomous regions across the country, accounting for 85% of the national population. The survey subjects are elderly people aged 65 years and older and adult children aged 35–64 years.

The questionnaire includes the basic status of elderly people and their families, socioeconomic background and family structure, economic resources and economic status, health and quality of life self-assessment, cognitive function, personality and psychological characteristics, daily activity ability, diet and other lifestyles, life care, and disease treatment, among other items. The survey was followed by a baseline survey in 1998 and follow-up surveys in 2000, 2002, 2005, 2008–2009, 2011–2012, 2014, and 2017–2018 (14). According to the CLHLS survey team, the study was approved by the Ethics Committee of Peking University (IRB00001052-13074), and all of the respondents signed an informed consent form before participating (15).

This study used demographic and health-related CLHLS data from 2011 to 2018, and a total of 9,765 respondents participated in the interviews in 2011. The inclusion criteria were as follows: (1) were aged ≥65 years, (2) had complete demographic data, required health-related data, and lifestyle data, among other information. The exclusion criteria: Respondents who did not participate in longitudinal tracking in the CLHLS. According to the inclusion and exclusion criteria, a total of 1,349 subjects participated in the 7-year follow-up.

2.2 Research method

2.2.1 General information survey

By querying various books and electronic information databases related to the diet and BMI of elderly people at home and abroad, as well as investigating the research situation in various databases, such as books, journals, master's and doctoral theses, newspapers and periodicals, the relevant variables were identified and sorted. The survey data that were collected included age, sex, education level, marital status, place of residence, economic status, smoking status, alcohol consumption status, cohabitation, exercise status, tooth loss status and the number and types of comorbidities.

2.2.2 Dietary assessment

According to the Dietary Guidelines for the Elderly (2022) (5), elderly people should ensure their energy supply, maintain a daily grain intake of 200–300 g, control salt, sugar and oil intake, and eat more fresh vegetables and fruits as well as foods that are rich in important nutrients such as protein. Furthermore, ensuring food diversity is essential for an adequate and balanced nutritional supply. Therefore, this study selected 14 foods that are relevant to the dietary guidelines based on the CLHLS database and the dietary scoring methods of previous researchers, which is consistent with the principle of selecting and evaluating food groups for a reasonable diet according to a specific purpose (16, 17). The respondents were asked to report their intake and frequency of consumption of grains and oils, as well as 12 other food groups, including vegetables, fruits, meat, aquatic products, eggs, soy products, dairy products, pickles, sweets, fungi and algae, nuts, and vitamins.

Cereals and oils are foods that reflect the calories of elderly people, and a reasonable diet should be controlled within the normal range; for this reason, cereals and oils should be scored according to the amount and type of intake. "The amount of staple food per day is controlled at 200–300 g" was counted as 1 point, and "the amount of staple food per day is more than 300 g" and "the amount of staple food per day is less than 200 g" was counted as 0 points. "Mainly edible vegetable oil" was recorded as 1 point, and "regular consumption of animal oil such as lard" was recorded as 0 points. The other 12 foods were scored according to the frequency of intake, with participants responding to five of them ("almost every day," "at least once a week," "at least once a month," "occasionally" and "rarely or never"), with 1 point being given if the answer to a food group was "almost every day" or "at least once a week"; otherwise, the score was 0. Moreover, pickled products and sweets were encouraged to be eaten less, and a reverse score was needed. The total score is the sum of the abovementioned 14 food scores, with a range of 0–14 points; a higher score indicated a more reasonable diet. The questionnaire was created to assess the adequacy of meals and the health of diets in older adults, and its scientific validity has been previously demonstrated (18). Based on the median total score, the respondents were divided into two groups: the reasonable diet group and the irreasonable diet group.

2.2.3 Body mass index assessment

Body mass index (BMI) was calculated based on the height and weight measured in the questionnaire, and BMI was calculated by dividing the weight by the square of the height (m^2) in kg/m^2. Numerous studies (both in China and abroad) have shown that being too thin in elderly people can lead to reduced resistance and an increased risk of death (18, 19). According to the Dietary Guidelines for the Elderly, the BMI cutoff value for assessing whether elderly individuals have a normal weight is different from that of young and middle-aged people. The basic consensus formed by experts and scholars is that the weight of elderly individuals should not be too low, and a BMI of the general elderly is more suitable at 20.0 kg/m^2–26.9 kg/m^2 (5), the appropriate range of body mass index for Chinese oldest old is 22.0 kg/m^2–26.9 kg/m^2 (13).

2.3 Covariates

Data related to a reasonable diet and BMI were selected and coded, including age (65–79 years = 1, ≥80 years = 2), sex (male = 1, female = 2), marital status (with spouse = 1, without spouse = 2), education (below primary school = 1, primary school and above = 2), place of residence (rural = 1, urban = 2), economic status (low to moderate income = 1, high income = 2), smoking status (yes = 1, no = 2), alcohol consumption status (yes = 1, no = 2), living together (living with family = 1, living alone = 2, nursing home = 3), exercise status (yes = 1, no = 2), tooth loss status (yes = 1, no = 2), and comorbidities of chronic disease (yes = 1, no = 2).

2.4 Statistical methods

Normally distributed data are expressed as the mean ± standard deviation (x ± s), nonnormally distributed data are expressed as the median (M) and interquartile range (IQR), and counts are described as the frequency and percentage. The latent variable growth mixed model (LGMM) was used to fit the dietary trajectories of the elderly participants. LGMM combines the features of the linear mixed model with additional components to divide the population into a limited number of potential classes (20). The evaluation indicators of LGMM models include the Aickeck information criterion (AIC), Bayesian information criterion (BIC), sample-corrected BIC (aBIC),

information entropy, likelihood ratio test (LMR), and bootstrap-based likelihood ratio test (BLRT) (21). Lower values of AIC, BIC, and aBIC indicated a better fit of the model. Moreover, a higher entropy value (≥0.8 indicates more than 90% classification accuracy) indicated a more accurate model classification. LMR and BLRT were used to compare whether the difference between the k and $k-1$ categories was significant, and a smaller p-value indicated a better model k category. A multivariate logistic regression model was used to test the relationships between different dietary trajectories and BMI changes. Statistical analysis was performed by using Mplus 8.3 and SPSS software version 26.0.

3 Results

3.1 General information of the research subjects

A total of 2,465 elderly people aged 65 years and older were included in this study at baseline, and a total of 1,349 respondents with complete data were followed after 7 years. There was no statistically significant difference between the baseline characteristics of the older adults who completed follow-up and the baseline characteristics of the overall study subjects, as shown in Table 1. Among the 1,349 elderly people, the average age was 81.21 (SD = 8.9) years, 45.96% were female, 42.40% received formal education, 83.99% were married, 56.34% were rural, 67.01% were low- and middle-income people, 74.65% were living with their families, 29.95% were smokers, 42.25% were drinkers, 32.39% were less active, and 20.31% of older people with 2 or more chronic diseases had tooth loss. General information on the study subjects is shown in Table 1.

3.2 Analysis of the development trajectory of the diet of elderly people

The LGMM results showed that the AIC, BIC and aBIC values were smaller and that the entropy values changed accordingly, which indicated that there was heterogeneity in the longitudinal data population. In principle, the 5-category model should be retained; however, only 0.1% of patients with categories were found in the 5-category model, 2 potential categories were found to be very similar, and the distinction was not obvious. When considering the simplicity of the model, the 4-category model was ultimately retained, as shown in Table 2.

3.3 Nomenclature and characteristics of the categories of dietary development trajectories of elderly people

A total of 1,349 elderly patients were included in this study; these patients could be divided into four groups, as shown in Figure 1. The first category was termed the "persistent unreasonable diet group," and the dietary evaluation of the elderly individuals in this category was unreasonable at baseline and follow-up, with a total of 272 people (accounting for 20.20%). The second category was termed the "Dietary Behavior Decline Group," and 389 elderly people in this category were evaluated as reasonable at baseline and unreasonable after 7 years of follow-up, accounting for 28.84%. The third category was the "continuous reasonable diet group," and the dietary behavior of the elderly individuals in this group was reasonable at baseline and follow-up, with a total of 510 people (accounting for 37.81%). The fourth category was the "dietary behavior improvement group," and there were 178 elderly people in this category, accounting for 13.19%; the dietary behavior of these individuals was unreasonable at baseline but improved after follow-up.

Univariate analysis of demographic and clinical characteristics among the four categories of dietary development trajectories of the elderly showed that there were significant differences in age, sex, place of residence, education level, marital status, economic status, alcohol consumption, cohabitants, physical exercise, and comorbidities among the different categories ($p < 0.05$). There was no significant difference in smoking status among the four categories, as shown in Table 2. The four categories determined via LGMM analysis were used as dependent variables; moreover, the meaningful variables of the univariate analysis were used as independent variables, and multivariate logistic regression analysis was performed with "continuous reasonable diet group" as the reference category, as shown in Table 3. The results showed that males (OR = 1.614, 95% CI = 1.167–2.233, $p = 0.004$), rural residents (OR = 0.498, 95% CI = 0.361–0.685, $p < 0.001$), people with no spouses (OR = 0.344, 95% CI = 0.195–0.609, $p = 0.011$), people with no formal education (OR = 1.480, 95% CI = 1.072–2.045, $p = 0.017$), people who were not wealthy (OR = 2.368, 95% CI = 1.496–3.749, $p < 0.001$), people who lived alone (OR = 2.652, 95% CI = 1.676–4.195, $p < 0.001$), and people who experienced tooth loss (OR = 1.036, 95% CI = 0.440–2.438, $p = 0.036$) were more likely to be in the "continuous unreasonable diet group" ($p < 0.05$) (see Table 4).

3.4 Relationship between dietary trajectory category and BMI change in elderly people

At baseline, the elderly individuals were divided into thin, normal, and obese groups according to the appropriate BMI range proposed in the Dietary Guidelines for the Elderly (5). The ratio of BMI at baseline to that at follow-up is shown in Figure 2. In this study, nine BMI change patterns were constructed according to the BMI at baseline and follow-up, including the "thin stable group" (156 patients), "normal stable group" (513 patients), "thin-normal group" (180 patients), "thin-obese group" (43 patients), "normal-thin group" (161 patients), "normal-obesity group" (109 patients), "obesity-stable group" (101 patients), "obese-thin group" (15 patients), and "obese-normal group" (71 patients).

Multivariate logistic regression was used to explore the relationship between dietary trajectory categories and BMI changes in elderly individuals, and the results showed that when the covariates were not adjusted, the BMIs of the elderly individuals in the "continuous reasonable diet group" and the "dietary behavior improvement group" tended to be normal compared with those in the "continuous unreasonable diet group" ("continuous reasonable diet group," "normal and stable group": OR = 1.071, 95% CI = 0.626–1.832, $p = 0.003$; "obesity-normal group": OR = 1.029, 95% CI = 0.437–2.426, $p = 0.041$). The inclusion criteria for the "dietary behavior improvement group" were also determined ("normal and stable group": OR = 0.796, 95% CI = 0.418–1.514, $p = 0.026$; "thin-normal" group: OR = 0.421,

TABLE 1 Baseline characteristics of the study subjects and those who completed follow-up.

Baseline characteristics	Baseline respondents (N = 2,465), n/(%)	Follow-up respondents (N = 1,349), n/(%)	χ^{2a}	p
Age			1.172	0.279
65–79	1763 (71.52)	987 (73.17)		
≥80	702 (28.48)	362 (26.83)		
Sex			3.628	0.057
Male	1,411 (57.24)	729 (54.04)		
Female	1,054 (42.76)	620 (45.96)		
Residence			1.426	0.232
Rural	1,438 (58.34)	760 (56.34)		
Town	1,027 (41.66)	589 (43.66)		
Marital status			0.064	0.801
With spouse	2078 (84.30)	1,133 (83.99)		
No spouse	387 (15.70)	216 (16.01)		
Education			0.001	0.985
Formal	1,046 (42.43)	572 (42.40)		
Nonformal	1,419 (57.57)	777 (57.60)		
Economic			0.280	0.597
Low and middle	1,631 (66.17)	904 (67.01)		
High	834 (33.83)	445 (32.99)		
Smoke			2.784	0.095
Yes	803 (32.58)	404 (29.95)		
No	1,662 (67.42)	945 (70.05)		
Drink			0.001	0.989
Yes	1,041 (42.23)	570 (42.25)		
No	1,424 (57.77)	779 (57.75)		
Living together			1.421	0.492
Living with family	1831 (74.28)	1,007 (74.65)		
Nursing home	52 (2.11)	21 (1.56)		
Living alone	582 (23.61)	321 (23.79)		
Exercise			0.004	0.949
Yes	801 (32.49)	437 (32.39)		
No	1,664 (67.51)	912 (67.61)		
Chronic disease			0.094	0.760
Yes	511 (20.73)	274 (20.31)		
No	1954 (79.27)	1,075 (79.69)		
Tooth loss			2.471	0.116
Yes	1,543 (62.60)	879 (65.16)		
No	922 (37.40)	470 (34.84)		

[a]The differences in these characteristics between the analyzed sample and baseline sample were evaluated using chi-square tests.

95% CI = 0.194–0.912, $p = 0.028$; and "obesity-normal group": OR = 1.136, 95% CI = 0.422–3.063, $p = 0.001$). The BMI of the elderly individuals in the "dietary behavior decline group" tended to be lean ("normal-lean group": OR = 2.567, 95% CI = 1.127–5.849, $p = 0.006$). After adjusting for age, sex, place of residence, education level, marital status, economic status, smoking status, alcohol consumption status, living with people, exercise status, tooth loss status, and comorbidities, improvements in continuous reasonable diet and dietary behavior were significantly correlated with the development of a normal BMI ("continuous reasonable diet group," "normal stable group": OR = 1.907, 95% CI = 1.356–2.682, $p < 0.001$; "obese-normal group": OR = 0.859, 95% CI = 0.350–1.458, $p = 0.039$) ("dietary behavior

TABLE 2 LGMM fitting information of the dietary trajectories of elderly people in the community.

Category	AIC	BIC	aBIC	Entropy	LMR	BLRT	Category probability
C1	6081.782	6063.113	6031.339				1
C2	5970.901	6022.972	5911.206	0.703	<0.001	<0.001	0.429/0.571
C3	5964.215	6031.907	5900.612	0.931	0.0013	<0.001	0.471/0.106/0.423
C4	5564.847	5648.161	5597.336	0.968	<0.001	<0.001	0.202/0.288/0.378/0.132
C5	4918.172	5017.107	4956.252	0.971	<0.001	<0.001	0.001/0.682/0.057/0.001/0.259

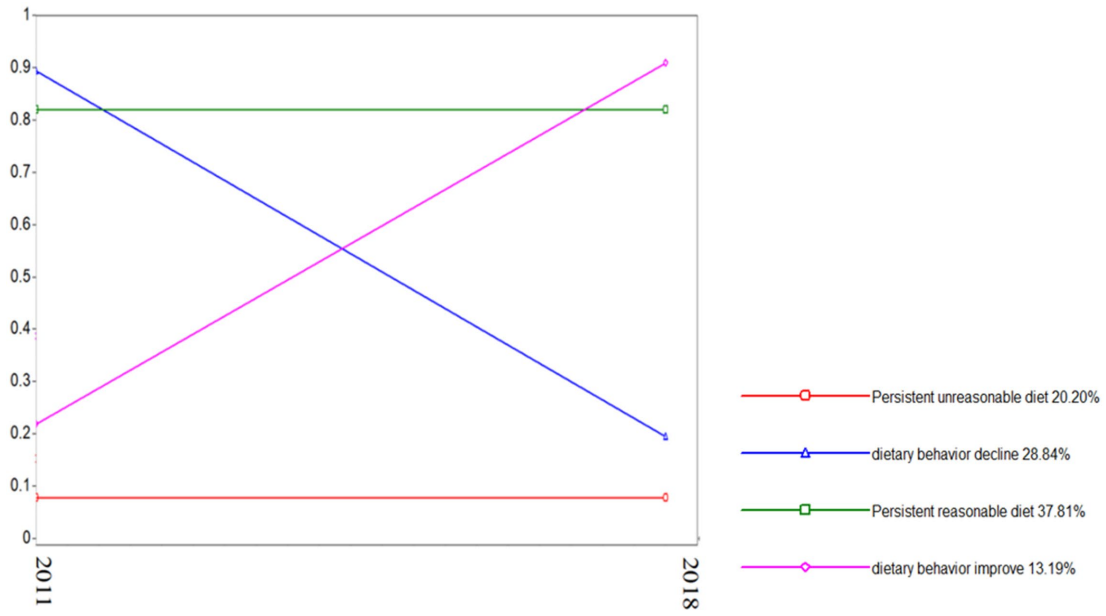

FIGURE 1
Reasonable diet trajectory for elderly people in the community.

improvement group," "thin-normal group": OR = 0.412, 95% CI = 0.188–0.902, $p = 0.027$; "obese-normal group": OR = 1.241, 95% CI = 0.448–3.437, $p < 0.001$). A decrease in dietary behavior was significantly associated with a change from a normal BMI to a lean BMI ("normal-lean group": OR = 1.117, 95% CI = 1.034–2.402, $p = 0.001$), as shown in Table 5.

4 Discussion

4.1 Categorical characteristics of dietary development trajectories in the elderly

In this study, the LGMM model was used to assess the change trajectory and factors influencing the diet of elderly people in the community. The model fit a total of four dietary trajectories: the continuous reasonable diet group, the dietary behavior decline group, the continuous unreasonable diet group, and the dietary behavior improvement group.

The "dietary behavior improvement group" accounted for the lowest proportion, which was 13.19%, and the baseline dietary evaluation of the elderly individuals in this category was unreasonable; however, their dietary behavior improved at follow-up. The results of regression analysis showed that this group was dominated by older people with comorbidities; specifically, 108 elderly people in this category had comorbidities, of which 81 (74.1%) had diabetes and hypertension at the same time. Dietary control is the main nonpharmacological treatment for diabetes and hypertension. With the promotion of the Healthy China Initiative and the promotion of dietary guidelines for residents, elderly people have begun to understand the importance of a reasonable diet; moreover, when they learn that they have diabetes or high blood pressure, they will consciously improve their dietary behavior. In this category, 129 (72.5%) of the elderly individuals reduced their intake of staple foods; 134 (75.3%) of the elderly individuals reduced their intake of sugar, salt and pickled products; and 152 (85.4%) of the elderly individuals increased their intake of vegetables, fruits, fish, eggs and other foods. For this group of elderly people, it is necessary to encourage them to continue to maintain the enthusiasm and continuity of a reasonable diet (22, 23).

The proportion of the "dietary behavior decline group" was 28.84%, and the baseline dietary evaluation of the elderly individuals in this category was reasonable; however, the dietary evaluation was unreasonable at follow-up. The results of regression analysis showed

TABLE 3 Relationships between dietary trajectories and sociodemographics of elderly people in the community.

Variable[a]	Total (n = 1,349)	Persistent unreasonable diet (n = 272)	Dietary behavior decline (n = 389)	Continuous reasonable diet (n = 510)	Dietary behavior improve (n = 178)	χ^2	p
Age						16.922	0.001
65–79	796 (59.01)	160 (58.82)	231 (59.38)	277 (54.31)	128 (71.91)		
≥80	553 (40.99)	112 (41.18)	158 (40.62)	233 (45.69)	50 (28.09)		
Sex						24.008	<0.001
Male	729 (54.04)	122 (44.85)	226 (58.10)	302 (59.22)	79 (44.38)		
Female	620 (45.96)	150 (55.15)	163 (41.90)	208 (40.78)	99 (55.62)		
Residence						16.898	0.001
Rural	739 (54.78)	179 (65.81)	209 (53.73)	275 (53.92)	116 (65.17)		
Town	610 (45.22)	93 (34.19)	180 (46.27)	235 (46.08)	62 (34.83)		
Marital status							
With spouse	1,061 (81.62)	229 (84.19)	304 (78.15)	411 (80.59)	117 (88.20)	23.867	<0.001
No spouse	288 (18.38)	43 (15.81)	85 (21.85)	99 (19.41)	61 (11.80)		
Education						11.046	0.011
Formal	572 (42.40)	94 (34.56)	173 (44.47)	235 (46.08)	70 (39.33)		
Nonformal	777 (57.60)	178 (65.44)	216 (55.53)	275 (53.92)	108 (60.67)		
Economic status						32.056	<0.001
Low and middle	1,104 (81.84)	244 (89.71)	302 (77.63)	396 (77.65)	162 (91.01)		
High	245 (18.16)	28 (10.29)	87 (22.37)	114 (22.35)	16 (8.99)		
Smoke or not						5.532	0.137
Yes	193 (14.31)	46 (16.91)	53 (13.62)	62 (12.16)	32 (17.98)		
No	1,156 (85.69)	226 (83.09)	336 (86.38)	448 (87.84)	146 (82.02)		
Drinking status						12.578	0.006
Yes	233 (17.27)	52 (19.12)	85 (21.85)	67 (13.14)	29 (16.29)		
No	1,116 (82.73)	220 (80.88)	304 (78.15)	443 (86.86)	149 (83.71)		
living together						43.439	<0.001
Living with family	947 (70.20)	170 (62.50)	265 (68.12)	361 (70.78)	151 (84.83)		
Nursing home	30 (2.22)	3 (1.10)	5 (1.29)	14 (2.75)	8 (4.49)		
Living alone	372 (27.58)	99 (36.40)	119 (30.59)	135 (26.47)	19 (10.68)		
Exercise						16.041	<0.001
Yes	543 (38.25)	86 (31.62)	147 (37.79)	229 (44.90)	81 (45.51)		
No	806 (61.75)	186 (68.38)	242 (62.21)	281 (55.10)	97 (54.49)		
Chronic disease						98.948	<0.001
Yes	398 (29.50)	79 (29.04)	90 (23.14)	121 (23.73)	108 (60.67)		
No	951 (70.50)	193 (70.96)	299 (76.86)	389 (76.27)	70 (39.33)		
Tooth loss						116.032	<0.001
Yes	902 (66.86)	218 (80.15)	317 (81.49)	271 (53.14)	96 (53.93)		
No	447 (33.14)	54 (19.85)	72 (18.51)	239 (46.86)	82 (46.07)		

[a]The number of sociodemographic variables in the population after 7 years of follow-up, and the number of variables at baseline and follow-up is shown in Table 1.

that this group of people was mainly unmarried, low- and middle-income, alcoholic, and elderly with tooth loss. With increasing age, the physical and mental functions of elderly people, such as the decline of smell, taste and other sensations, absorption and digestion functions, coupled with the loss of teeth, as well as modulation of some food choices, decline to varying degrees. This results in a gradual

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TABLE 4 Factors influencing the dietary trajectories of elderly people in the community.

Variable	Persistent unreasonable diet			Dietary behavior decline			Dietary behavior improvement		
	OR 值	95% CI	*p*-值	OR 值	95% CI	*p*-值	OR 值	95% CI	*p*-值
Age									
65–79	Ref			Ref			Ref		
≥80	1.047	0.762–1.438	0.777	1.544	1.065–2.238	0.022	1.144	0.794–1.648	0.471
Sex									
Female	Ref			Ref			Ref		
Male	1.614	1.167–2.233	0.004	1.113	0.837–1.479	0.462	0.364	0.220–0.601	0.552
Residence									
Town	Ref			Ref			Ref		
Rural	0.498	0.361–0.685	<0.001	0.788	0.600–1.034	0.085	0.712	0.417–1.214	0.212
Marital status									
With spouse	Ref			Ref			Ref		
No spouse	0.344	0.195–0.609	0.011	0.277	0.141–0.546	<0.001	0.997	0.579–1.715	0.990
Education									
Formal	Ref			Ref			Ref		
Nonformal	1.480	1.072–2.045	0.017	1.016	0.772–1.336	0.910	1.175	0.815–1.694	0.387
Economic									
High	Ref			Ref			Ref		
Low and middle	2.368	1.496–3.749	<0.001	0.983	0.711–1.361	0.020	0.606	0.369–0.995	0.058
Living together									
Living with family	Ref			Ref			Ref		
Nursing home	0.701	0.186–2.635	0.599	0.366	0.046–2.933	0.344	2.052	1.221–3.449	0.097
Living alone	2.652	1.676–4.195	<0.001	2.446	1.475–4.057	0.051	1.192	0.739–1.923	0.471
Drinking status									
No	Ref			Ref			Ref		
Yes	2.071	1.359–3.156	0.091	1.944	1.354–2.790	<0.001	1.654	1.007–2.718	0.082
Exercise									
No	Ref			Ref			Ref		
Yes	1.620	1.141–2.302	0.007	2.616	1.487–4.602	0.061	1.584	1.141–2.200	0.056
Chronic disease									
No	Ref			Ref			Ref		
Yes	1.137	0.784–1.647	0.059	1.296	0.980–1.713	0.069	0.740	0.465–1.179	0.025
Tooth loss									
No	Ref			Ref			Ref		
Yes	1.036	0.440– 2.438	0.036	1.084	0.665–1.768	<0.001	0.648	0.418–1.002	0.078

decrease in dietary intake and types, especially the insufficient intake of fruits, dairy products, nuts and soy products. A total of 274 (70.4%) elderly people in this category reduced their intake of fruits, dairy products, nuts and soy products. Marriage has a considerable impact on the diet of older adults, which is consistent with the findings of most studies (24). Among the unmarried elderly individuals in this category, 82 (82.83%) were widowed. Zhao and Li (25) used 6-phase CLHLS data to analyze the impact of widowhood on multiple health outcomes and health behaviors and showed that widowhood can lead to changes in the original living status of elderly people, as well as reduce the available psychological and social support resources, increase the risk of depression and cognitive decline in elderly people, and lead to decreased appetite. Older adults who live alone after widowhood may reduce their intake of nutritious food due to a lack of financial support (26). Furthermore, widows are more likely to engage in health-risk behaviors such as alcohol consumption, which is due to the need to relieve widowhood stress and the lack of spousal supervision (27).

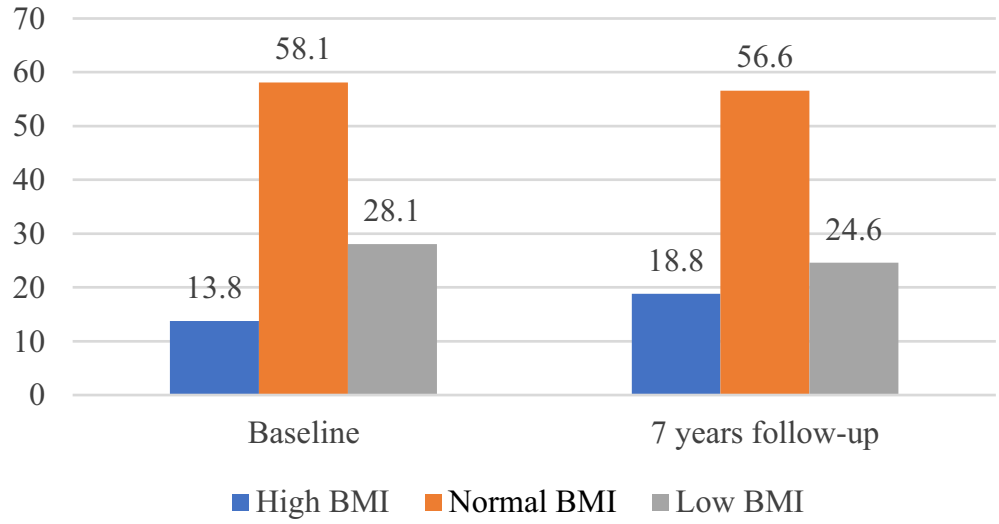

FIGURE 2
BMI status of elderly people in the community at baseline and at the 7-year follow-up.

The "persistent unreasonable diet group" accounted for 20.16% of the sample, and the dietary evaluation of the elderly individuals in this category was unreasonable at baseline and at follow-up. The results of regression analysis showed that this group of people was mainly male, lived in rural areas, did not have formal education, had low incomes, lived alone, and had tooth loss. The dietary habits of older men were worse than those of older women, which was consistent with the findings of most studies. Feraco et al. (28) investigated sex differences in the eating habits of 2,388 adults and showed that women had better eating habits than men. In a study of healthy eating among 262 respondents conducted by Razaz et al. (29), women were more likely to adopt a healthy diet than men were (OR = 1.85, 95% CI = 1.02–3.35). The analysis of the sex differences in this study may be due to the following reasons. First, differences in dietary choices between men and women. In this category, men preferred spicy and salty foods, and the number of people who regularly consumed lard (76 cases, 27.94%) was significantly greater than that of women (28 cases, 10.29%). Only 16.91% of men regularly consumed soy products, fruits, and vegetables, which may be related to evolutionary dietary roles and current social norms (28). Second, men have a greater rate of social participation than women and often rely on out-of-home gatherings to build or strengthen their social support networks, which also indirectly leads to poorer eating control behaviors. Older people living in rural areas, with no formal education and with low incomes, have less access to information on healthy diets and lack knowledge about nutrition and health, although the state is actively publicizing the impact of a reasonable diet on health. Due to the limitations of the living environment, some elderly people may not be aware of the important role of nutrition in health and are unwilling to accept nutritional knowledge and change their dietary habits for reasonable nutrition. Most of the elderly people are mainly engaged in farm work, with greater energy consumption and increased intake of staple foods, oil and salt but less intake of milk, eggs and fruits. Second, due to economic constraints, low-income elderly people will reduce their demand for dairy products, meat, eggs, fish and nuts, thus resulting in a greater risk of malnutrition. Older people who live alone may have irregular diets and lower intake of important nutrients; thus, they are more likely to suffer from malnutrition due to lack of care from family members or financial constraints.

4.2 Relationship between dietary trajectory category and BMI change in older adults

The results of this study demonstrated that a "continuous reasonable diet group" and "dietary behavior improvement group" were significantly associated with the development of obesity in individuals with a normal BMI. For obese older adults, a reasonable diet has a positive effect on maintaining a normal BMI, which is consistent with the results of most studies. Acharya et al. (30) conducted a one-year dietary intervention in 80 obese middle-aged and elderly people and showed that a low-oil, low-fat, and low-calorie diet could reduce body weight by 2.9%, which was meaningful for maintaining normal body weight (OR = −2.5, 95% CI = −6.289 to 1.289). Lu and Zhang (31) conducted a 4-month nondrug nutritional intervention on 68 overweight and obese elderly people and compared body weight and other indicators before and after the intervention. After 4 months of nonpharmacological nutritional intervention, the weight of the elderly individuals decreased to varying degrees; moreover, the BMI also improved, and most of the elderly individuals changed from being obese to having a normal weight. According to the Weight Loss Action of Healthy Weight Management in China, a reasonable diet is the basis for scientific weight loss (32). The National Health Commission also proposed that the most important way to scientifically lose weight is to "keep your mouth shut," 80% of which rely on a reasonable diet; furthermore, exercise is only used as an auxiliary function. The reasonable diet mentioned in the "Dietary Guidelines for the Elderly" should include cereals and potatoes, vegetables and fruits, livestock, poultry, fish, eggs and milk and legumes as a daily diet; moreover, individuals should reduce the intake of oil, salt and sugar, as well as appropriately increase the intake of dairy products. With age, older people eat less and eat cereals and potatoes as staple foods, which reduces the intake of other high-calorie foods, such as high

TABLE 5 The relationship between the trajectory of reasonable diet behavior and changes in BMI among elderly people in the community.

Group	Model 1			Model 2			Model 3		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Continued reasonable diet									
Lean stable	Ref			Ref			Ref		
Normal stable	1.071	0.626–1.832	0.003	0.937	0.539–1.630	0.001	1.907	1.356–2.682	<0.001
Thin-normal	0.692	0.379–1.266	0.052	0.753	0.405–1.401	0.074	1.824	1.138–2.923	0.092
Thin-obese	0.535	0.230–1.240	0.145	0.487	0.202–1.175	0.220	0.509	0.209–1.240	0.137
Normal-lean	0.836	0.445–1.570	0.577	0.775	0.404–1.485	0.442	0.754	0.390–1.458	0.402
Normal-obese	0.623	0.308–1.259	0.187	0.576	0.278–1.191	0.136	0.586	0.281–1.224	0.155
Stable obese	0.879	0.435–1.776	0.719	0.768	0.368–1.603	0.482	0.736	0.349–1.554	0.421
Obesity-lean	1.415	0.352–5.684	0.055	2.216	0.503–8.976	0.092	2.614	0.605–11.295	0.150
Obesity-normal	1.029	0.437–2.426	0.041	0.877	0.360–2.133	0.049	0.859	0.350–1.458	0.039
Dietary behavior decline									
Lean stable	Ref			Ref			Ref		
Normal stable	0.801	0.466–1.376	0.422	0.763	0.438–1.328	0.339	0.567	0.431–1.324	0.328
Thin-normal	0.836	0.536–1.304	0.430	0.573	0.296–1.112	0.100	0.635	0.307–1.312	0.220
Thin-obese	0.123	0.037–0.410	0.051	0.638	0.312–1.307	0.220	0.551	0.283–1.076	0.081
Normal-lean	2.567	1.127–5.849	0.006	0.114	0.033–0.389	0.001	1.117	1.034–2.402	0.001
Normal-obese	0.595	0.311–1.138	0.067	0.489	0.258–0.925	0.028	0.464	0.244–0.885	0.120
Stable obese	0.630	0.312–1.269	0.055	0.560	0.261–1.200	0.074	0.534	0.247–1.156	0.112
Obesity-lean	0.309	0.048–1.965	0.213	0.433	0.066–2.816	0.381	0.509	0.077–3.381	0.485
Obesity-normal	1.010	0.429–2.379	0.982	0.923	0.382–2.230	0.859	0.864	0.355–2.104	0.748
Dietary behavior improve									
Lean stable	Ref			Ref			Ref		
Normal stable	0.796	0.418–1.514	0.026	0.788	0.412–1.508	0.031	0.835	0.434–1.605	0.058
Thin-normal	0.421	0.194–0.912	0.028	0.410	0.189–0.893	0.025	0.412	0.188–0.902	0.027
Thin-obese	0.486	0.169–1.400	0.181	0.472	0.161–1.385	0.172	0.485	0.164–1.430	0.189
Normal-lean	0.565	0.256–1.247	0.018	0.560	0.253–1.240	0.053	0.573	0.257–1.276	0.173
Normal-obese	0.708	0.308–1.629	0.417	0.696	0.300–1.612	0.398	0.746	0.320–1.741	0.498
Stable obese	0.521	0.209–1.301	0.162	0.515	0.203–1.308	0.163	0.567	0.221–1.452	0.237
Obesity-lean	0.347	0.034–3.574	0.374	0.334	0.032–3.478	0.359	0.386	0.037–4.072	0.429
Obesity-normal	1.136	0.422–3.063	0.001	1.180	0.430–3.234	<0.001	1.241	0.448–3.437	<0.001

Model 1, not adjusted; Model 2, adjusted for age and sex; Model 3, corrected for sex, age, place of residence, education, smoking status, alcohol consumption status, marital status, economic status, exercise status, tooth loss status, and history of comorbidities.

oil and sugar. High-protein diets such as livestock, poultry, fish, and eggs mainly use the satiety effect of protein to reduce energy intake and body fat mass and improve the metabolic status of elderly people (33). Milk and its products are the best sources of dietary calcium, thus providing a variety of essential nutrients; moreover, an appropriate daily increase in dairy products in elderly people can help to reduce weight (32). Vegetables, fruits and soy products can help to increase the satiety of elderly people, as well as reduce the intake of high-calorie, high-fat foods that are rich in dietary fiber and slow the increase in blood sugar after meals. This scenario ultimately plays an important role in weight control. This study did not demonstrate an effect of a reasonable diet on the development of a lean to normal weight, which may be due to the fact that the change in BMI trajectory in elderly individuals is not easy to considerably change in a short period of time; moreover, in elderly individuals, a thin weight at baseline, tooth loss, a decrease in chewing function and other factors lead to a decrease in food intake, insufficient nutrient intake, and difficulty in returning to normal weight in a short period of time due to physical fitness and other reasons. In the future, other studies will investigate the dietary trajectory of thin older adults and explore its relationship with BMI.

4.3 Future recommendations for older populations with different dietary trajectory categories

This study explores the trajectory of reasonable diet among the elderly in the community in China, and finds the characteristics of

different trajectory categories, which should not only be observed from the old age, but should be examined throughout the life course of the individual (34). In the context of promoting healthy ageing in the world, we must adopt active and effective personalized strategies to improve the existing problem of unreasonable diets of the elderly with different characteristics.

The basic health rights and interests of elderly people in low social classes should be protected; moreover, elderly people in rural areas who are old, have a low level of education, and have a poor economic status should be considered as the bottom group of China's basic social security system. Therefore, the health service system for elderly people should be improved, and the quality of health services for elderly people should be expanded in terms of content, region, and coverage of infrastructure. These interventions should include the prevention and treatment of overnutrition or malnutrition, as well as local medical and health service policies, the government should strengthen food security for vulnerable groups, and the "Health and Nutrition Report for the Elderly" proposes that food stamps can be used as a meal assistance program (2), which can provide more choices to recipients, increase food spending for low-income people, release part of their purchasing power, ensure their healthy diet and improve their nutritional level.

At present, most parts of the country have set up canteens for elderly people. The purpose of these canteens is not only to provide rich and healthy nutritious meals for elderly people to meet their nutritional needs but also to provide a place for them to exchange ideas and gather together (35). However, the development status of the elderly canteen is not optimistic. This may be related to food not meeting the habits or needs of different older people. Thus, government departments should actively optimize the structure of the canteen for elderly people and provide personalized meal services for elderly people of different ages according to their needs and dining tastes, especially elderly people who have lost their teeth and who should be provided with soft and fine food, nuts or fruits that can be ground into powder or juiced for consumption. Canteens for elderly people should provide preferential policies for these individuals. For elderly people who live far from the canteen, the community can provide them with free meal delivery services to avoid the intake of food and drink due to inconvenient activities. Moreover, in the case of reduced dietary intake, according to the guidance of professionals, appropriate nutrients can be selected to meet the needs of elderly people for trace elements.

The community has gradually established and standardized the health records of elderly people with chronic diseases in the community and has provided elderly people with an inclusive package of contracted family doctor services; in particular, elderly people with chronic disease or hypertension are provided with free follow-up visits four times a year, which include regular blood sugar and blood pressure measurements and disease-related health education and health literacy services (36). Due to the fact that the participation of family doctor contract services is voluntary, the participation rate of elderly people may be low for various reasons; therefore, community workers should actively publicize and popularize family doctor contract services to elderly people so that elderly people can actively participate and improve their ability to perceive the disease to better manage their diet.

The communities should actively respond to the national campaign policy, carry out community mobilization activities in the form of posters or banners, encourage the elderly in the community to actively participate in reasonable dietary health actions, make them aware of their own health responsibilities, change unhealthy health-related behaviors and lifestyles, enhance the awareness of reasonable diet among the elderly in the community, strengthen dietary and nutrition education, and provide various opportunities for them to regularly participate in health education activities, learn and master dietary health-related knowledge and skills in the participation. Choose to vigorously publicize in a form that is easily accepted by the elderly, such as television and broadcasting, to provide the elderly with more specific, practical and easy-to-operate nutritional information, as well as free and authoritative dietary guidance and consultation.

4.4 Strengths and weaknesses

This study discussed the dietary development trajectory of the elderly in the community in China, analyzed the influencing factors of different dietary trajectories of the elderly. Diet is significantly correlated with BMI, and reasonable dietary behavior is an important measure to prevent and improve overweight or obesity in the elderly. This study provides a reference for the elderly in the community to formulate scientific personalized interventions and cultivate healthy living habits. The advantages of this study are as follows. First, the participants of this study were elderly individuals in the CLHLS database, and the respondents originated from multiple regions; therefore, the study population is more representative. Second, this study explored the dietary trajectory of elderly individuals for the first time; additionally, based on the Healthy China Action (2019–2030), it was shown that a reasonable diet is the most effective way to maintain normal weight. This study verified that the correlation between different dietary trajectories and BMI of the elderly people in the community, thus providing insights for elderly individuals to formulate scientific and reasonable dietary interventions. There are also some shortcomings in this study. First, the self-reported information that was collected by using the Food Frequency Questionnaire is prone to recall bias. Second, the questionnaire only collected information about the frequency of food intake, rather than the specific amount of food intake, especially the lack of food intake such as oil, salt, and meat, which led to the failure to account for the problem of excessive or too little caloric intake in the unreasonable diet when classifying whether it is a reasonable dietary behavior, which may bias the results. Thirdly, the BMI range of the general elderly (65–79 years old) in this study is defined as 20 kg/m^2–26.9 kg/m^2, but some guidelines or studies have found that the optimal BMI range for the elderly is 22 kg/m^2–26.9 kg/m^2, and it is believed that the lower BMI range of the elderly should be increased, which may be due to the influence of geography or cultural customs, in the future, this study will continue to explore the optimal BMI range for the elderly. At present, there are very few studies on sex or age differences in the dietary nutrition trajectories of elderly people in the community; moreover, due to differences in physical constitution or body structure, the manner of how men and women differ in dietary nutrition trajectories should be the focus of our future research. Past studies have typically explored the effects of dietary management on obese older adults. Currently, the incidence of malnutrition in elderly individuals is gradually increasing, and malnutrition can also cause a variety of chronic diseases and even increase the risk of death;

therefore, malnourished elderly individuals are still the key group to which we need to pay attention, and the trajectory of weight change in malnourished elderly individuals needs to be further explored.

5 Conclusion

Based on the framework of the Healthy China Action (2019–2030), this study discussed the development trajectory of four community diets for the elderly population, indicating the heterogeneity of the elderly population's dietary behavior, thus suggesting that we should formulate or adopt different intervention strategies according to different categories of elderly populations. Regularly carry out nutritional screening and assessment, according to the nutritional status of elderly people, combined with their daily diet and living habits, to provide appropriate and targeted nutritional knowledge and daily dietary advice. This study also explored the relationship between different trajectories and changes in BMI in elderly people, and the results confirmed that the correlation between different dietary trajectories and BMI of the elderly people in the community, which will help to provide an appropriate entry point for the formulation of public health policies. However, this study has not yet investigated the effect of a reasonable diet on low-BMI elderly individuals, and we will further explore the effect of a reasonable diet on the weight change trajectory of malnourished older adults in the future.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The data used in this study was obtained from the CLHLS, which was managed by the Peking University Center for Healthy Aging and Development Studies. All procedures were carried out in accordance with relevant guidelines and regulations (Declaration of Helsinki). All individuals provided written informed consent before participating in the study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

ML: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. YC: Data curation, Writing – review & editing. WG: Formal analysis, Writing – review & editing. SZ: Data curation, Writing – review & editing. MZ: Methodology, Writing – review & editing. XM: Software, Writing – review & editing. XJ: Supervision, Writing – review & editing. YL: Data curation, Writing – review & editing. LZ: Formal analysis, Funding acquisition, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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EDITED BY
Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Jordan Maximillian Wilkins,
Mayo Clinic, United States
Marcelo Muniz,
Federal University of Espirito Santo, Brazil

*CORRESPONDENCE
Zhen Wang
✉ wang798110510@163.com
Ajay Kumar
✉ ajaykumar_bhu@yahoo.com

†These authors have contributed equally to this work

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Precision nutrition-based strategy for management of human diseases and healthy aging: current progress and challenges forward

Vipin Kumar Singh[1†], Xiao-Hu Hu[2†], Amit Kishore Singh[3], Manoj Kumar Solanki[4], Pooja Vijayaraghavan[5], Rajpal Srivastav[5], Naveen Kumar Joshi[6], Madhuree Kumari[7], Sandeep Kumar Singh[8], Zhen Wang[2]* and Ajay Kumar[5]*

[1]Department of Botany, K.S. Saket P.G. College, Ayodhya, India, [2]Guangxi Key Laboratory of Agricultural Resources Chemistry and Biotechnology, Agricultural College, Yulin Normal University, Yulin, China, [3]Botany Department, B.N. College, T.M. Bhagalpur University, Bhagalpur, India, [4]Department of Life Sciences and Biological Sciences, IES University, Bhopal, Madhya Pradesh, India, [5]Amity Institute of Biotechnology, Amity University, Noida, India, [6]Amity Institute of Microbial Biotechnology, Amity University, Noida, India, [7]Department of Biochemistry, Indian Institute of Science, Bengaluru, India, [8]Department of Microbiology, Indian Agriculture Research Institute, New Delhi, India

Currently, the treatment of various human ailments is based on different therapeutic approaches including traditional and modern medicine systems. Precision nutrition has come into existence as an emerging approach considering the diverse aspects such as age, sex, genetic and epigenetic makeup, apart from the pathophysiological conditions. The continuously and gradually evolving disciplines of genomics about nutrition have elucidated the importance of genetic variations, epigenetic information, and expression of myriads of genes in disease progression apart from the involvement in modulating therapeutic responses. Further, the investigations have presented the considerable role of gut microbiota comprising of commensal and symbionts performing innumerable activities such as release of bioactive molecules, defense against pathogenic microbes, and regulation of immunity. Noteworthy, the characteristics of the microbiome change depending on host attributes, environmental factors, and habitat, in addition to diet, and therefore can be employed as a biomarker to unravel the response to given food. The specific diet and the components thereof can be suggested for supporting the enrichment of the desired microbial community to some extent as an important part of precision nutrition to achieve not only the goal of human health but also of healthy aging.

KEYWORDS

biomarker, microbiota, bioactive constituents, machine learning, algorithm, immunity

1 Introduction

The rising pressure of different disorders including chronic diseases ensuing from ever changing complex epidemiological events has long been highlighted (1) to pose risks to health and life span (2) in addition to those resulting from mineral imbalances. Surprisingly, the mortality and disabilities caused by chronic diseases are comparatively higher than infectious

diseases and injuries (3). The risk factors for such diseases are identified as lifestyle modification at the individual level, variation in diet at global scale, declining physical activities, lack of preventive measures, and nutrient deficient foods. Noteworthy, sufficient intake of nutrients promotes good health, whereas, the deficiency of essential nutrients has tens diverse diseases (4). Therefore, several developed countries like United States, European Union, across the globe have made the implementation of essential minerals and vitamins mandatory. Apart from the suggestion of recommended diets comprising of plant and animal based products such as vegetables and meat, providing essential minerals, amino acids, vitamins, and fatty acids known to be required for sustaining the health of a given populace. Moreover, the continued qualitative and quantitative modifications in human diet owing to technological advances meant for food generation as well as processing have resulted in substantial perturbations of metabolic activities leading to varied human health disorders (5–7) including cancer, allergies, and cardiovascular diseases. Such perturbations resulting from modulations in dietary contents are much pronounced in developed countries.

The alleviation and treatment of human diseases can be divided broadly into traditional (Ayurveda, Unani, Siddha, etc.) and modern medicine systems (Allopathic). Traditional medicine relying to a greater extent on natural products of plant origin has long been recognized for treating different human disorders (8, 9). The development of strategies for prevention of innumerable diseases through improvement of immunity as well as offering the ways for produce valuable drugs (10, 11) is important approach of disease management. Traditional medicine has also been differently referred to as complementary and alternative medicine (12). The modern medicine is characteristically marked by the continued advances in technology aimed toward refining diagnostic methodologies and treatment of disorders started from 1946 to the current period (13). Modern medicine employing a single or mixture of a few purified bioactive compounds could have profound undesirable effects in comparison to traditional medicine generally prescribing crude mixtures of plants causing minimum side effects rendered by modulatory action of other components. Further, the isolated bioactive used in modern medicine systems to treat human health disorders should rather be used for deciphering the mechanism of action (14).

Precision nutrition is an emerging research frontier for managing health and treating human diseases through extensive investigations on bodily metabolic responses so as to suggest optimum dietary plans (15). The science of precision nutrition involves major factors such as environmental exposures, lifestyle, plausible interaction between gene and nutritional components (nutrigenomics), gut microbial communities, and processes influencing gene expression not only at the intra-individual level, but also at the inter-individual level (16, 17). The implementation of precision nutrition can be successful through analysis of individual features, continuous nutrient availability, and control as well as site-specific delivery (16), in addition to the introduction of different omics technologies.

Recently, the contribution of metabolomics in achieving the targets of precision nutrition has been reviewed by Brennan and de Roos (17). In this context, the strategy of metabolomics may comprise analyzing metabolic constituents (18) to reveal the knowledge concerning the effect of nutrients on metabolic activities, and available bioactive molecules. The variations in metabolic profiles, therefore, can be used for identifying metabotypes to advise diet plan. Furthermore, the data available on metabolite patterns can be combined with additional factors to gain insight into an individual's response to dietary intake. The precise identification and analysis of metabolites using mass spectrometry (MS), infra-red (IR), and Raman spectroscopy, as well as nuclear magnetic resonance (NMR) in combination with modern computational approaches, can further advance the progress in the discipline of metabolomics (19, 20). Additionally, different approaches including nutrigenetics, epigenetics, and nutriepigenetics (21, 22), proteomics (23), gut microbiota (24), dietary interventions (25), nutraceuticals (26), lifestyle (27), and machine learning tools (28) have shown promise in the field of precision nutrition focused toward better human health (Figure 1).

Most of the previous articles have included only a few aspects of precision nutrition. The holistic information to our knowledge is still lacking. Therefore, the present review has attempted to provide updated information about different strategies adopted for precision nutrition. The limitations and future opportunities in the discipline of precision nutrition given good human health are finally discussed.

2 Different omics technology and precision nutrition

2.1 Nutrigenomics and management of human health in the era of the 21st century

The successful launch of human genomics in the 2000s led to the emergence of novel research frontier including nutrigenomics which deals with the study of interaction between dietary components and the genome, proteome, and metabolome. However, the continuous development of several omics like metabolomics, proteomics genomics, etc. has provided ample information not only for nutrigenomics but also mainstream to the nutritional values at individual level recognized as precision nutrition.

Nutrients are environmental factors having (i) the potential to alter gene expression, and (ii) increase the risk of diseases through impairing the epigenome of the developing organisms. Exceedingly increasing interest in such interactions led to the emergence of nutrition genetics or nutrigenetics, which allow us to understand the relation between diet and gene expression although they follow different approaches. Nutrigenomics deals with the study of the effect of nutrients on gene expression, while nutrigenetics describes the cellular response to the nutritional components apart from other external factors by observing metabolism and the site of action (29).

2.2 Metabolomic profiles (metabolizing)

Different metabolic constituents can be regarded as biomarkers to provide real-time information about the dietary food intake and quality of the food consumed by the individual (17). Clark et al. (30) in a review reported the potential biomarkers for whole grains, soy, and sugar that have been validated primarily based on several criteria such as biological plausibility, time and dose–response, robustness, reliability, stability, and performance of the method which have used to explore the biomarker potential.

Recently, some of the studies have indicated the use of biomarkers as a tool for establishing dietary patterns. For example, multiple plasma metabolites have been used as a signature biomarker in the Mediterranean diet and further assessed for their association with

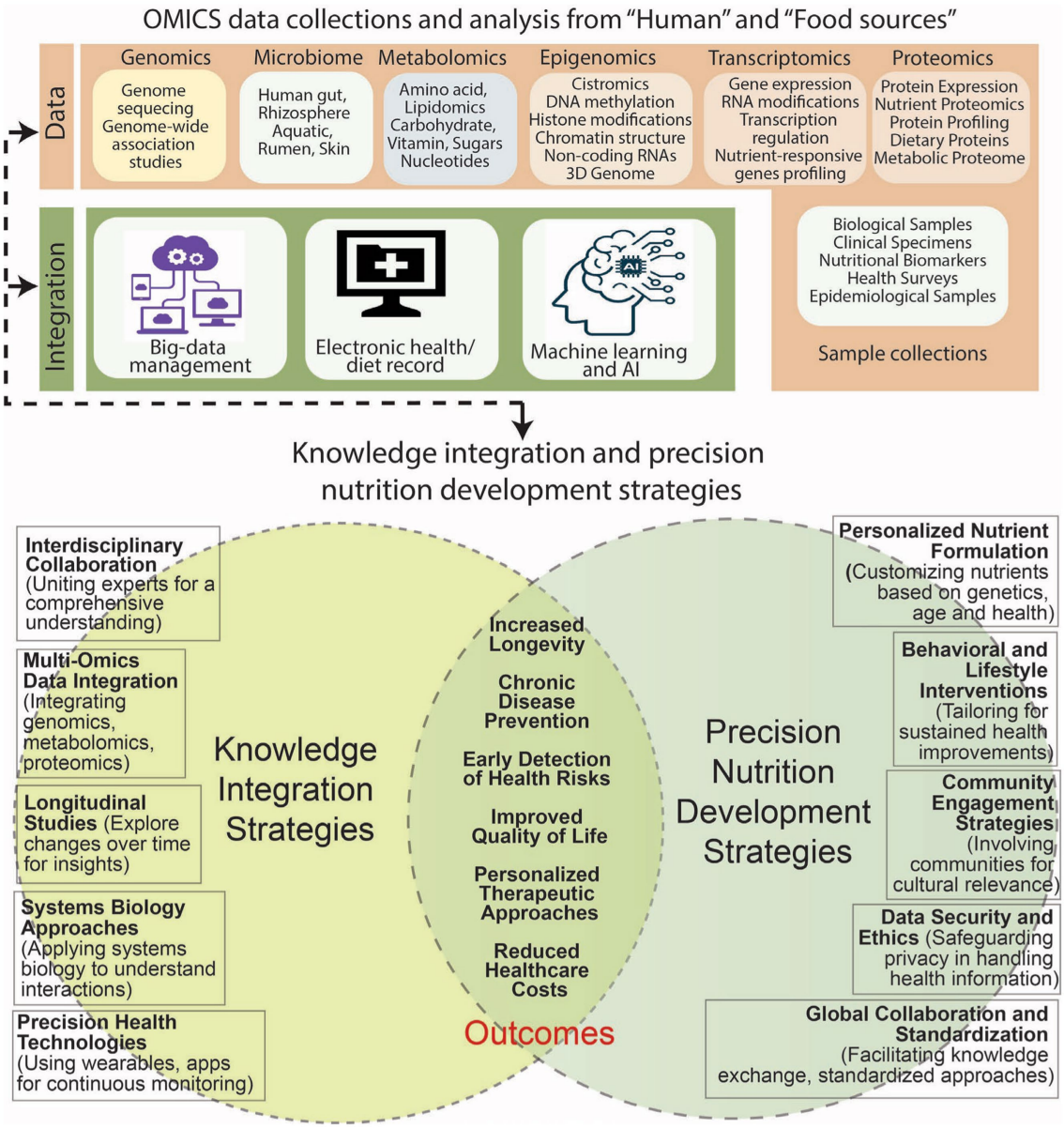

FIGURE 1
Strategies in knowledge integration and precision nutrition against aging and diseases involve interdisciplinary collaboration, multi-omics data integration, longitudinal studies, systems biology, and precision health technologies. The development includes personalized nutrient formulation, behavioral interventions, community engagement, data security, and global collaboration. Major outcomes: increased longevity, disease prevention, improved quality of life, reduced healthcare costs, and personalized therapeutic approaches.

cardiovascular disease (CVD) risk (31). Furthermore, several studies also indicated the influence of metabolic profile-based biomarkers in the assessment of disease risk (32). However, it has been concluded that factors such as age, body mass index (BMI), etc., play a significant role in influencing the potential of the biomarker of the individual.

The metabolomics approach is further applied to classify the individuals based on their metabolic profiles. This approach allows for the comprehensive analysis of metabolites, thereby providing a detailed understanding of the metabolic processes and pathways active in different. In precision nutrition, metabotyping plays a vital role in the development of tailored precision nutrition via categorizing individuals based on their unique metabolic profiles (33). Generally, the metabolizing approach is based on several biomarkers (triacylglycerol, cholesterol, HDL-cholesterol, and glucose) to classify the population of definite size into metabotypes that are further subjected to delivering tailored advice (34). However, the concept of metabotypes further needs to be redefined considering the dietary requirements and the economic status of the population because these factors significantly influence metabolic profiles and health outcomes.

2.3 Metagenomic profiles

Development of cutting-edge sequencing tools like next-generation sequencing (NGS)which explore the hidden information concerning spatial and temporal variation of microbiota present in

any biological samples. Metagenomic profiling of the gut microbiome of an individual's mid gut play a vital role in nutrigenomics. Furthermore, studies indicated that gut microbiota changes from birth to successive stages (35). Besides this, microbiome profiling also helps to decipher the type of food preferred by certain age groups. The presence of Firmicutes- and Bacteroides-dominant patterns in adult age groups indicated the long-term ingestion of carbohydrate and animal fat and/or protein-rich diet, respectively (35, 36). These findings revealed how factors like age, and food habits affect the structure and functions of gut microbiome dynamics and therefore should be considered while handling metagenomic data. However, integration of other "omics" such as genomics, transcriptomics and metabolomics will provide more comprehensive overview of an individual variability in response to diet and enables the development of personalized nutritional strategies that are more effective in promoting health and preventing disease.

2.4 Nutrigenetics

The interaction of personalized diet or nutrition and genes with the objective of achieving sound health is the ultimate goal of nutrigenetics. Nutrients that we intake are one of the environmental factors that interact with the genes and affect the DNA metabolism, repair mechanism, and gene expression of individuals. Recent published reports further confirmed that single nucleotide polymorphisms (SNPs) can be used as molecular tools to gain the information on the interaction between human diseases and the nutrition diet (37). For example, phenylketonuria (PKU) disorder is the result of altered gene expression by SNPs, interaction with metabolite leads to the deficiency of the phenylalanine hydroxylase gene (38). Other examples of polymorphism include Lactase-phlorizin hydrolase gene (LPH) polymorphism, glutathione peroxide gene polymorphism, Manganese superoxide dismutase (MnSOD) in which substitution or deletion of the specific genes resulted in an increased risk of liver and breast cancer, respectively (39). There is growing evidence that multiple pathways may be involved in the cause of multiple diseases where transcription factors alter gene expression patterns via interaction with bioactive food components (40). The influence of transcriptomic on gene expression is not only dose-dependent but also time-dependent. Future aspects of nutrigenetics can be helpful in knowing which genetic factors should be given to particular genetic subgroups that may reduce the risk of emergence of chronic diseases.

2.5 Nutriepigenetics

Epigenetics involves the switch on or switch off the gene expression without affecting the DNA sequences. In general, epigenetics involves DNA methylation, histone modifications, and non-codingRNA regulation to influence cellular metabolism. Bioactive food components such as micronutrients and chemicals are known to be involved in DNA methylation (41). Several studies indicated the role of dietary factors in the provision of methyl for the formation of S-adenosylmethionine that may alter the DNA methyltransferase activity and impair folate metabolism. Disruption in foliate metabolism eventually causes risk of cardiovascular diseases, neurological disorders, and other developmental anomalies (41, 42). In addition to DNA methylation, the role of non-coding RNAs [microRNAs (miRNAs)] and long noncoding RNAs (lncRNAs), has also been reported in the epigenetic process. Recently, miRNAs and lncRNAs, are known to have links with chronic disorders like cardiovascular diseases and obesity (43). In nutshell, DNA methylation and miRNAs can be treated as target markers for future precision dietary interventions.

3 The role of microorganisms (gut microbiome)

3.1 Human microbiome and role in human health management

The human microbiome influences human physiology through different mechanisms. The gut microbiome regulates digestion, metabolism, colonization resistance, immune modulation, and cellular functions in various ways (44). The dysregulation of microbial community functions may induce inflammations and disease development. The pathogenesis of opportunistic microbes may occur in these conditions of gut dysbiosis. However, imbalance in the composition of normal gut microbiota represents dysfunction or disorders (45). The association of gut microbiota with human health and diseases is now evident by various investigations (46). The existence of gut-brain and gut-lung axis is now correlated with illnesses, and associated with brain and respiratory tracts respectively, suggesting the importance of gut microbes in human health. However, there are still many aspects to explore and to better understand the association between gut microbiome and human health in complex disorders including cancers and other serious illnesses like respiratory illness, i.e., COVID-19 infections.

Current disease-specific therapeutic approaches may miss the large portion of the microbial populations, whose impact may be significant on human health. Thus, personalized medicine has been focused on therapeutics now (45). The personalized medicine is a future path of diagnostics and therapeutics as it takes care of individuals' physiological and genetic factors (45, 47). Further, each patient has different biological habits, lifestyle, metabolic profile, food environments, and gut microbiome. So, precision nutrition could help design comprehensive diets plans based on individual variables. It also takes care of socioeconomic parameters during recommendations of diet plans (48). Further, the modern lifestyle has influenced our dietary patterns and food habits adversely leading to obesity and other related health problems (49). Therefore, the dietary recommendations can play an important role in disease management. The role of personalized nutrition is to manage diseases by diet monitoring and recommendations (50). There are many layers of the dietary recommendations. The genetic and biological characteristics of the individual are taken care of while determining the dietary recommendations in personalized nutrition (45). The fat content of the diet, and other modifications in obese or diabetic individuals is one of the such interventions while fixing for the course of personalized medicine. The same type of the diet may have different metabolic responses in different patients. The difference in glycemic responses in different patients

has also been observed (51). The gut microbiome affects human metabolism in different ways and thus influences the manifestation of the diseases.

The chronic disease of arteries identified as atherosclerosis is responsible for significant mortality worldwide. The use of hypoglycemic, antiplatelet, and lipid lowering drugs are the current therapies for the treatment of atherosclerosis (52). The role of trimethylamine-N-oxide (TMAO) is associated with gut microbiota and can provide strategies for management of the atherosclerosis (53, 54). The consumption of red meat leads to the formation of TMAO by gut microbial activities. Thus, avoiding red meat is suggested for managing atherosclerosis (55, 56). In the case of chronic kidney disease (CKD), the prevalence of atherosclerotic events is higher. Higher TMAO levels are positively correlated with serum creatine and urea in CKD patients (57). Further, it is found that glucose intolerance susceptibility has an association with gut microbiota and non-caloric artificial sweeteners (NAS) can increase glucose intolerance (58). These artificial sweeteners are not absorbed by the gut and are thus speculated to interact directly with the gut microbiota and may affect physiological functions (59, 60). Thus, avoiding artificial sweeteners is considered a subset of personalized nutrition in such patients.

The gut microbes help in the catabolism of food, appetite alteration, and harvesting of nutrients. The live microbes in the form of "probiotics" when administered are useful in providing health benefits to the host. The microbes like *Bifidobacterium*, *E.coli*, and *Lactobacillus* are being used for disease management including gut dysbiosis, diarrhea, inflammatory bowel disease, Crohn's disease, and recurrent *Clostridium difficile* infection (61, 62). The advancements in technology helped to develop strategies for microbiota transplantation, which has been proven to be useful in treating the illness associated with gut dysbiosis. Here, gut microbiota can be altered by a novel approach called fecal microbiota transplantation (FMT), a promising approach to alter gut microbiomes.

4 Precision nutrition and their characteristics

Each individual requires some specific amount of nutrients depending on genetic makeup, metabolisms, and microbiomes (63). Therefore, precision nutrition can be recommended for the individuals irrespective of the population level. Precision nutrition provides a detailed overview of the genetics, metagenome, microbiome, metabolome, and epigenetics of the individuals through latest next-generation analytical techniques. The generation of the analytical data and their assessment via computational-aided methods help in sharing the connection between the diet, lifestyle of the person, and health of the individuals (64).

Different populations of the world have some specific characteristics depending on cultivated crops, climate, and geographical location. These differences also lead to variations in the genetic makeup of the population. Although various governmental institutions have proposed different types of nutritional guidelines for the population, these guidelines give a brief overview of nutrient composition, nutrients needed, and a particular guideline for the population (65). Moreover, the differences in the population, regional diversity, and the genetic makeup of the person allow variation in the guidelines among different regions (66).

Recognizing the needs of individuals in view of precision nutrition is much challenging. The identification and development of nutritional advice for individuals require a broad analytical instrumentation, a computer-generated database, and extensive research analysis. Noteworthy, the differences in developmental stages, physiology, and health conditions contribute to the varied nutritional and caloric requirements of individuals. During the critical growth phase, adolescents require higher levels of proteins, and carbohydrates in comparison to adults (67). Similarly, pregnant women require some unique diet plan to nourish the growing infant. However, the elderly person facing challenges related to bone and muscle aging is advised to consume foods abundant in bioavailable calcium and proteins to address these age-related issues (68). Additionally, with the passage of age, physical activity often decreases, making it necessary to opt the foods having lower calorie density to prevent weight gain and obesity. On the contrary, individuals in demanding professions like army men, fire fighters, and athletes require calorie-dense, nutrient-rich foods (69). Variations in the gastrointestinal physiological patterns of the individual persons may also necessitate different nutrient profiles and levels of digestibility in their food (70).

The symbiotic relationship between the human body and the intestinal flora is crucial for the maintenance of normal physiology and metabolic function. The variations in normal microflora including intestinal flora of the individuals can led to genetic differences (71). However, the some of the studies have revealed that the composition and diversity of the intestinal microflora is influenced by the diets standing out as one of the most easily modifiable external factors (72).

The variations in dietary patterns significantly influence the microflora composition of population (73). For example, Japanese individuals harbor a distinct microbial strain in their intestinal tracts capable of secreting metabolic enzymes capable to digest algal constituents, a trait attributed to regular consumption of seaweed (74). This study underscores the direct impact of dietary interventions on the intestinal microflora and their functional aspect required for the normal functioning of human health.

5 Nutritional omics and systems biology

In the early stages of food nutrition, nutrigenomics research primarily focused on the exploration of new mechanisms related to nutrition and diet through the application of transcriptomics. The oxidative stress and inflammation can lead to changes in the transcriptomeas compared to the normal. So, the investigation of the proteome and the transcriptome will help in understanding the food patterns of a healthy person (75). Similarly, the advanced metabolomic approaches are gaining prominence in nutrition research because metabolites directly reflect the products of dietary intake and metabolism, which further help in the assessment of the relation and molecular pathways between diet metabolisms and the diseases (17).

The metabolism of the food in the human body is a complex phenomenon. Different metabolomic approaches may lead to identification of the new metabolites in the body that have prominent role in the functioning of colonic microflora and therefore impact on normal functioning of the human health (76). For example, in his study Rådjursöga et al. (77) reported that intake of breakfast cereals leads to enhancement of some specific amino acids like proline,

tyrosine, N-acetylaminoacids in serum of the adults human body. However, the ingestion of ham and eggs leads to the enhancement of creatine, methanol, and isoleucine in the serum. Similarly, the lipid peroxidation metabolites considered as the markers to differentiate stable angina pectoris and myocardial infarction (78).

The metabolomics study has also provided an insight into individual's biological age (79). Under the conditions of chronic diseases, the biological age becomes older than the actual age. The dietary intervention indicated that the ingested food and metabolites thereof affect the metagenome, metabolome, and transcriptome. Thus, the detection of changes in the metabolome, transcriptome or the metagenome at the early stages of the disease development can be helpful in developing the formulation of the new dietary patterns as a part of precision nutrition to achieve the goals of human health. Nutriomics involves the investigation of interactions between the human diet and genes, and their influence on the human health at the both molecular and population levels. This knowledge serves as a basis for creating personalized dietary interventions and healthcare strategies by analyzing individual's genome structures. In the early stages, nutriomics research primarily focused on exploration of new mechanisms concerned with the nutrition through the application of transcriptomics and proteomics (17).

Modern food industry is facing a significant challenge in terms of food safety and waste, given the global production and transportation of ingredients and food items (80). It is imperative for the nutraceutical and food industries as well as government to adopt a plan (i) to prevent the food contamination, (ii) control minimize postharvest storage loss from the pathogenic microbes, and (iii) minimize the application of hazardous chemicals. In addition, authorities should introduce plans to enhance the nutrients composition of the food in order to maintain health and improve immunity.

Nowadays, the food industries and the academia are searching for alternative of various food ingredients from the proteins rich animal products like red meat, fish, eggs to plant based products, fermentation products, and cell cultures (65). Such kind of shift in food pattern may help in reducing biodiversity loss, greenhouse gas emission, and the maintenance of natural resources (81). However, it is crucial that foods derived from alternative protein sources are not only environmentally friendly but also nutritionally sound. While the macronutrient composition of many alternative protein sources resembles that of animal-derived foods, considerations, along with digestibility, are important. Additionally, the affordability, convenience, and taste of the food products constituted of alternative protein source are crucial factors of consumer acceptance (65).

6 The latest strategy to reduce the diet burden

The quality of the diet has major influence on the health of human beings. The population served with improved diet quality showed better resistance against the diseases and infections with improved health outcomes (82, 83). However, the healthy and the beneficial pattern of diets are the results of the presence of nutritional factors in the food. For instance, nowadays the healthy nutrient foods consisting of fresh fruits, vegetables, and fish are considered as the rich source of vitamins, minerals, antioxidants, etc. (83). However, the processed meat, refined grains, and sugar rich drinks have been considered as an unhygienic or unhealthy dietary pattern (84). The nutrients rich foods are considered to support the growth of gut microbiome and directly or indirectly affect the microbiome functioning with the resultant prevention of chronic diseases (85, 86).

Although the impact of nutritional content on health may be observed at any stage of disease, diet quality has been considered as one of the prime factors during diseases developments and the chances of infection can be reduced by modifying the diet pattern (87, 88). Further, the nutrient composition of the diet also impacts the recovery after the surgery (89). In addition, the diet quality also play pivotal role in aging (90). The evidence underscores the crucial role of diet quality, encompassing the composition of macro and micronutrients, in maintaining overall health. Diet influences disease occurrence, complication development, disease management, recovery, and the quality of life across a spectrum of health conditions (91–95). Dietary intervention trials frequently demonstrate that improving diet quality leads to enhanced health outcomes, independent of changes in weight (96). For instance, the plant based and low protein diet help control the chronic kidney diseases (97). The diet devoid of gluten and dairy products may have beneficial effects on children suffering from specific kidney disorders, and glomerulosclerosis (98). Similarly, the consumption of fish based diet enriched in omega-3 fatty acids could have positive effects on the management of IgA nephropathy (99). Thus, the inclusion of specific diets and components thereof as the part of precision nutrition may not only improve the human health, but also help reduce the globally rising risks of fatal diseases. The future of precision nutrition in the management of human diseases is presented in Table 1.

In the last few years, various international organization like Food and Drug Administration (FDA), started to issue a national guidelines to obtain the healthier food and nutrition information for their population. The enhanced information concerned with the healthier foods and nutrition profile will help in improving the health and wellness.[1]

Recently USA government released a national strategy to identify the nutrient profile of the food and improve the health hygiene so as to improve everyone's health and wellness up to 2030 and control the diet related diseases, especially the obesity, diabetes, and hypertension.[2] In light of the meetings held, the government encouraged the population to reduce the intake of sodium and sugar in the food, because the level of salt and sugar play a prominent role in diseases development. it has been observed that most of the population of U.S do not use enough amounts of healthy foods like fruits, dairy products, whole grains and also consume higher amount of sodium and sugar in the food. In the last few years, the world has faced the challenges of pandemic and huge number of global population. The developed countries were also hot spot of that pandemic. The poor nutrition and weak immune system are one of the major causes of such infections. Beside these, other diet specific epidemic like obesity, diabetes, and other cardiovascular diseases are also recognized to affect the U.S. population.

1 https://www.fda.gov/food/food-labeling-nutrition/fdas-nutrition-initiatives

2 https://health.gov/our-work/nutrition-physical-activity/white-house-conference-hunger-nutrition-and-health

TABLE 1 Role of precision nutrition (PN) in the management of human disease.

Approaches of nutrition method	Omics and other technologies described	Disease managed	References
Precision nutrition	Nutrigenetics, metabolomics, metagenomics, behavioral aspects	Obesity and type 2 diabetes	Antwi (100)
Precision nutrition	Epigenetics, metabolomics, phenotypic anthropometrics	Aging and brain health	Chen and Small (101)
Precision nutrition	Environment, gut microflora, epigenetics	Female reproductive health	Dumesic et al. (102)
Precision nutrition	Lipoprotein analysis	Cardiovascular diseases	Hong et al. (103)
Precision nutrition	Genomics, proteomics	SARS-CoV-2	Naidu et al. (104)
Precision nutrition	The Genome, epigenome, and microbiome	Treatment of cardiovascular diseases	Ordovás (105)
Precision nutrition and omics tools approach	Genomics, epigenomics and metabolomics	Lactose intolerance management	Pratelli et al. (106)
Precision nutrition	Nutrigenomic, and Nutriepigenetic	Chronic diseases linked to obesity	Ramos-Lopez et al. (107)
Precision nutrition and dietary intervention	Metabolic phenotyping	Cardio-metabolic health management	Trouwborst et al. (108)
Precision nutrition	Biomarkers of food consumed, microbiome, lipidomics, genomics, transcriptomics	Obesity	Ulusoy-Gezer and Rakıcıoğlu (109)
Precision nutrition	Genomics, metabolomics, and gut microbiome technologies	Type 2 diabetes	Wang and Hu (110)
Precision nutrition	Target delivery of food functional factors	Chronic diseases like cancer, obesity, atherosclerosis	Yu et al. (16)

7 Machine learning and other digital technologies based approaches

Recent advances in digital technologies like machine learning (ML), deep learning, big data and artificial intelligence (AI) play a pivotal role in progression and usage of precision nutrition. Machine learning (ML) with the help of current digital technologies can venture into the unknown of nutraceuticals, identify valuable nutrients within our food and personalize the nutritional requirements. Machine learning can be quite useful in gathering dietary data inputs such as metabolomics, meal timing, meal uptake, physical activities, nutrigenomics, health conditions, genetics and personal health data. Further integrating the dietary data inputs, it can make a maximum likelihood prediction about the outcome using ML algorithms. The four types of ML considered in precision nutrition are supervised learning, unsupervised learning, semi-supervised learning and reinforcement learning (111). ML applies multiple algorithms, linear and logistic regression, data clustering analysis, artificial neural networks, deep learning, principal component analysis and data assessment to build a computational model for maximum output in understanding, characterization and precision nutrition in chronic dietary diseases (27, 112). Indeed, it has emerged as a quick solution to gather useful information from omics data, interpret it and predict the personalized dietary requirement and management. Moreover, it can also act as a biomarker monitoring tool assessing dietary intake, correlating with current health conditions and recommending precise nutraceutical for each individuals (27).

One of the recent example of application of ML in precision nutrition is the PREDICT 1 clinical trial (PersonalisedREsponses to Dietary Composition Trial; NCT03479866), where an ML model "robust to overfitting" was developed that predicted both triglyceride and glycemic responses to food intake. The predictions can further be used for precision nutrition and preparing dietary plans (113). Similarly, in a personalized diet study, hypocaloric diet was provided to overweight patients with pre-diabetic and moderately controlled diabetes type-2 using an ML based algorithm (114). In a comparison between statistical and machine-learning techniques used to evaluate the cardio-metabolic risks observed with dietary intake for 10 years (ATTICA study), ML techniques (k-nearest-neighbor's algorithm and random-forests decision tree) were found to be superior than traditional linear regression model (115). ML algorithms have also been found useful in predicting the hereditary and environmental risks of lifestyle diseases, gene–gene, gene-nutrition interactions, change in microbiota and factors affecting the nutraceuticals (27, 116).

Artificial intelligence has unleashed a new arena in every possible field, including precision nutrition. AI-driven food interventions can diagnose the disease, assess the morbidity and mortality risk of a patient, discuss disease outbreak and surveillance and help in policy and planning using precision nutrition (117). AI, along with ML, can revolutionize the field of nutritional epidemiology in terms of precise nutrition measurement and addition of complex tools to model complexity of diet (118). Recently, Lee et al. (116) reported about two AI models (semantic and nutritional analysis models) which were developed and integrated into precision nutrition analysis using five different algorithms. The results showed that AI models could be used for nutritional survey and precision nutrition with high accuracy and reliability (116). Apart from working efficiently for large datasets, AI combined with big data and ML can generate nutrition-driven hypothesis and test them accurately, accounting for multiple factors at the same time (119).

Advancement in analytical and digital techniques have also helped to monitor and interpret nutraceutical data simultaneously. A number of smart phone- based apps have been developed which are replacing the traditional pen and paper-based databases for precision nutrition

(120). Non-invasive wearable chemical and physical sensors and mobile and app-based electrochemical sensors can provide accurate real-time monitoring of dietary behavior changes toward a managed nutritional balance (121). Similarly, analytical techniques such as sensor-based vibrational spectroscopy, Raman, and terahertz spectroscopy, as well as hyperspectral imaging coupled with data analysis (ML, AI, and big data), can not only generate huge set of nutritional data on fluid-based biomarkers but also cut down the incurred cost substantially (19). Indeed, the dual use of continuous health monitoring and evaluation of continuously generated dynamic data can identify and provide recommendations on dietary requirements, which set a bright future for precision nutrition.

Despite being able to bring about revolutionary changes in precision nutrition by MI, AI and digital technologies, they still need certain hurdles huddles to overcome. Guidelines, and recommendations on the uses of AI are not very specific yet, and it can be misused easily. The generation of large set of data will further require protection of intellectual property and personal information. Further, ethical issue related to the use of AI also needs to be addressed. Collaboration between academics, industry and government and continuous upgrading of guidelines will further be required to AI-assisted precision nutrition.

8 Conclusion

Precision nutrition has been considered as one of the emerging approach in the field of human health management. The goal of precision nutrition research is to provide nutritional advice to individuals or populations. Although the nutritional profile that needs to be explored varies and depends upon genetics, sex, age, and geographical locations, it is now considered superior to generic advice. Currently, treatment of various human ailments is based on different therapeutic approaches, including traditional and modern medicine system. The continuously and gradually evolving disciplines of genomics in relation to nutrition have elucidated the importance of genetic variations, epigenetic information, and expression of myriads of genes in disease progression, apart from their involvement in modulating therapeutic responses. Although precision nutrition now includes the integrative study of latest omics of Nutrigenomics *like* metagenomics, metabolomics, and next-generation sequencing to understand the relationship between nutrition profile and human health management. However, the management of huge amounts of data generated by omics approaches is still a challenging task and warrants the application of latest artificial intelligence and machine learning tools for in depth understanding.

Author contributions

VS: Conceptualization, Methodology, Writing – original draft. X-HH: Funding acquisition, Writing – review & editing. AS: Data curation, Writing – review & editing. MS: Data curation, Formal analysis, Visualization, Writing – review & editing. PV: Writing – review & editing. RS: Data curation, Writing – review & editing. NJ: Writing – review & editing. MK: Writing – review & editing. SS: Writing – review & editing. ZW: Funding acquisition, Writing – review & editing. AK: Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

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Conflict of interest

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EDITED BY
Luciane Bresciani Salaroli,
Federal University of Espirito Santo, Brazil

REVIEWED BY
Virginia Maria Muniz,
Secretaria de Estado da Saúde do Espírito Santo, Brazil
Marcelo Muniz,
Federal University of Espirito Santo, Brazil

*CORRESPONDENCE
Ning Yan
✉ 800033@hospital.cqmu.edu.cn

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Association between the geriatric nutritional risk index and cognitive functions in older adults: a cross-sectional study from National Health and Nutrition Examination Survey

Zhichun Tan, Yaxin Nie and Ning Yan*

Neurology Department, The Affiliate University-Town Hospital, Chongqing Medical University, Chongqing, China

Objective: To investigate the associations between the geriatric nutritional risk index (GNRI) with cognitive functions among U.S. older adults. (Patients were classified into two nutrition risk groups based on the GNRI).

Methods: Our analysis utilized data from the cross-sectional National Health and Nutrition Examination Survey (NHANES) conducted between 2011 and 2014. Cognitive function was measured using CERAD test, AFT and DSST. Composite *z*-scores were obtained by summing test-specific *z*-scores of the above three cognitive tests and were used to assess the global cognitive function. We employed weighted logistic regression models to evaluate the associations between GNRI and nutritional status (low and high GNRI) with cognitive function among older participants. The non-linear relationship was described using fitted smoothed curves and threshold effect analyses. Subgroup analysis and interaction tests were also conducted.

Results: This study included 2,592 older participants aged 60 years and older. After adjusting for confounding variables, the GNRI was positively associated with AFT (β = 0.05, 95% CI 0.005–0.096, *p*-value = 0.0285), DSST (β = 0.192, 95% CI 0.078–0.305, *p*-value = 0.0010) and the composite *z*-scores (β = 0.027, 95% CI 0.010–0.044, *p*-value = 0.0024). The results also showed that the high-GNRI group was significantly associated with AFT (β = 0.922, 95% CI 0.166–1.677, *p*-value = 0.0169), DSST (β = 2.791, 95% CI 0.884–4.698, *p*-value = 0.0042) and composite *z*-scores (β = 0.405, 95% CI 0.115–0.695, *p*-value = 0.0062) likewise had significant positive correlations, using the low-GNRI group as a reference. In addition, inflection points with CERAD and composite *z*-scores were found at GNRI of 108.016, and 105.371, respectively. Specifically, on the left side of the inflection point GNRI levels were positively correlated with CERAD and composite *z*-scores (CERAD β = 0.087, 95% CI 0.024–0.150, *p*-value = 0.0070; composite *z*-scores β = 0.065, 95% CI 0.040–0.091, *p*-value <0.0001), while on the right side of the inflection point were significantly negatively associated (CERAD β = −0.295, 95% CI −0.529 to −0.062, *p*-value = 0.0133, composite *z*-scores β = −0.050, 95% CI −0.091 to −0.008, *p*-value = 0.0184).

Conclusion: Lower GNRI was associated with poorer performance in several cognitive domains. Additionally, there was a non-linear positive association between GNRI and cognitive function in normal nutritional states, for excessive GNRI may cause cognitive decline.

KEYWORDS

cross-sectional study, geriatric nutritional risk index, older adults, cognitive function, nutritional status, NHANES

1 Introduction

The increasing incidence of cognitive function deterioration is becoming a significant concern in the context of global aging (1). Cognitive decline refers to the worsening of abilities across various cognitive domains, such as memory, language, judgment, executive functions, visuospatial skills and computational capabilities (2). Without timely prevention and intervention, this decline can evolve into mild cognitive impairment (MCI) and ultimately progress irreversibly to different forms of dementia, predominantly Alzheimer's disease (3, 4). This progression poses substantial challenges to the quality of life of not only the affected individuals but also their families and society at large (5). Once dementia is established, the outcomes from existing treatments are frequently unsatisfactory (6). However, preemptive measures including lifestyle modifications like enhanced nutrition and increased physical activity can effectively manage and potentially prevent the deterioration of cognitive functions (7).

Previous studies have shown that diet and nutrition, as a common lifestyle, are significantly associated with CI and dementia (8–10). Two studies have relied on specific nutritional markers like vitamin and albumin levels (11, 12) or utilized scales such as the mini nutritional assessment (MNA) and its short form (MNA-SF) to investigate the link between malnutrition and cognitive function (13, 14). However, some of the above criteria for assessing nutritional status are subjective and do not fully reflect the overall nutritional status, so the relationship between nutritional status and cognitive function is still controversial. The geriatric nutritional risk index (GNRI), which is a more straightforward dietary index that evaluates the nutritional status of older adults using objective criteria such as height, weight, ideal body weight, and albumin levels (15), has recently been acknowledged as equally effective as the MNA in determining malnutrition (16).

To date, research examining the link between the GNRI and normal nutritional status with cognitive function remains scarce. In this investigation, we evaluated the relationship between GNRI and cognitive performance using a representative cohort of older U.S. adults from the 2011–2014 National Health and Nutrition Examination Survey (NHANES). Additionally, we analyzed how GNRI levels correlate with cognitive domains, through the application of three tests among older adults who are in a normal nutritional state.

Abbreviations: GNRI, Geriatric nutritional risk index; NHANES, National Health and Nutrition Examination Survey; CERAD, Alzheimer's Disease Registry; AFT, Animal fluency test; DSST, Digit symbol substitution test; CI, Cognitive impairment; MNA, Mini nutritional assessment; MNA-SF, Mini nutritional assessment-short form; NCHS, National Center for Health Statistics; PIR, Poverty-to-income ratio; BMI, Body mass index; CVD, Cardiovascular diseases.

2 Methods

2.1 Study population

The cohort for our study was sourced from the NHANES, which assesses the health and nutritional status of a representative segment of the U.S. populace through complex and multistage stratified random sampling. NHANES data has been collected continuously since 1999, and data are released publicly in 2-year cycles. The study's protocol was sanctioned by the National Center for Health Statistics (NCHS), and all participants provided informed consent. We can find NHANES database from the link: https://www.cdc.gov/nchs/nhanes/index.htm.

Our analysis incorporated individuals from the 2011 to 2014 NHANES cycles, as these were the periods during which the latest assessments of cognitive function were available. Initially, we included 19,931 participants. Exclusions were made for those under the age of 60, resulting in 16,299 participants being omitted. Additionally, participants missing cognitive function test data ($n = 698$), GNRI-related data ($n = 206$), and necessary covariates ($n = 136$) were also excluded. Eventually, 2,592 participants remained eligible for inclusion in our research (Figure 1).

2.2 GNRI assessment

GNRI is a newly nutritional assessment tool designed to evaluate the nutritional risk and its associated morbidity and mortality in older adults. According to previous studies (17, 18), the GNRI is composed of the individual's height (m), weight (m), ideal weight (kg), and serum albumin (g/L). The calculation formula as follows (18): $\text{GNRI} = 1.489 \times \text{albumin (g/L)} + 41.7 \times (\text{weight/ideal weight})$, $\text{ideal weight} = 22 \times \text{height (m)} \times \text{height (m)}$. In cases where the actual weight exceeded the ideal weight, the set weight/ideal weight was 1. In our study, the total GNRI was treated as a continuous variable and participants were divided into two categories based on their GNRI levels (18): a low-GNRI group (GNRI <98) and a high-GNRI group (GNRI ≥98). The low-GNRI group included individuals identified as malnourished, whereas the high-GNRI group comprised those with normal nutritional status. The GNRI was designated as the exposure variable for the research.

2.3 Cognitive function assessment

To assess the cognitive performance in participants, we employed the following three cognitive function tests, with higher scores indicative of better cognitive function.

The consortium for the establishment of an Alzheimer's Disease Registry (CERAD) test involves three consecutive learning trials and one delayed recall trial, aimed at evaluating the immediate and delayed

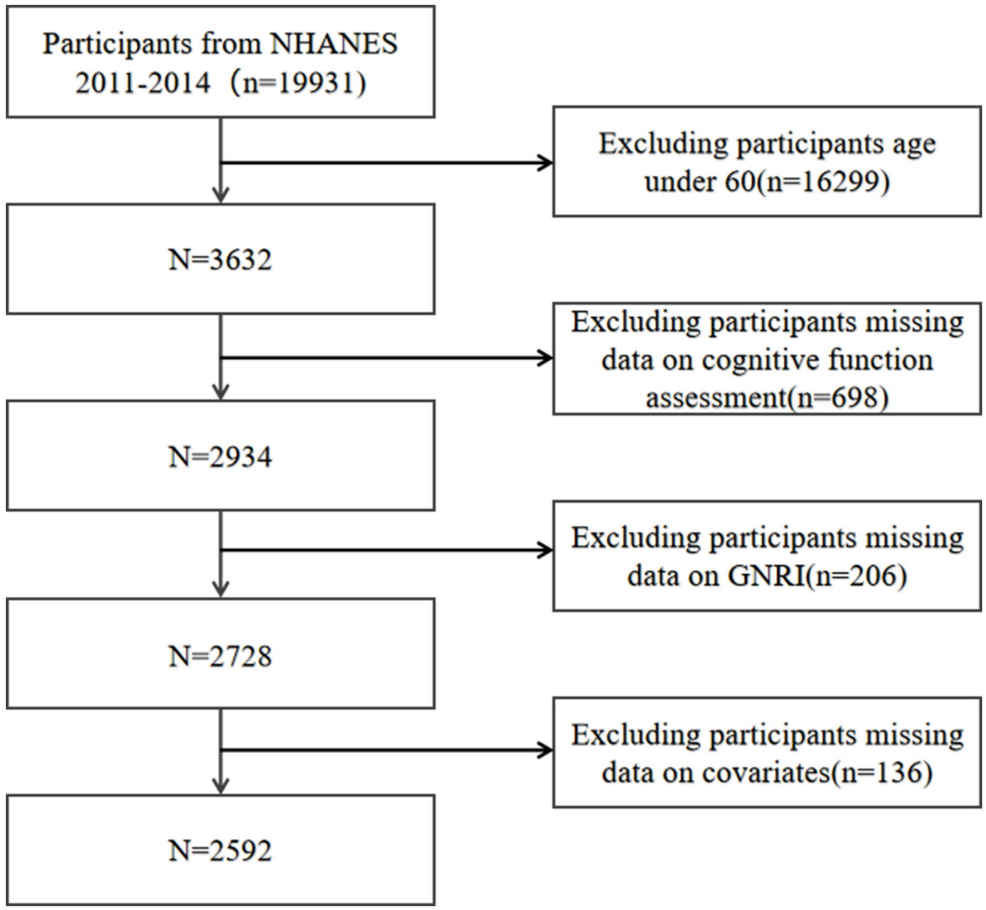

FIGURE 1
Flow chart of participants selection. NHANES, National Health and Nutrition Examination Survey.

acquisition of new verbal information (19), with scores from 1 to 40. The animal fluency test (AFT) assesses categorical language fluency (20), with scores ranging from 3 to 40. The digit symbol substitution test (DSST), a component of the Wechsler Adult Intelligence Scale, measures processing speed, sustained attention, and working memory (21), with scores between 0 and 105.

Additionally, we calculated test-specific *z*-scores for each cognitive test by using the sample mean and standard deviation of the scores from each of the three listed cognitive tests, based on the prior reference [22]. These specific *z*-scores were then aggregated to create a composite *z*-score. The composite *z*-score was utilized to assess the global cognitive function of the study participants.

2.4 Covariates

We included relevant covariates that could potentially influence the association between GNRI and cognitive function in three categories: sociodemographic variables, lifestyle, and common diseases in older adults (23, 24).

Sociodemographic variables included sex (male/female), age (years), race (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, other), poverty-to-income ratio (PIR), education levels (less than high school, high school and above), and body mass index (BMI, kg/m^2). Lifestyle factors comprised physical activity (active/inactive), smoking status (yes/no) and drinking status (yes/no). Common diseases in older adults that were considered included diabetes, hypertension, self-reported cardiovascular diseases (CVD) and stroke. Physically active was defined as engaging in at least 10 consecutive minutes of moderate or vigorous intensity activities not related to work or transport. While activities lasting less than 10 min were classified as physically inactive (25). Smoking status was assessed based on whether an individual had smoked at least 100 cigarettes in their lifetime. Drinking status was identified by whether an individual had at least 12 drinks per year. Self-reported CVD included congestive heart failure, coronary heart disease, angina/angina pectoris, and heart attack. Hypertension was determined either through a mean systolic blood pressure exceeding 140 mmHg or a mean diastolic blood pressure over 90 mmHg from the last three measurements, or by self-reported history. Diabetes was diagnosed either through physician diagnosis or the glycosylated hemoglobin level exceeding 6.5%.

2.5 Statistical analysis

In the weighted baseline table, continuous variables were described using the mean ± standard deviation, while categorical

variables were represented as percentages. To explore differences across subgroups defined by varying GNRI levels, we applied *t*-tests for continuous variables and chi-squared tests for categorical variables. We also conducted analyses using weighted multivariate logistic regression to compute beta values and 95% confidence intervals, aiming to assess the association between GNRI and cognitive function. In our analytical models, no covariates were adjusted in model 1. Model 2 included adjustments for gender, age, and race. Model 3 accounted for all covariates. Furthermore, we performed smoothed curve fitting and threshold effects analyses to further investigate the non-linear relationship between GNRI and cognitive function, including identifying potential inflection points, adjusting for all covariates. Finally, to assess the stability of the correlation between high-GNRI and global cognitive function, we conducted further subgroup analyses and interaction tests, adjusting for all confounding factors in the process. Missing values for continuous variables in this study were entered from the median or mean of available cases for these variables. All study analyses were completed in EmpowerStats (versions 2.0; http://www.empowerstats.com) and R software (version 4.2.2; http://www.r-project.org).

3 Results

3.1 Baseline characteristics of participants

The baseline characteristics of the 2,592 participants in our study, stratified by GNRI levels, are summarized in Table 1. The weighted average age of the study was 69.08 ± 6.63 years, with a slightly higher proportion of females (53.69%) compared to males (46.31%). Compared with the low-GNRI group, the high-GNRI group was younger and more likely to be male, had a higher proportion of other Hispanics and non-Hispanic White people; was more likely to be overweight (BMI ≥25); had higher alcohol consumption and physical activity status; and had a lower prevalence of stroke and diabetes. In addition, the high-GNRI group scored higher on all three cognitive function tests and had higher composite *z*-scores compared to the low-GNRI group.

3.2 Composite *z*-scores distribution of participants in the high-GNRI and low-GNRI group

Participants in the high-GNRI group had higher composite *z*-scores compared to the low-GNRI group, suggesting higher global cognitive function in the high-GNRI group population. And the difference was statistically significant (p-value <0.0001) (Figure 2).

3.3 The association between GNRI levels and cognitive function

The outcomes of the multivariate logistic regression analyses are detailed in Table 2. After adjusting for all covariates, the significant positive correlation was observed between total GNRI and scores from the AFT, DSST, and composite *z*-scores. Specifically, for each unit increase in total GNRI, there was an increase of 0.050 points in AFT scores (β = 0.050, 95% CI 0.005–0.096, p-value = 0.0258), 0.192 points in DSST scores (β = 0.192, 95% CI 0.078–0.305, p-value = 0.0010), and 0.027 points in composite *z*-scores (β = 0.027, 95% CI 0.010–0.044, p-value = 0.0024). Additionally, when analyzed by GNRI levels, the GNRI levels in the high-GNRI group were significantly associated with better outcomes in cognitive functioning. Compared to the low-GNRI group, the high-GNRI group exhibited significantly higher AFT scores (β = 0.922, 95% CI 0.166–1.677, p-value = 0.0169) and DSST scores (β = 2.791, 95% CI 0.884–4.698, p-value = 0.0042). Furthermore, the higher GNRI levels were also significantly and positively correlated with higher composite *z*-scores, reflecting overall cognitive functioning (β = 0.405, 95% CI 0.115–0.695, p-value = 0.0062).

3.4 Non-linear relationship between the GNRI and cognitive performance

The non-linear positive association between the GNRI and the three cognitive test scores, as well as the composite *z*-scores, were confirmed through smoothed curve fitting analyses, as shown in Figure 3. Furthermore, the non-linear U-shaped relationship between GNRI and global cognitive function was identified using a two-segment linear regression model, with calculated threshold effects presented in Table 3.

The smoothed curve depicting the relationship between GNRI and the global cognitive function revealed an inflection point at a GNRI value of 105.37. On the left side of this inflection point, there was a positive association with an increase in GNRI associated with improved cognitive scores (CERAD β = 0.087; 95% CI: 0.024, 0.150; p-value = 0.0070; composite *z*-scores β = 0.065; 95% CI: 0.040, 0.091; p-value <0.0001). Conversely, on the right side of the inflection point, the association turned negative, indicating that higher GNRI values beyond this point were associated with cognitive decline (CERAD β = −0.295; 95% CI: −0.529, −0.062; p-value = 0.0133, composite *z*-scores β = −0.050; 95% CI: −0.091, −0.008; p-value = 0.0184).

3.5 Subgroup analysis

Finally, we implemented adaptive subgroup analyses and interaction tests stratified by all confounders to evaluate the consistency of the correlation between high GNRI and overall cognitive functioning, and to identify potential differences among specific populations, as depicted in Figure 4. The results indicated that participants with diabetes exhibited a significant positive correlation between overall cognitive function and GNRI. This positive correlation was notably absent in non-diabetic patients, with the interaction effect reaching statistical significance (p for interaction = 0.0423). Furthermore, participants with a history of cardiovascular disease (CVD) demonstrated a tendency to have higher cognitive functioning with increased GNRI, which was marginally significant (p-value = 0.0498).

Among the other covariates examined, the association between GNRI and global cognitive function remained consistent across the remaining subgroups, with no significant interactions observed (p for interaction >0.05). The analysis suggested that GNRI's impact on cognitive function may vary depending on the presence of specific health conditions like diabetes and CVD.

TABLE 1 Weighted characteristics of study population based on different GNRI levels.

Variables	Low-GNRI (*N* = 225)	High-GNRI (*N* = 2,367)	*p*-value
Age (years)	70.86 ± 7.09	68.94 ± 6.57	0.0001
Gender (%)			<0.0001
Male	32.18	47.40	
Female	67.82	52.60	
Race (%)			0.0073
Mexican American	3.99	3.21	
Other Hispanic	2.88	3.63	
Non-Hispanic White	73.32	81.10	
Non-Hispanic Black	14.59	7.24	
Other race	5.22	4.82	
Education level (%)			0.2198
<High school	18.76	15.37	
High school, or >high school	81.24	84.63	
PIR (%)			0.1137
≤1	11.29	7.98	
>1	88.71	92.02	
BMI (%)			0.0024
<25	36.29	25.44	
≥25, <30	27.69	37.15	
≥30	36.02	37.41	
Smoking status (%)			0.6125
Yes	48.31	50.24	
No	51.69	49.76	
Drinking status (%)			0.0033
Yes	64.15	74.05	
No	35.85	25.95	
Physical activity (%)			<0.0001
Active	31.24	46.86	
Inactive	68.76	53.14	
CVD (%)			0.2942
Yes	20.15	17.13	
No	79.85	82.87	
Stroke (%)			0.0002
Yes	12.37	5.53	
No	87.63	94.47	
Hypertension (%)			0.5630
Yes	64.58	66.66	
No	35.42	33.34	
Diabetes (%)			0.0326
Yes	31.87	24.80	
No	68.13	75.20	
Composite *z*-score	−0.10 ± 2.35	0.84 ± 2.41	<0.0001
CERAD test score	25.04 ± 6.84	26.13 ± 6.30	0.0243
AFT score	16.20 ± 4.83	18.30 ± 5.64	<0.0001
DSST score	46.36 ± 17.43	53.11 ± 16.37	<0.0001

Mean ± SD for continuous variables: *p*-value was calculated by weighted linear regression model. % for categorical variables: *p*-value was calculated by weighted chi-square test.
PIR, poverty-income ratio; BMI, body mass index; CVD, cardiovascular disease; CERAD, the consortium to establish a registry for Alzheimer's disease; AFT, animal fluency test; DSST, digit symbol substitution test.
The composite *z*-score was calculated by summing the *z*-scores [(test score − mean score)/SD] of the three individual tests.

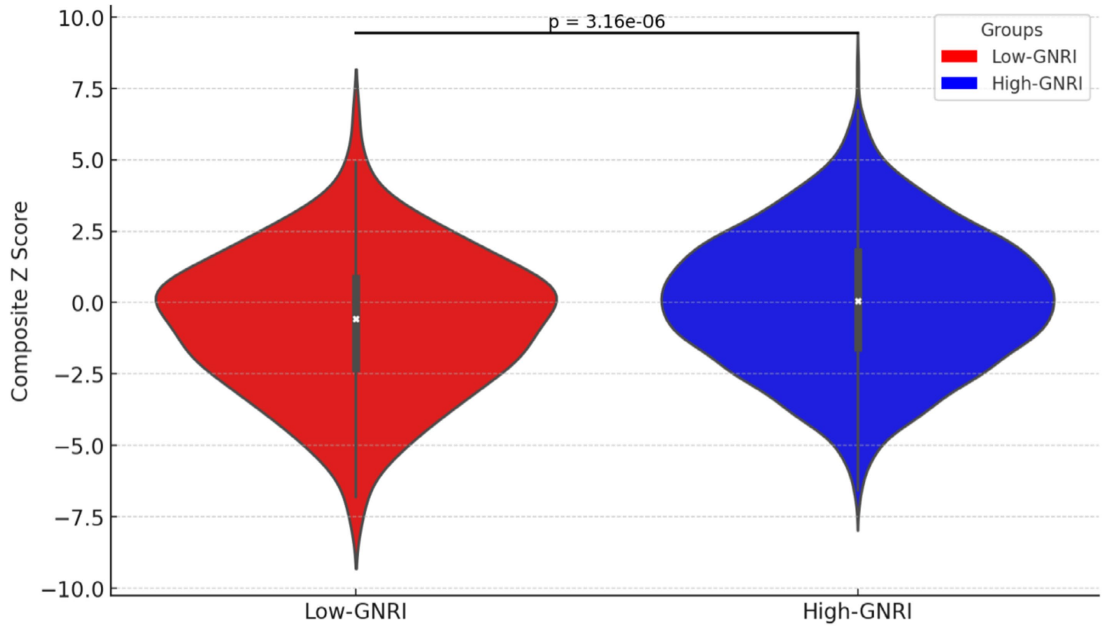

FIGURE 2
Violin plot of composite *z*-scores distribution in high-GNRI and low-GNRI group participants.

TABLE 2 Logistic regression analysis for associations between GNRI and cognitive function scores.

Cognitive function	Model 1 [β (95% CI)]	*p*-value	Model 2 [β (95% CI)]	*p*-value	Model 3 [β (95% CI)]	*p*-value
CERAD						
Total GNRI	0.089 (0.033, 0.144)	0.0018	0.061 (0.009, 0.112)	0.0222	0.041 (−0.011, 0.093)	0.1185
Low-GNRI	Reference		Reference			Reference
High-GNRI	1.089 (0.142, 2.035)	0.0243	0.654 (−0.223, 1.532)	0.1441	0.474 (−0.396, 1.343)	0.2860
AFT						
Total GNRI	0.014 (0.091, 0.189)	<0.0001	0.083 (0.037, 0.129)	0.0004	0.050 (0.005, 0.096)	0.0285
Low-GNRI	Reference		Reference		Reference	
High-GNRI	2.097 (1.262, 2.931)	<0.0001	1.252 (0.473, 2.032)	0.0017	0.922 (0.166, 1.677)	0.0169
DSST						
Total GNRI	0.495 (0.351, 0.638)	<0.0001	0.339 (0.217, 0.461)	<0.0001	0.192 (0.078, 0.305)	0.0010
Low-GNRI	Reference		Reference		Reference	
High-GNRI	6.749 (4.292, 9.205)	<0.0001	4.343 (2.270, 6.416)	<0.0001	2.791 (0.884, 4.698)	0.0042
Composite *z*-score						
Total GNRI	0.068 (0.047, 0.089)	<0.0001	0.044 (0.026, 0.062)	<0.0001	0.027 (0.010, 0.044)	0.0024
Low-GNRI	Reference		Reference		Reference	
High-GNRI	0.946 (0.588, 1.305)	<0.0001	0.584 (0.275, 0.893)	<0.0001	0.405 (0.115, 0.695)	0.0062

Model 1: no adjustment for covariates.
Model 2: age, gender, and race adjusted.
Model 3: age, race, gender, BMI, education level, PIR, physical activity, smoking and drinking status, CVD, stroke, diabetes, hypertension. CERAD, the consortium to establish a registry for Alzheimer's disease; AFT, animal fluency test; DSST, digit symbol substitution test.
The composite *z*-score was calculated by summing the *z*-scores [(test score − mean score)/SD] of the three individual tests.

4 Discussion

Our results demonstrated that the GNRI is significantly and positively correlated with the AFT, DSST and composite *z*-scores, even after adjusting for potential confounding variables. These findings indicated that a lower GNRI is linked to declines across multiple cognitive domains and global cognitive deterioration.

Upon categorizing participants based on their nutritional status (GNRI <98; GNRI ≥98), our analysis revealed a positive correlation between GNRI and cognitive functioning in older adults who

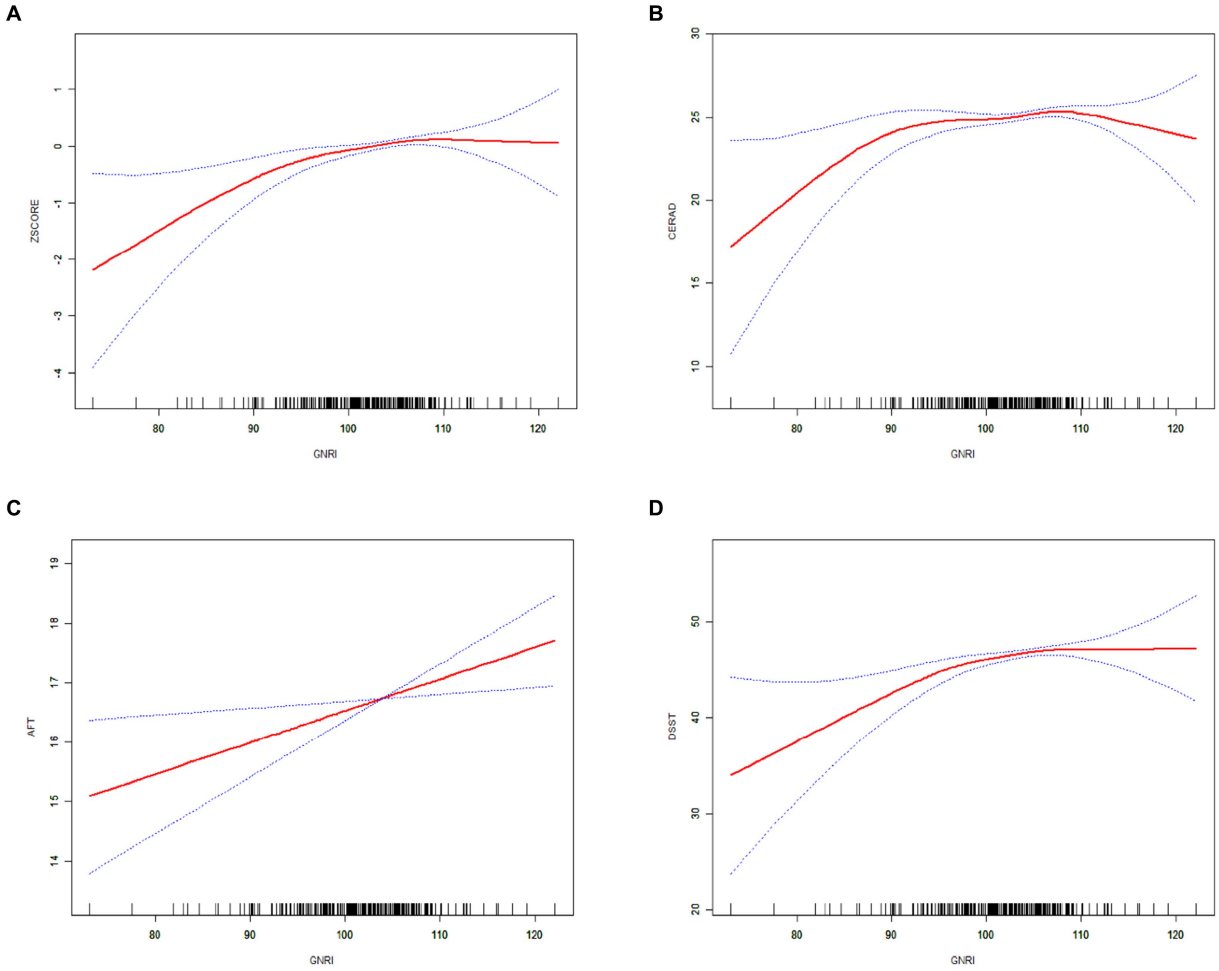

FIGURE 3
The solid red line indicates a smooth curve fit between the GNRI and cognitive performance. Blue bars indicate 95% of the fitted confidence intervals. **(A)** GNRI and composite *z*-score. **(B)** GNRI and CERAD. **(C)** GNRI and AFT. **(D)** GNRI and DSST.

TABLE 3 Threshold effect analysis of GNRI on cognitive function using a two-segment linear regression model.

Outcomes	CERAD β (95% CI) *p*-value	AFT β (95% CI) *p*-value	DSST β (95% CI) *p*-value	Composite *z*-score β (95% CI) *p*-value
Linear effect model				
	0.041 (−0.011, 0.093) 0.1185	0.050 (0.005, 0.095) 0.0285	0.192 (0.078, 0.305) 0.0010	0.027 (0.010, 0.044) 0.0024
Non-linear model				
Inflection point (K)	108.016	104.219	96.793	105.371
GNRI <K	0.087 (0.024, 0.150) 0.0070	0.156 (0.082, 0.230) <0.0001	1.119 (0.643, 1.595) <0.0001	0.065 (0.040, 0.091) <0.0001
GNRI >K	−0.295 (−0.529, −0.062) 0.0133	−0.089 (−0.178, 0.001) 0.0514	0.062 (−0.069, 0.192) 0.3549	−0.050 (−0.091, −0.008) 0.0184
Log likelihood ratio	0.013	<0.001	<0.001	<0.001

Age, race, gender, BMI, education level, PIR, physical activity, smoking and drinking status, CVD, stroke, diabetes, and hypertension were adjusted. CERAD, the consortium to establish a registry for Alzheimer's disease; AFT, animal fluency test; DSST, digit symbol substitution test.
The composite *z*-score was calculated by summing the *z*-scores [(test score − mean score)/SD] of the three individual tests.

maintain a normal nutritional status (GNRI ≥98), as opposed to those considered malnourished (GNRI <98).

Previous investigations into the association between the GNRI and cognitive function in older adults have been limited, with most research focusing on malnutrition as assessed by GNRI and yielding mixed results. For instance, a longitudinal analysis from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) found a linear relationship between malnutrition risk (GNRI ≤98) and declining cognitive function, indicating that worsening malnutrition correlates with deteriorating cognitive abilities (26). Additionally, a study of an elderly Chinese stroke population identified a low GNRI (<98) as a predictive marker for post-stroke cognitive impairment (27). However,

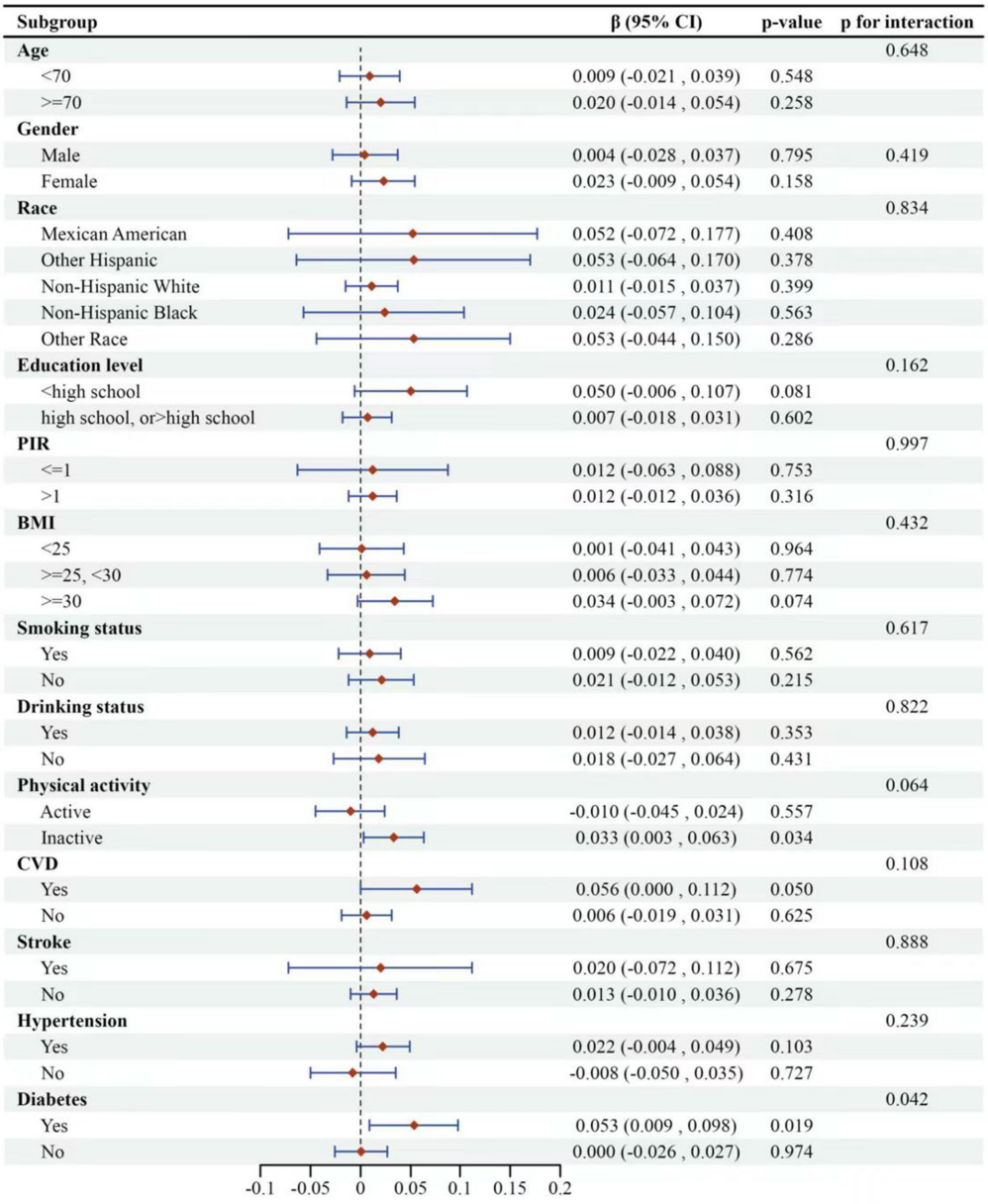

FIGURE 4
Subgroup logistic regression analysis for the association between high-GNRI and global cognitive function. The global cognitive function was represented by composite *z*-scores. Low-GNRI was the control group.

other studies have reported differing outcomes; for example, Lee et al. (28) found no significant association between GNRI and cognitive impairment risk among hemodialysis patients. And Xu et al. (29) observed no significant link between GNRI and cognitive function indicators in elderly patients with coronary artery disease. These divergent findings may be attributable to the specific diseases affecting the study populations or the varying methodologies employed in assessing cognitive function. Consistent with some prior studies, our research also observed lower cognitive function among malnourished participants, highlighting the ongoing need for extensive research to further elucidate the relationship between GNRI and cognitive function.

Additionally, previous evidence suggested that cognitive decline and the progression of dementia can potentially be mitigated through nutritional supplementation and maintaining a healthy diet (30). Notably, the combined intake of multiple B vitamins such as folic acid, vitamin B6, and vitamin B12 has been shown to prevent cognitive decline by inhibiting the accumulation of homocysteine (31–33). Furthermore, there is an expanding body of evidence supporting the role of $n-3$ fatty acids, vitamins D and E, and plant-derived vitamins in preventing cognitive deterioration and potentially dementia (33–36). On the other hand, an increasing number of studies have identified a negative correlation between the consumption of trans fats and added sugars and cognitive function (37, 38), suggesting that higher nutritional status may paradoxically lead to diminished cognitive performance. This aligns with our findings where smoothed curve fitting and threshold effect analyses revealed that higher GNRI levels were negatively associated with both CERAD scores and composite *z*-scores as GNRI increased. Consequently, a higher nutritional status does not necessarily

eliminate the risk of cognitive decline. Effective prevention might be achievable through maintaining an optimal GNRI by adopting a balanced nutritional intake and following a healthy dietary pattern (39).

The mechanism by which the GNRI appears to be associated with cognitive function is unclear. The main reason may be that GNRI is a valid indicator for assessing nutritional status, which has been shown to be strongly associated with cognitive function (16–18), although the exact mechanism is still unclear. GNRI is calculated on the basis of height (cm), body weight (kg), ideal body weight (kg), and serum albumin (18). Therefore, the relationship between GNRI and cognitive function may be related to albumin and BMI. Recent studies have shown that higher albumin levels are associated with a lower risk of cognitive impairment, suggesting that maintaining high levels of albumin may benefit cognitive function in older adults (12, 40, 41). This may be because albumin itself is closely related to nutritional status (42). Reduced albumin levels may interfere with the blood supply to the central nervous system and may disrupt the oxidant/antioxidant balance, contributing to the development of cognitive impairment (43–46). Similarly, BMI, an assessment index for obesity, has been consistently shown to be strongly associated with cognitive function, but the findings were controversial. Some studies have suggested that overweight older adults have a lower risk of developing CI or dementia (47, 48). However, recent studies have shown that higher BMI is associated with poorer cognitive functioning in older adults (49, 50), which may also account for the cognitive decline seen in participants with excessive GNRI. And some studies have found significant correlations between GNRI and the prevalence of diabetes, stroke, and depression (18, 51, 52). Therefore, it is possible that GNRI indirectly affects cognitive function through the above factors (53–55).

The study addressed the underexplored relationship between the geriatric nutritional risk index (GNRI) and cognitive function among a representative cohort of U.S. older adults. We found a significant positive correlation between GNRI and cognitive function. However, excessively high GNRI values were also associated with declines in cognitive performance. This suggested that GNRI could potentially serve as a reliable predictor of cognitive decline in clinical settings, further emphasizing the link between malnutrition and cognitive function.

Our research, a cross-sectional analysis based on data from the NHANES, benefited from the representativeness of the NHANES sample, providing a more accurate reflection of the older American population compared to other studies. We utilized various cognitive tests to evaluate different cognitive abilities among older adults, alongside composite *z*-scores for an overall assessment of cognitive function. The substantial sample size facilitated subgroup analyses, enhancing our understanding of the GNRI-cognitive function relationship across different demographics. Nonetheless, our study is not without limitations. The cross-sectional nature of NHANES restricts our ability to track changes in nutritional status and cognitive function over time or to establish a causal relationship between these variables. Additionally, some variables in NHANES come from questionnaires and self-reports, which are prone to biases. And the evidence from the U.S. may not be generalizable to other populations due to differences in genetic origin and socioeconomics conditions. Furthermore, of a total 3,632 elderly people, 1,040 (28%) were excluded due to missing data on covariates, which may have affected the results. Consequently, future multicenter longitudinal clinical trials with extended follow-ups are essential to more definitively determine the relationship between GNRI and cognitive function in the aging population.

5 Conclusion

In a representative cohort of older Americans, our study reinforced the link between malnutrition and cognitive decline. Additionally, our findings indicated that higher geriatric nutritional risk index (GNRI) levels correlate with improved cognitive function. However, there may be instances where increased GNRI levels within a normal nutritional status could lead to cognitive deterioration. This implies that GNRI could serve as a valuable tool for predicting changes in cognitive function in clinical environments in the future.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by National Center for Health Statistics. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ZT: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. YN: Data curation, Formal analysis, Methodology, Software, Writing – original draft, Writing – review & editing. NY: Methodology, Software, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Paulo Neves,
University of Toronto, Canada
Romina Buffarini,
Federal University of Rio Grande, Brazil

*CORRESPONDENCE
Yonatan Menber
✉ nataniem21@gmail.com

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Validation of the minimum dietary diversity for women as a predictor of micronutrient adequacy among lactating women in Ethiopia

Yonatan Menber[1]*, Selamawit Gashaw[1], Tefera Belachew[2] and Netsanet Fentahun[1]

[1]Department of Nutrition and Dietetics, School of Public Health, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia, [2]Department of Nutrition and Dietetics, Faculty of Public Health, College of Public Health, Jimma University, Jimma, Ethiopia

Background: The Minimum Dietary Diversity for Women (MDD-W) indicator is used as a proxy indicator for assessing micronutrient adequacy among women of the reproductive age group. Variations were observed in studies, and there was also a lack of evidence regarding the performance of this proxy indicator in Ethiopia, a country with diverse dietary consumption practices. This study aimed to validate the performance of the MDD-W in predicting micronutrient intake adequacy among lactating women in Ethiopia.

Methods and materials: A community-based cross-sectional study was conducted among randomly selected 457 lactating women in Northwest Ethiopia from February 2 to 18, 2023. A multistage sampling technique was used to select 457 study participants. A single multiphasic interactive 24-h dietary recall was used to collect dietary intake data. Ten food groups were used to compute the Minimum Dietary Diversity for Women, and the Mean Adequacy Ratio was used to assess nutrient intake adequacy. Spearman's rank correlation test, Cohen's kappa statistics, and ROC curve analysis were conducted. The optimal cutoff points for Minimum Dietary Diversity for Women were determined by selecting the points that maximized the Youden index.

Results: MDD-W had poor positive correlation ($\rho = 0.19$, $p < 0.001$) and poor predictive ability (AUC = 0.62, 95% CI: 0.56, 0.67) ($p < 0.001$) with the Mean Adequacy Ratio in determining micronutrient intake adequacy. The sensitivity and specificity of the MDD-W in the ≥5 food groups standard cutoff were 25.2 and 82.3%, respectively. The optimal cutoff point for MDD-W to predict micronutrient intake adequacy was ≥3 food groups.

Conclusion: Minimum Dietary Diversity for Women had a poor correlation and poor predictive ability in predicting micronutrient intake adequacy. The variations noted in studies and differences from the Food and Agriculture Organization recommendations regarding the cutoff and level of performance of MDD-W in defining micronutrient adequacy warrant further investigation.

KEYWORDS

minimum dietary diversity, nutrient adequacy, validation, lactating women, Ethiopia

1 Introduction

Lactating women experience nutritional vulnerability due to the high physiological demands of lactation. Inadequate intake of micronutrients during this phase can have detrimental effects on both the women themselves and the development of their children (1–4). Various global and national efforts have been made to improve the overall quality of women's diets (5–8). However, a significant proportion of women still experience poor dietary intake with monotonous diets that do not provide sufficient micronutrients, resulting in malnutrition (9–12). To effectively intervene and prioritize actions for Women of Reproductive Age (WRA), it is crucial to enhance the availability and accessibility of high-quality, accurate, and reliable data (13).

Various dietary assessment methods or indicators offer valuable insights into the nutritional adequacy of individuals and populations. However, these approaches can be costly and demand well-trained enumerators and a significant time investment for preparation and data collection. Therefore, they May not be suitable for large-scale surveys. As a result, implementing these methods regularly in Low- and Middle-Income Countries (LMIC) poses significant challenges, hindering the tracking of progress in nutrition interventions (14). To bridge this gap, the Minimum Dietary Diversity for Women (MDD-W) indicator has been developed by the Food and Agriculture Organization of the United Nations (FAO) to evaluate diet quality among WRA. This user-friendly, food-based indicator serves as a tool for monitoring dietary diversity and contributes to the achievement of the Sustainable Development Goals (SDGs) (5, 13, 15).

The MDD-W is a dichotomous indicator of food group diversity that is used as a proxy measure for assessing the adequacy of 11 micronutrients, including vitamin A, B1, B2, B3, B6, B9, B12, C, calcium, iron, and zinc. It determines whether women aged 15 to 49 years have consumed a minimum number of specified food groups within the past 24 h (13). The concept of nutrient adequacy refers to consuming an appropriate amount of vital nutrients necessary to meet the body's nutritional needs and maintain overall well-being at its best (16). Nutrient adequacy is evaluated through the analysis of quantitative dietary data. It is calculated using the Nutrient Adequacy Ratio (NAR), which compares an individual's nutrient intake to the nutrient requirement at the Recommended Daily Allowance (RDA) levels to determine their nutrient adequacy (17, 18). Additionally, the Mean Adequacy Ratio (MAR) is used as a comprehensive measure to indicate the overall quality of an individual's diet (18).

MDD-W has been validated across six countries (Bangladesh, Philippines, Burkina Faso, Mali, Mozambique, and Uganda) to determine the probability of meeting the requirements for 11 essential micronutrients (9, 19). Other studies validated dietary diversity against different numbers of micronutrient intake adequacy among women. The results of studies in Latin America, Thailand, Nigeria, and Burkina Faso exhibited a positive and significant correlation between MDD and the overall MAR of micronutrients, except for the NAR of some nutrients, which displayed a negative correlation. However, the demonstrated conclusion was found to have a low correlation coefficient (20–23).

Moreover, it is crucial to recognize that variations in dietary practices and cultural disparities among different countries worldwide lead to inconsistencies in the findings of studies concerning the actual utilization of MDD-W as proxy indicators to evaluate nutrient intake adequacy (13, 14, 18, 24, 25). The existence of these variations emphasizes the necessity for further validations of MDD-W in the Ethiopian context, where considerable sociocultural differences in dietary consumption practices persist compared to other regions of the world. Bold flavors and distinctive spices, a wide range of dishes, a communal eating approach, and a distinctively dynamic and diversified culinary tradition are all characteristics of Ethiopian food (26, 27). Additionally, there is a lack of evidence regarding the performance of the MDD-W indicator in predicting micronutrient adequacy among Ethiopian lactating women. Therefore, this study aimed to validate the performance of the MDD-W as a predictor of adequate micronutrient intake among lactating women in the North Mecha District, Northwest Ethiopia.

2 Materials and methods

2.1 Study setting and study design

The study was conducted in the North Mecha District in the Amhara Regional State, Northwest Ethiopia. This particular district is approximately 530 kilometers away from Addis Ababa, the capital city of Ethiopia. Agriculture is prominent in the district, serving as the main means of sustenance for 85% of the local community. The district is widely recognized for its remarkable cultivation of crops such as teff, maize, barley, wheat, beans, and peas. Farmers in the district employ a combination of both rainfall and irrigation techniques to cultivate these crops (28). The district is home to Koga Dam, which can irrigate 7,000 acres of land. The Koga Irrigation and Watershed Management Project, initiated by the government, aims to enhance agricultural productivity and water management in the Koga watershed area of the region. This project focuses on reducing poverty and improving food security. Its execution is anticipated to have a favorable influence on food consumption and dietary practices and also promote socio-economic progress in the region (29). A community-based cross-sectional study design was utilized from February 2nd to 18th, 2023, during the dry season following the autumn harvest and preceding the spring.

2.2 Population and eligibility criteria

The source population for this study consisted of lactating women residing in the North Mecha District. On the other hand, the study population consisted of lactating women residing in selected kebeles (local administrative units) within the district. Only lactating women who had lived in the study area for at least six months were eligible to participate. Women who had fasted or were engaged in special events such as festivals or periods of mourning within the last 24 h were also excluded from the study.

2.3 Sample size determination and sampling techniques

A sensitivity estimation formula (30) was utilized to determine the sample size based on the following assumptions: a 95% confidence

level, a 5% margin of error (d), an anticipated 90% sensitivity (Sn), and a 50% proportion (P). After multiplying in a design effect of 1.5 and accounting for a 10% non-response rate, the final sample size was determined to be 457. The study participants were selected using a multistage sampling technique. Seven kebeles were randomly chosen from a total of 38 kebeles. A systematic random sampling approach was then employed to select the study participants from the chosen Kebeles.

$$N = \frac{\left(Z_{\alpha/2}\right)^2 Sn\left(1-Sn\right)}{d^2 P}$$

2.4 Operational and term definitions

2.4.1 Minimum dietary diversity for women

It is a dichotomous indicator that was developed by the FAO to be used as a proxy indicator reflecting the micronutrient adequacy of diets for WRA. It is assessed using ten food groups, which include: grains, white roots and tubers, and plantains; pulses (beans, peas, and lentils); nuts and seeds; milk and milk products; meat, poultry, and fish; eggs; dark green leafy vegetables; other vitamin A-rich fruits and vegetables; other vegetables; and other fruits. If a woman consumed at least five of the ten defined food groups, at least 15 g/day of each food group, within the preceding 24 h, she was considered to have adequate MDD; otherwise, she was considered to have inadequate MDD (13).

2.4.2 Recommended dietary allowances/ reference nutrient intake

This represents the recommended daily consumption of nutrients that satisfy the nutritional needs of nearly all (97.5%) lactating women (31).

2.4.3 Nutrient adequacy ratio

It refers to the ratio of a subject's micronutrient intake to the current RDA for each sex and age category (18).

2.4.4 Mean adequacy ratio

It is a comprehensive measure that serves as an indicator of overall diet quality. It was derived by dividing the sum of all NAR values by the total count of computed micronutrients (18).

2.4.5 Micronutrient intake inadequacy

The occurrence occurred when lactating women consumed less than 100% of the RDA for a specific micronutrient and the NAR for that micronutrient was less than 1 (18).

2.4.6 Overall micronutrient intake inadequacy

The ideal MAR cut-off for nutrient intake inadequacy should be one (100%), which would mean that the intake of all 12 nutrients, namely vitamin A, vitamin B1, vitamin B2, vitamin B3, vitamin B6, vitamin B9, and vitamin B12, vitamin C, calcium, iron, zinc, and selenium, is equal to or greater than the RDA and the requirements for all the nutrients are met. Since no participant had a MAR score of 1 in this study, overall micronutrient intake inadequacy was operationalized to be <0.75 (18, 32–34).

2.5 Data collection tools and procedures

A structured interviewer-administered questionnaire was used to collect data on socio-demographic and economic factors and household food security. The data were collected using the Kobo Tool Box, an electronic data collection toolkit. FAO-standardized tools were used to assess the dietary data (14, 35). A team of ten skilled data collectors, supported by two experienced supervisors with expertise in public health nutrition, actively participated in the data collection and supervision process.

2.6 24-h dietary recall assessment

Before collecting actual data, home surveillance and market inspections were conducted to gather information about the types of foods consumed, cooking techniques, and kitchen utensils used in the study area. During the surveillance, photographs of household utensils and food portions eaten during a single meal were taken, and a code was assigned to each item. In the nutrition laboratory, utensils used for serving food were standardized using a digital food portion weighing scale and a measuring cylinder with food portions and water (34).

During the data collection process, the respondents were questioned about the utensils they used by referring to a photographic atlas. The atlas contained pictures of various household utensils, such as spoons, ladles, cups, and glasses, as well as food portions. These photographs aided the participants in remembering and determining the types and sizes of the consumed food items. An interactive single multiple-pass 24-h recall method was employed for this purpose. Additionally, the quantities of consumed foods were assessed using household utensils and specific numbers (such as oranges, bananas, mangoes, and potatoes). Foods expressed in numbers were categorized as large, medium, or small (34).

2.7 Data quality control

The questionnaire was originally formulated in English and then translated into Amharic before being translated back into English to ensure consistency. The data collection instrument consisted of standard questions developed by the FAO as well as questions adapted from various sources (14, 35). These adapted questions were included in the tool after being validated by experts in the field, and any necessary modifications were made based on their recommendations. A pretest was conducted on approximately 5% of the sample. Supervisors and data collectors received training sessions, and the data collection process was closely monitored to ensure the quality of the data. To assist participants in recalling and identifying the types and quantities of food they had consumed, photographs of food portions and common household utensils such as spoons, ladles, cups, and glasses were utilized.

A multiple-pass, 24-h recall was conducted to collect dietary intake data, consisting of three passes. This procedure involved three sequential stages: first, a "quick list" was created; second, a detailed description of all food and beverage items consumed was recorded; and finally, a review was conducted.

2.8 Data processing and analysis

After the data collection process was completed, the food consumption data were converted into nutrient intake data using NutriSurvey 2007 software. The Ethiopian food composition tables were used to evaluate the nutrient values per 100 grams of each food item (36, 37). When certain food items were not specified in the Ethiopian food composition tables, alternative tables from different African countries like Kenya (38) and Tanzania (39) were utilized as points of reference. The analysis was conducted using SPSS version 25, specifically employing NutriSurvey 2007 software to analyze the intake of nutrients.

In 2004, the World Health Organization (WHO) and the FAO established the RDA as a means to compare and evaluate the actual intake of nutrients. The NAR was then calculated to determine the inadequacy of a particular nutrient. Additionally, the MAR was used to assess the overall inadequacy of micronutrient intake. The MAR considered 12 micronutrients that were chosen based on their significance to public health. These micronutrients included vitamin A, thiamin, riboflavin, niacin, vitamin B-6, folate, vitamin B-12, vitamin C, calcium, iron, zinc, and selenium (17, 18).

$$\text{NAR} = \frac{\text{Actual intake of the nutrient per day}}{\text{RDA of that nutrient}}$$

To determine the overall adequacy of micronutrients, the MAR was computed as follows:

$$\text{MAR} = \frac{\sum \text{NAR}\left(\text{each truncated at 1}\right)}{\text{Number of nutrients}}$$

The NAR was truncated at 1, implying that a nutrient with a superior NAR was unable to compensate for a nutrient with an inferior NAR. To ensure adequacy for NAR, the intake of each nutrient is needed to meet or exceed the RDA. On the other hand, adequacy for the MAR was determined using a ratio. This ratio calculates the sum of the NAR for each nutrient divided by the total number of nutrients, intending to achieve a value of 1 (18, 34). The evaluation of the adequacy of data on micronutrient intake was conducted by employing the Kolmogorov–Smirnov and Shapiro–Wilk tests to assess normality (p-value >0.05). The assessment revealed that the data were not distributed normally, and the results were presented using the median and interquartile range.

The validity of MDD-W was assessed by comparing it to MAR, which serves as a gold standard for high accuracy. Since the MAR distribution was skewed, Spearman's rank correlation test was employed to investigate the correlation between MDD-W and MAR. The strength of the correlation was interpreted using the correlation coefficient as follows: poor (0–0.29), fair (0.30–0.59), moderate (0.60–0.79), and strong (0.80–1.00) correlation (40, 41). To assess the level of agreement between MDD-W and MAR, Cohen's kappa statistics were employed. The kappa scores were interpreted as follows: poor agreement (<0.00), slight agreement (0.00–0.20), fair agreement (0.21–0.40), moderate agreement (0.41–0.60), substantial agreement (0.61–0.80), and almost perfect agreement (0.81–1.00) (42).

Additionally, sensitivity and specificity analyses were carried out to assess the accuracy of MDD-W in correctly identifying lactating women with high MAR values. The Area Under the Curve (AUC) was calculated using the Receiver Operating Characteristic (ROC) curve based on the nutrient adequacy as either yes (MAR ≥0.75) or no (MAR <0.75). Additionally, further analyses were conducted to assess the performance of the MDD-W at different MAR thresholds, which were set between 0.50 and 0.85. The AUC values were then interpreted according to predefined criteria, which categorized them as fail (0.5–0.6), poor (0.6–0.7), fair (0.7–0.8), good (0.8–0.9), or excellent accuracy (0.9–1.0) (43). The optimal cutoff points were identified by selecting the points that maximized the Youden J statistic (sensitivity + specificity – 1) (the larger the better) (44). A p-value less than 0.05 was considered statistically significant. Texts, tables, and graphs were used to present the final results.

3 Results

3.1 Socio-demographic and socioeconomic characteristics

A total of 430 lactating women participated in the study, with a 94.1% response rate and a mean age of 29.46 ± 5.55 years. Three hundred nineteen (74.2%) participants were unable to read and write in terms of their educational status. The mean family size was 5.81 ± 1.90. All study participants were followers of the Orthodox Christian religion (Table 1).

3.2 Minimum dietary diversity and nutrient adequacy of lactating women

The range of food groups consumed varies from a minimum of one food group to a maximum of ten food groups. The prevalence of the MDD-W score (≥5 food groups) was 19.8% (95% CI: 16.1, 23.9). The median MDD-W score was 3.0 ± 2.0 (Figure 1). A large majority of study participants had consumed starchy staple foods and pulses (beans and peas), while the least consumed food group was nuts and seeds (Figure 2). The overall prevalence of adequate micronutrient intake, defined as MAR ≥0.75, was 27.7% (95% CI: 23.5, 32.2). This prevalence was calculated among the 11 nutrients after excluding iron, which was adequate for all participants.

3.3 Validation of the MDD-W in predicting adequacy of micronutrient intake

The Spearman correlation test revealed a statistically significant poor positive correlation between the MDD-W and the MAR in determining the adequacy of micronutrient intake ($\rho = 0.19$, $p < 0.001$). According to the ROC analyses, MDD-W exhibited poor predictive ability for micronutrient adequacy concerning 11 micronutrients at MAR ≥0.75 (AUC = 0.62, 95% CI: 0.56, 0.67) ($p < 0.001$) (Figure 3; Table 2).

3.4 Determination of the cutoff for dietary diversity

The optimal cutoff was determined to be food groups of three, and this remained consistent regardless of the MAR threshold set between 0.50 and 0.85. The agreement levels were generally slight for each

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TABLE 1 Socio-demographic characteristics among lactating women in North Mecha District, Northwest Ethiopia, 2023 (N = 430).

Variables	Frequency	Percentage
Maternal age in years		
18–25	119	27.7
26–35	258	60.0
36–50	53	12.3
Maternal education		
Unable to read and write	319	74.2
Primary school incomplete	40	9.3
Primary school completed	42	9.8
Secondary school completed	24	5.6
University or college completed	5	1.2
Maternal occupation		
Farmer	333	77.4
Merchant	17	4.0
Housewife	78	18.1
Employee	2	0.5
Maternal marital status		
Married	423	98.4
Widowed	7	1.6
Partner education (423)		
Unable to read and write	193	44.9
Primary school incomplete	165	38.4
Primary school completed	44	10.2
Secondary school completed	17	4.0
University or college completed	4	0.9
Partner occupation (423)		
Farmer	390	90.7
Merchant	15	3.5
Student	4	0.9
Daily laborer	7	1.6
Other[#]	7	1.6
Family size		
≤4	123	28.6
5–7	224	52.1
≥8	83	19.3
Parity		
≤2	123	28.6
3–5	209	48.6
≥6	98	22.8

[#]Driver, soldier, veterinarian.

MAR threshold. However, the highest level of agreement was achieved when the MAR value was ≥0.75 (Table 2).

The MDD-W score (≥5 food groups), which is a proxy indicator developed by FAO to reflect micronutrient adequacy, showed a sensitivity of 25.2% and a specificity of 82.3%. The optimal cutoff point for MDD-W to predict micronutrient intake adequacy based on the findings of the present study, determined by considering the Youden index, was ≥3 food groups, resulting in a sensitivity of 82.4% and a specificity of 41.5%. The Kappa statistics also demonstrated a relatively higher Kappa value when examining the dietary diversity of ≥3 food groups. This suggests a slight agreement between the consumption of ≥3 food groups and meeting the essential micronutrient requirements (Table 3).

Compared to all the studied micronutrients, dietary diversity for women demonstrated relatively high performance in predicting nutrient intake adequacy for Vitamin B12 (NAR = 1). The Spearman rank correlation indicated that dietary diversity for women showed a fair positive correlation with vitamin B12 intake adequacy and a poor positive correlation with the adequacy of other micronutrients that had a significant correlation (vitamin B2, B3, B12, zinc, and selenium). Except for vitamin B1, which showed a poor negative correlation, the AUC of all micronutrients with significant values ranged from 0.57 to 0.69, with the highest score exhibited for vitamin B12. Taking into consideration the Youden index, the optimal cutoff point for MDD-W to predict micronutrient intake adequacy was determined to be ≥3 food groups for all micronutrients with significant values, except vitamin B1 (Table 4).

4 Discussion

This study aimed to validate the performance of the MDD-W as a predictor of adequate micronutrient intake among lactating women in the North Mecha District, Northwest Ethiopia. The present study revealed that the occurrence of a satisfactory MDD-W (≥5 food groups) as suggested by FAO was 19.8% within the 24 h preceding the survey. The findings of this study demonstrate a lower rate when compared to the most recent findings from studies conducted in Ethiopia (45–50). The potential difference could be explained by various factors, including seasonal variations that affect food availability, particularly vegetables, differences in study settings such as urban versus rural areas, divergent sociocultural practices in dietary consumption, and disparities in nutrition-related knowledge and attitudes.

The MAR for lactating women fell within the range of 0.29 to 0.94, indicating that none of the participants reached the RDA for all essential nutrients and had a MAR of one, which is supported by other studies (51, 52). This study also showed that the overall prevalence of micronutrient intake adequacy (MAR ≥0.75) among lactating women was 27.7%. This is significantly lower than the findings of the study conducted in Bahir Dar City, Ethiopia (52), as well as in rural areas of Indonesia (53). The potential explanation for the low adequacy of micronutrient intake includes factors such as the dominant consumption of cereals with low micronutrient density, such as teff, maize, and sorghum, and seasonal variations. Moreover, there is insufficient consumption of food items from other food groups, such as animal-source foods, pulses, fruits, vegetables, and nuts and seeds, which are rich in essential micronutrients (54). In contrast to other studies, the variation observed in this study can also be attributed to disparities in study settings, encompassing rural and urban areas (52), as well as disparities in dietary reference intakes, such as RDA and Estimated Average Requirement (EAR) (31). This discrepancy can

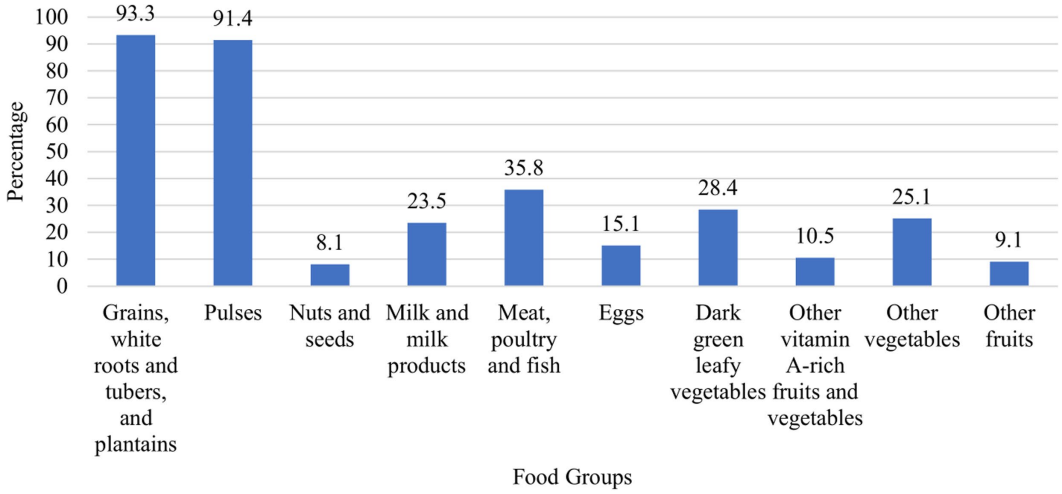

FIGURE 1
Number of consumed food groups among lactating women in North Mecha District, Northwest Ethiopia (*N* = 430).

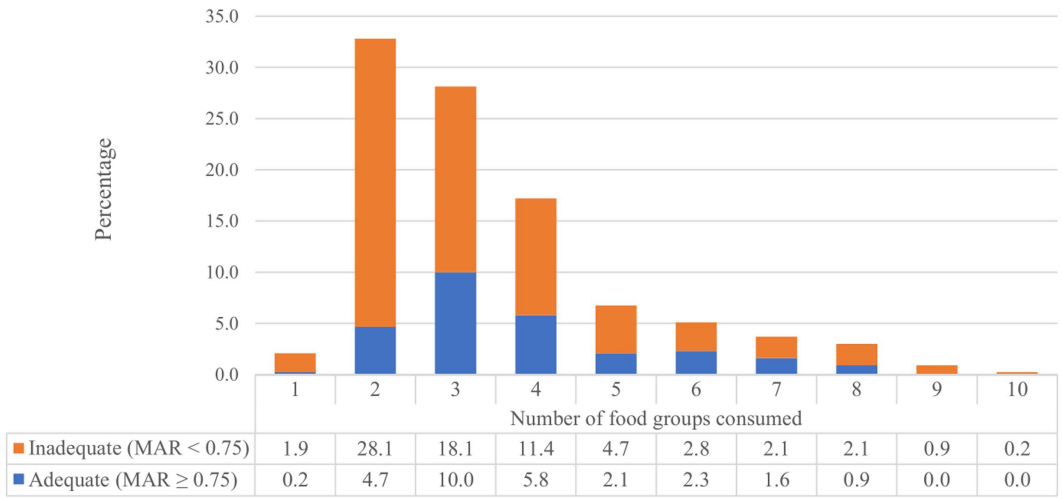

FIGURE 2
Types of consumed food groups among lactating women in North Mecha District, Northwest Ethiopia (*N* = 430).

be observed as one instance of disparity between studies employing RDA (21, 52, 55) and EAR (51, 53, 56–59).

A variety of validation tests were utilized to assess the validity of the MDD-W. The Spearman correlation analysis of this study indicated a statistically significant but poor positive correlation between MDD-W and the adequacy of intake for 11 micronutrients (MAR ≥0.75). Additionally, in the ROC analyses, MDD-W exhibited poor predictive ability for micronutrient adequacy. Likewise, a Latin American study revealed that the Dietary Diversity Score exhibited a significant weak positive correlation with the MAR score (20). Additionally, this study finding was relatively comparable to a study conducted in Burkina Faso, which found a moderate correlation between MDD-W and the adequacy of micronutrient intake in lactating women (23). Other studies conducted in Nigeria and Thailand also revealed a significant correlation between the dietary diversity score and nutrient adequacy. It was observed that as the dietary diversity score increased, so did the nutrient intake adequacy (21, 22). Furthermore, studies conducted among WRA from low- and middle-income countries have consistently revealed a notable correlation between MDD-W and Mean Probability of Adequacy (MPA) at each respective site (9, 19).

The MDD-W score (≥5 food groups), a proxy indicator endorsed by the FAO to assess the adequacy of micronutrients (13), exhibited a sensitivity of 25.2% and a specificity of 82.3%, according to the current study. This suggests that MDD-W is a specific measure for assessing micronutrient adequacy at the defined threshold. It indicates that when the MDD-W indicator is used with a cutoff of ≥5 food groups, it is more likely to ensure that those who have adequate MDD-W and test positive are most likely to have adequate intake of micronutrients according to the MAR score. As a result, it reduces the likelihood of false positive results, such as incorrectly identifying women as having micronutrient adequacy when they have a low probability of it,

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especially if their diet consists of a less diverse range of foods from at most four different food groups. On the other hand, the low sensitivity of the indicator suggests that it performs poorly in identifying women with adequate levels of micronutrient adequacy and has a high chance of producing false negative results, failing to identify those who have adequate micronutrient intake at the defined MDD-W cutoff.

In comparison to the findings of the Women's Dietary Diversity Project (WDDP II), led by the FAO, the sensitivity of the MDD-W indicator (≥5 food groups) was significantly lower in the present study than the sensitivity of a similar indicator calculated from 10 food groups (restricted) with an MPA >0.7, compared to the results of each study site in the included countries. On the contrary, the specificity of the MDD-W indicator (≥5 food groups) in the present study was higher than the specificity results obtained for the similar indicator calculated from 10 food groups (restricted) with an MPA >0.7 among women, compared by study site in each country (19).

The optimal cutoff point for MDD-W to predict micronutrient intake adequacy based on the findings of the present study, determined by considering the Youden index, was ≥3 food groups, resulting in a sensitivity of 82.4% and a specificity of 41.5%. The Kappa statistics also demonstrated a relatively higher Kappa value when examining the dietary diversity of ≥3 food groups. The finding suggests a slight agreement between the consumption of ≥3 food groups and meeting the essential micronutrient requirements. Similarly, the optimal cutoff point for MDD-W in predicting the adequacy of micronutrient intake was found to be ≥3 food groups for all micronutrients with significant values (vitamin A, B2, B3, B12, zinc, and selenium), except for vitamin B1. In line with the slight agreement observed between the MDD-W (≥3 food groups) and the overall adequacy of micronutrients using MAR, the MDD-W (≥3 food groups) for individual micronutrients also showed slight agreement with the adequacy of each micronutrient using NAR. The best cutoff determination, considering the maximum Youden index value, revealed a better sensitivity for the MDD-W (≥3 food groups) indicator than for the MDD-W (≥5 food groups) indicator, which had high specificity but low sensitivity.

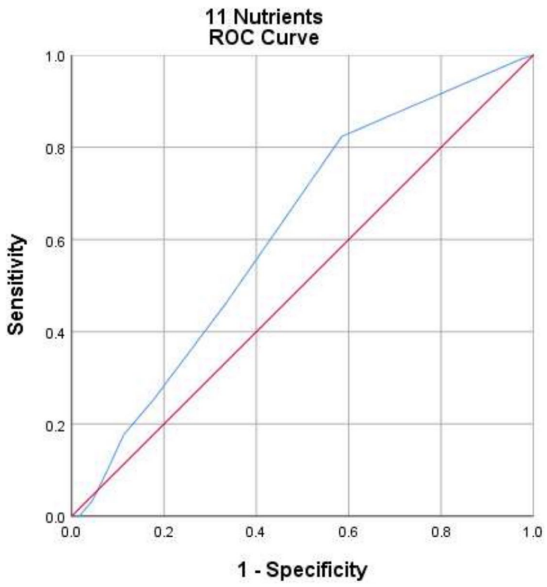

FIGURE 3
The ROC curve illustrates the performance of dietary diversity for women in predicting adequate micronutrient intake among lactating women in North Mecha District, Northwest Ethiopia, 2023 (MAR ≥ 0.75) (*N* = 430).

The cutoff derived from this study is lower than what has been revealed by other studies. A study in Burkina Faso demonstrated the effectiveness of MDD-W in accurately predicting the MPA value >0.6 in women who were not pregnant or breastfeeding. Moreover, it was observed that setting a threshold of a four-food-group cutoff for MDD-W for a food group score of 10 resulted in a better balance between sensitivity, specificity, and the accuracy of classification compared to MDD-W with a five-food-group cutoff, thereby reflecting improved adequacy of micronutrients. However, this study highlights that the levels of MPA for pregnant and breastfeeding women were insufficient to determine the best cutoff points effectively (23). Another study conducted among WRA from low- and middle-income countries demonstrated that using a cutoff of ≥5 food groups in the measurement of MDD-W yielded the best balance between sensitivity and specificity across study sites. This was observed for both indicators derived from nine and ten food groups, with a MPA >0.6 (9).

One possible explanation for this variation could be related to the threshold of MAR selected to define the level of adequacy required to be considered satisfactory. When validating the MDD-W indicator with a uniform cutoff, sensitivity increases as the MAR cutoff increases, while specificity decreases. This had little effect on determining the best balance of sensitivity and specificity and defining the best cutoff. Additionally, cultural disparities, methodological discrepancies, individual dietary patterns, and socioeconomic influences all play a significant role in shaping these variations.

However, since lactating women have higher micronutrient requirements than other WRA, a higher cutoff of MDD is expected to

TABLE 2 Summary of dietary diversity for women indicator characteristics at various MAR thresholds among lactating women in North Mecha District, Northwest Ethiopia, 2023 (*N* = 430).

Threshold	*p*	AUC	MDD optimal cutoff (≥)	Value at the optimal cutoff			
				Sensitivity (%)	Specificity (%)	J	Kappa
MAR ≥ 0.50	0.11*	0.60 (0.51, 0.70)*	3	66.6	0.50	0.17	0.071*
MAR ≥ 0.65	0.11*	0.56 (0.51, 0.62)*	3	69.9	41.4	0.11	0.116*
MAR ≥ 0.67	0.14**	0.58 (0.52, 0.63)**	3	72.4	43.1	0.15	0.157**
MAR ≥ 0.75	0.19***	0.62 (0.56, 0.67)***	3	82.4	41.5	0.24	0.168***
MAR ≥ 0.85	0.12*	0.63 (0.54, 0.72)*	3	91.7	36.5	0.28	0.047**

ρ: spearman rank correlation coefficient rho, AUC: area under the curve, J: youden index, MDD: minimum dietary diversity, MAR:mean adequacy ratio.
**p* value < 0.05, ***p* value < 0.01, ****p* value < 0.001.

TABLE 3 Summary of dietary diversity for women indicator characteristics for 10 food groups among lactating women in North Mecha District, Northwest Ethiopia, 2023 (*N* = 430).

Food groups	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	J	Kappa
≥1	100	0	27.7	0	0	0.000
≥2	99.2	2.6	28.0	88.9	0.02	0.010
≥3	82.4	41.5	35.0	86.0	0.24	0.168***
≥4	46.2	66.6	34.6	76.4	0.13	0.116*
≥5	25.2	82.3	35.3	74.2	0.08	0.083
≥6	17.6	88.7	37.5	73.8	0.06	0.076
≥7	9.2	92.6	32.4	72.7	0.02	0.024
≥8	3.4	95.5	22.2	72.1	−0.01	−0.015
≥9	0	98.4	0.0	72.0	−0.02	−0.023
10	0	99.7	0.0	72.3	<−0.01	−0.005

PPV: predictive value positive, NPV: negative predictive value, J: youden index.
*p value < 0.05, **p value < 0.01, ***p value < 0.001.

TABLE 4 Summary of dietary diversity for women indicator characteristics for each micronutrient among lactating women in North Mecha District, Northwest Ethiopia, 2023 (NAR =1) (*N* = 430).

Micronutrient	ρ	AUC	MDD optimal cutoff (≥)	Value at the optimal cutoff			
				Sensitivity (%)	Specificity (%)	Youden Index	Kappa
Vitamin A	0.09	0.59 (0.51,0.69)*	3	77.2	36.7	0.14	0.052*
Vitamin B1	−0.19***	0.38 (0.32,0.44)***	2	98.6	3.4	0.02	0.027
Vitamin B2	0.16**	0.61 (0.55,0.66)***	3	76.0	42.9	0.19	0.177***
Vitamin B3	0.19***	0.64 (0.58,0.70)***	3	86.9	40.2	0.27	0.144***
Vitamin B6	0.06	0.55 (0.48,0.62)	5	21.3	87.2	0.09	0.036
Vitamin B9	0.08	0.57 (0.52,0.63)*	3	72.8	39.8	0.13	0.113**
Vitamin B12	0.33***	0.69 (0.63,0.75)***	3	93.4	41.0	0.34	0.167***
Vitamin C	0.05	0.59 (0.43,0.76)	3	85.7	35.2	0.21	0.010
Calcium	0.06	0.54 (0.44,0.64)	3	71.0	35.3	0.06	0.013
Iron	–	–	–	–	–	–	–
Zinc	0.13**	0.58(0.52,0.64)**	3	69.0	44.4	0.13	0.125**
Selenium	0.15**	0.62(0.55,0.70)**	3	67.9	52.5	0.21	0.124**
11 Nutrients	0.19***	0.62(0.56, 0.67)***	3	82.4	41.5	0.24	0.168***

ρ: spearman rank correlation coefficient rho, AUC: area under the curve, J: youden index.
*p value < 0.05, **p value < 0.01, ***p value < 0.001.

predict MAR ≥0.75 compared to other study findings that evaluated MDD at MPA >0.6 and concluded the best cutoff of four or five food groups (9, 19, 23), including what is endorsed by FAO (13). Furthermore, when taking into account the necessary level of micronutrient requirements to meet the RDA as utilized in this particular nutrient analysis study, it is worth noting that the requirement level exceeds that of micronutrients necessary to meet the EAR as employed in other research studies (9, 19, 23). This elevated requirement level consequently leads to a higher MDD-W cutoff to achieve RDA-based adequacy. Conversely, it is significant that this anticipation contrasts with the findings of previous studies once again.

The variations noted in studies and differences from FAO recommendations regarding the cutoff and level of performance of MDD-W in defining micronutrient adequacy have several implications. These include improved identification of individuals with adequate micronutrient intake, effective allocation of resources, enhanced monitoring and evaluation, and policy considerations. Therefore, as countries are implementing the FAO-endorsed MDD-W guideline in their health systems, discrepancies in its performance have been observed in various studies, including the current one. Hence, further investigation is required in different settings with diverse dietary consumption practices to fully comprehend the reasons behind these controversies and adapt management strategies accordingly. Along with the relevant findings of this study in the northwest part of Ethiopia, additional comprehensive analysis of dietary intake data is necessary for other parts of Ethiopia, a country with a diverse population and varying dietary consumption practices.

This community-based study validated the performance of MDD-W, which is endorsed by FAO for low- and middle-income countries (13), in defining micronutrient intake adequacy. The study specifically focuses on lactating women in Ethiopia, as their consumption plays a significant role in determining the nutritional

status of both the mother and child. Also, the study addresses a lack of evidence regarding the performance of the MDD-W indicator in Ethiopia, where considerable sociocultural differences in dietary consumption practices persist compared to other regions of the world. Nevertheless, relying solely on a single 24-h recall May introduce potential inaccuracies due to variations in daily dietary patterns and memory biases. To minimize these biases, significant efforts have been made to incorporate standardized quality-control procedures throughout the entire study process. Well-trained nutrition experts have been involved to ensure accuracy and consistency. Additionally, days of special events are excluded from the data collection process to ensure that the findings reflect regular dietary patterns.

5 Conclusion

A statistically significant, yet poor, positive correlation was found between MDD-W and MAR when determining the adequacy of micronutrients. Moreover, in the ROC analyses, MDD-W exhibited poor predictive ability for micronutrient adequacy. The optimal cutoff point for MDD-W in predicting adequate intake of micronutrients was established as ≥3 food groups. The variations noted in studies and differences from the FAO recommendations regarding the cutoff and level of performance of MDD-W in defining micronutrient adequacy are crucial and have several implications. These include enhanced monitoring and evaluation, effective allocation of resources, and policy considerations. In light of this consideration, along with the pertinent findings of this study in the northwest part of Ethiopia, further investigations are needed to determine the reasons behind the deviations and reexamine the recommendation of using MDD-W as a proxy indicator for predicting micronutrient adequacy. This should incorporate more study sites in a multicounty context, including Ethiopia, a country with a diverse population and varying dietary consumption practices.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethical Review Board of the College of Medicine and Health Science at Bahir Dar University. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

YM: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. SG: Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft. TB: Conceptualization, Investigation, Methodology, Validation, Visualization, Writing – review & editing. NF: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Henry Lukaski,
University of North Dakota, United States
Luciane Bresciani Salaroli,
Federal University of Espirito Santo, Brazil

*CORRESPONDENCE
Ailema González-Ortiz
✉ ailejgo@gmail.com

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Postoperative complications in the pediatric population. Malnutrition or phase angle? Which one do we use?

María José Díaz-Amaya[1], Laura Fernanda Rosales-Arreola[1,2], Jennifer Hernández-Licona[1], Beatriz Pérez-Guillé[1], Karen Ignorosa-Arellano[3], Silvio Carmona-Librado[4], José González-Zamora[1] and Ailema González-Ortiz[1]*

[1]Translational Research Center, Instituto Nacional de Pediatría, Mexico City, Mexico, [2]Master Program in Clinical Nutrition, Universidad del Valle de México, Mexico City, Mexico, [3]Department of Gastroenterology, Instituto Nacional de Pediatría, Mexico City, Mexico, [4]Department of General Surgery, Instituto Nacional de Pediatría, Mexico City, Mexico

Background and Aims: Malnutrition increases post-operative risks like infections and prolonged stays. Pediatric assessment challenges require using anthropometric measurements and phase angle, which reflects body cell mass and health outcomes. Phase angle varies by maturation stages, making it crucial for pre-surgical evaluations alongside BMI. This study aimed to determine the relationship between nutritional status, phase angle, and postoperative complications in pediatric patients who underwent surgery.

Methods: Prospective study with patients aged 3–17 undergoing major non-ambulatory surgery. Anthropometric measurements (weight, height, BMI *Z*-scores) hand grip strength, dietary intake and body composition via bioimpedance to assess phase angle were recorded. Postoperative complications were monitored, including surgical site infections, morbidity (pneumonia, inotropic support, infections, thromboembolism), and mortality. Surgical risks and pre- and postoperative conditions were documented.

Results: After the application of the selection criteria, a total of 391 patients who underwent surgery were included; 60% ($n = 235$) were within the range of the preschool and school-age groups. During the follow-up period, 51 (13%) patients developed at least one postoperative complication, with surgical site infections being the most common. Moreover, as phase angle decreased, the length of stay (LOS) increased in all the participants. Among children aged ≤12 years old, malnutrition was a risk factor for complications [OR 3.86 (1.61–9.27 95%CI)], whereas among adolescents, phase angle served as a protective factor [OR 0.63 (0.42–0.94 95%CI)].

Conclusion: Significant associations were observed between nutritional status, by BMI z-score, and post-surgical complications in younger patients. Additionally, in adolescents, the phase angle emerged as a protective factor against these complications.

KEYWORDS

postoperative complications, malnutrition, phase angle, pediatric surgery, body composition

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Introduction

Malnutrition is a critical concern in pediatric patients due to its significant impact on clinical outcomes. Unlike adults, where it has been identified as an independent risk factor contributing to infection development, prolonged hospital stay, post-operative complications, mortality, and high costs among surgical patients (1, 2); pediatric patients face unique challenges, including variations in growth patterns, developmental needs, and the impact of malnutrition on long-term health outcomes (3). Results indicate that up to 25% of hospitalized patients experience postoperative complications (4, 5), with the most common occurrences including superficial surgical site infections (SSIs), deep SSIs, urinary tract infections, and unplanned returns to the operating room (6). However, defining pediatric malnutrition within the context of surgical disease poses a significant challenge due to the distinct nutritional requirements of pediatric patients (7). Additionally, there is ongoing debate regarding the most effective method for assessing malnutrition in children, given that the clinical parameters established for adults often do not align well with those for pediatric malnutrition (8). Consequently, extrapolating the relationship between adult outcomes and post-surgery outcomes in the pediatric population becomes challenging.

Traditionally, malnutrition was assessed through deviations from standard growth curves, necessitating at least two data points (9). However, challenges arise when multiple data points are not readily available during the initial presentation of pediatric patients. Consequently, anthropometric growth indices such as weight-for-height, length/height, and body mass index (BMI)-for-age z scores are now recommended to evaluate nutritional status (9).

To accurately assess and categorize nutritional status in children, the Body Mass Index (BMI) must be adjusted according to age-specific *Z*-scores. The BMI *z*-score adjusts a child's Body Mass Index for age and sex by comparing it to a reference population. A BMI *z*-score below −2.0 indicates underweight, between −2.0 and + 1.0 represents normal weight, between +1.0 and + 2.0 signifies overweight, and above +2.0 indicates obesity. These cut-off points help evaluate nutritional status in pediatrics (10).

Similarly, the incorporation of body composition assessment, which includes Phase angle (PhA), becomes crucial when evaluating these patients. Beyond the nutritional dimension, body composition appears to be indicative of clinical prognosis (11, 12). PhA, a directly measured variable in bioelectrical impedance analysis, is considered an indicator of body cell mass and the ratio of extracellular to intracellular water, and is associated with cellular integrity and function (13). PhA has shown positive correlations with various nutritional indicators, such as current weight, arm muscle area (AMA), and percentage of ideal body weight (%IBW). These correlations are especially strong in malnourished children, indicating that a lower PhA may be associated with poorer nutritional condition. In fact, it has a predictive value that exceeds that of some nutritional screening tools, such as STRONGkids (14). Assessing body composition in children and adolescents is essential for evaluating their nutritional status during growth and may impact health outcomes. Furthermore, PhA has been reported to exhibit non-linear behavior. Differences between school-aged children and adolescents are observed, potentially due to varying stages of sexual maturation. Previous studies show a correlation between BMI and PhA in the pediatric population, suggesting that both tools could be used in pre-surgical evaluation throughout life (13).

PhA is a variable derived from bioelectrical impedance analysis that has emerged as a significant indicator in the assessment of nutritional status and overall health, as it reflects body cell mass and the ratio of extracellular to intracellular water (15).

In the pediatric population, PhA increases with age, particularly after puberty, and may differ between sexes due to pubertal development. Additionally, it is positively associated with physical fitness and lean body mass (13).

Incorporating PhA into clinical assessment can provide an additional perspective beyond traditional indices, aiding in the customization of nutritional and intervention strategies to improve postoperative outcomes in the pediatric population.

Recognizing patients with nutritional deficiencies enables the development of treatment strategies aimed at achieving improved outcomes, potentially reducing the risk of postoperative mortality in future patients. Additionally, it is important to note that there is no single tool available for evaluating patients. Both PhA and BMI are generally practical and easy to apply. However, it remains unclear whether they perform equally well in school-aged children and adolescents (12). Therefore, our aim is to determine the relationship between nutritional status, PhA, and post-surgical complications in pediatric patients undergoing surgery.

Materials and methods

Study design

This prospective cohort study was conducted from March to November 2022, involving patients who underwent major non-ambulatory surgery. The study was carried out in a third level hospital where surgeries in different areas are performed, general surgery, orthopedic surgery, plastic surgery, urology, otorhinolaryngology, oncology, cardiology and stomatology. However, for this study only major elective surgery was considered. The inclusion criteria comprised patients aged 3–17 years, while the exclusion criteria encompassed patients scheduled for vascular access placement, closed reduction for bone fractures, ophthalmologic exploration under sedation, and non-therapeutic endoscopic procedures, as well as those who had undergone surgery within 2 months prior to evaluation. The protocol received approval from the institutional review board (IRB protocol number 2021/070). All participants provided their assent and parental or guardian-signed informed consent.

Nutritional status

Anthropometrical measurements were recorded upon admission, before the surgery, including weight and height, obtained from participants dressed in light-weight clothing and without shoes, measured using methods previously described by the World Health Organization (WHO) (9), before the patient entered the operating room. BMI was categorized into age-*Z*-scores for patients, classifying malnutrition as: none: > −1, mild: −1 to −1.9, moderate: −2 to −2.9,

severe: <−3 (9). Additionally, we categorized BMI into three categories: normal weight, overweight, and obesity, according to CDC 2022 for 2–20 years (16) and with the support with app https://peditools.org/growthpedi/.

We obtained weight and height measurements just before their surgical procedure, using the SECA scale the same scale for all patients, and the same metric ruler for height. For younger patients or those with disabilities, we used a metric ruler for stretcher and the same SECA scale used for wheelchairs. With the patients with disabilities or minors, the family members supported us.

Body composition for phase angle

Measurements were performed by the operator using an impedance device (Bioelectric RJL Systems Quantum IV).[1] Bioimpedance is a method used to assess body composition by measuring the resistance and reactance of body tissues to an imperceptible multifrequency electrical current. This helps determine the distribution of body fluids and tissue mass. One of the key variables obtained from bioimpedance analysis (BIA) is the PhA, which reflects the relative ratio of extracellular to intracellular water and is considered an indicator of cell membrane integrity and overall cellular health. It was measured using the previously described standardized method (15). All patients fasted for at least 4 h before the measurement and before surgery, and they were requested to remove metal objects that were in direct contact with the body and could potentially interfere with the test. Subjects were positioned in a supine posture, with arms and legs extended away from the body and palms facing downward. Electrodes were positioned in pairs on the right extremities, located at the back of the hand and foot, through which an imperceptible multifrequency current was introduced (15). After we obtaining the anthropometric and analyzer data, these were entered into the system https://www.realbia.com/interactive-online-bia/, where the "New-Pediatric" equation was selected and with that the values of fat-free mass and muscle mass were obtained.

Outcomes

General complication was defined as the presence of the following characteristics within 30 days after surgery: death, unplanned return to the operating room, morbidity (including pneumonia, inotropic support, urinary tract infection, venous thromboembolism, respiratory failure, postoperative mechanical ventilation, and oxygen support), or SSIs (17).

Postoperative morbidity was defined as the presence of pneumonia or urinary tract infection, the requirement for inotropic support (using medications necessary to increase cardiac output), mechanical ventilation, or oxygen supplementation within the first 48 h after surgery, or the diagnosis of venous thromboembolism or renal failure (17). Regarding SSIs, characteristics of the surgical wound were assessed, including pain or tenderness, localized inflammation, redness, heat, purulent drainage, dehiscence, fever exceeding 38°C, or the presence of an abscess in the surgical wound.

Follow-up

The primary outcome of interest was the development of postoperative complications within 30 days after surgery.

Covariates

Upon admission, demographic characteristics and dietary intake of the enrolled children were recorded, including their age, which was grouped into pre-school children aged 3–12 years old and adolescents older than 12 years old. Surgical risk factors, including hematological disorders, neuromuscular disorders, cardiac risk factors, structural abnormalities of the central nervous system, and developmental delays, were assessed. Pre-operative conditions, including sepsis 48 h prior to surgery, mechanical ventilation, oxygen supplementation, inotropic support, and parenteral nutrition, were documented. Postoperative conditions were categorized by discharge status (outpatient or inpatient), type of surgical wound (clean, clean-contaminated, or contaminated), number of procedures, and duration of surgery in minutes.

Statistical analysis

Values are presented as mean and standard deviation (SD) for continuous variables with a normal distribution, median (interquartile range, IQR) for non-normally distributed variables, and as a percentage of the total for categorical variables. Differences between groups were assessed using the Chi-squared test, Student's t-test, or Mann–Whitney U test, as appropriate. We used logistic and linear regression to calculate the odds ratio of post-surgical complications associated with nutritional characteristics. Multiple imputation analyses were performed for missing data. Those variables that were potentially confounding and statistically significant in the bivariate analysis were included in the logistic regression.

A p value <0.05 was considered statistically significant. All statistical analyses were performed using STATA software (version 17.1; Stata Corp., College Station, TX).

Results

During the study period, a total of 1,233 surgeries were performed, of which 404 met the criteria and were invited to participate, 12 of them accepted but their surgeries were canceled or their phone number changed, a total of 391 patients who underwent surgery in 2022 were included, with 60% (n = 235) being schoolchildren and preschoolers and the majority of all the sample were male (n = 230, 59%).

In children ≤12 years old, considering the critical stages of neurological and muscular development, neuromuscular disorders and developmental disabilities were the most common comorbidities,

1 https://cdn.shopify.com/s/files/1/0829/4989/8550/files/quantum_4-manual1.pdf?v=1694476372

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whereas central nervous system structural abnormalities were predominant in those >12 years old. Regarding surgical-related conditions, the study revealed that most outpatient cases ($n = 251$, 64%) were discharged. Additionally, the duration of procedures (measured in minutes) was notably extended in individuals aged >12 years, with a comparison of 70 min versus 90 min (p-value <0.05). This suggests that surgical procedures in adolescents may be more complex or involve longer preparation times. The most common services were general surgery, orthopedics, and plastic surgery (Table 1).

By the end of the follow-up period, 51 (13%) patients had developed post-surgical complications, with surgical site infection being the most common complication (Table 2). Although the overall complication rates did not significantly differ between age groups, specific complications like surgical site infections were prevalent across all the participants.

Table 3 presents the general characteristics of nutritional status and body composition according to post-surgical complications. We observe in younger participants a higher prevalence of complications in malnutrition by BMI and according to PhA it was lower in adolescents with complications ($p < 0.05$ for both). Regarding hydration status, patients with postoperative complications have a higher extracellular water, with a median of 10.9 liters compared to 8.3 liters in those without complications ($p = 0.036$).

After applying linear regression models, we identified an association between dietary fat intake and duration of surgery in younger patients (≤ 12 years old), as well as an association between length of stay (LOS) and PhA across the population (Table 4).

In the logistic regression model, for children (≤ 12 years old), malnutrition, as indicated by the z-score, was a significant risk

TABLE 1 General characteristics of the population.

Characteristics	All participants $n = 391$	Preschoolers and schoolers $n = 235$	Adolescents $n = 156$	p-value
Gender				
Female *n*, (%)	161 (41)	97 (41)	64 (41)	0.99
Surgical risk factors				
Comorbidities				
Neuromuscular disorder *n*, (%)	29 (7)	20 (9)	9 (6)	0.31
Hematological disorder *n*, (%)	21 (5)	12 (5)	9 (6)	0.78
Cardiac risk factor *n*, (%)	22 (6)	15 (6)	7 (4)	0.43
Central Nervous System structural abnormality *n*, (%)	22 (6)	10 (5)	12 (8)	0.15
Developmental delay n, (%)	25 (6.5)	19 (8)	6 (4)	0.09
Conditions associated with surgery				
Pre-surgery condition* *n*, (%)	6 (1.5)	4 (2)	2 (1)	0.99
Postoperative condition				
Postoperative stay				
In-patient *n*, (%)	140 (36)	74 (31)	66 (42)	<0.05
Out-patient *n*, (%)	251 (64)	161 (69)	90 (58)	
Type of surgical wound				
Clean *n*, (%)	336 (86)	201 (86)	135 (86)	0.88
Clean-contaminated/contaminated** *n*, (%)	140 (36)	29 (14)	21 (14)	
Number of procedures (IQR)				
One procedure	283 (72)	169 (72)	114 (73)	0.82
More than one procedure	108 (28)	66 (28)	42 (27)	
Duration of surgery in minutes, median (IQR)	80 (50–130)	70 (50–120)	90 (60–150)	<0.05
Days of preoperative stay, median (IQR)	1 (1–3)	1 (1–3)	1 (1–5)	0.47
Hospital stays (days)	0.4 (4.5)	0.2 (3.5)	0.6 (5.3)	0.36
Treating service				
General surgery *n*, (%)	97 (25)	65 (28)	32 (21)	0.14
Orthopedics *n*, (%)	100 (26)	56 (24)	44 (28)	
Plastic surgery *n*, (%)	74 (19)	38 (16)	36 (23)	
Others *** *n*, (%)	120 (30)	76 (32)	44 (28)	

*Sepsis 48 h prior, mechanical ventilation, oxygen supply, inotropic support, parenteral nutrition. **No dirty-infected wound events. ***Urology, Otorhinolaryngology, Oncological surgery, Cardiology surgery, Stomatology.

TABLE 2 Post-operative complications.

Complications	All participants $n = 391$	Preschoolers and schoolers $n = 235$	Adolescents $n = 156$	p-value
Any complication *n*, (%)	51 (13)	27 (12)	24 (15)	0.26
Morbidity * *n*, (%)	10 (2.6)	5 (2)	5 (3)	0.53
Death *n*, (%)	1 (0.3)	0 (0)	1 (0.5)	0.22
Surgical site infection *n*, (%)	41 (10.5)	23 (10)	18 (12)	0.58
Unplanned return to the operating room *n*, (%)	6 (1.5)	2 (1)	4 (3)	0.18

*Pneumonia, inotropic support, urinary tract infection, venous thromboembolism, respiratory failure, postoperative mechanical ventilation and oxygen support were considered.

factor for surgical site infections, morbidity, and general complications ($p < 0.01$). Conversely, for patients >12 years old, PhA emerged as a protective factor against the same post-operative complications (Table 5). All models were adjusted for gender and comorbidities, highlighting the differential significance of malnutrition and PhA in postoperative complications according to patient age (Table 5).

Discussion

This study identified that PhA is associated with hospital stay time in all the participants. We found an association between malnutrition assessed by BMI *z*-score, and postoperative complications in children under 12 years old, whit no association in older patients. Regarding, PhA and dietary fat emerged as a protective factor against postoperative complications in adolescents. These findings underscore the importance of preoperative assessment that considers both. No association founded with hand grip strength or FFM.

Moreover, tailoring interventions based on age-specific risk factors may improve the effectiveness of postoperative care. It has been observed that PhA is a valuable marker in pediatric populations, with lower PhA values associated with malnutrition in younger children. They highlighted the need for standardized PhA measurements to improve comparability and diagnostic accuracy. Their review reinforces the importance of integrating PhA into preoperative assessments (14).

It has been reported that up to 50% of patients undergoing surgery experience some complications related to the procedure (7, 18–20). An observation was made in this study that 14% of the participants experienced some form of complication within the first 30 days after surgery (all elective), with the majority originating from orthopedic and general surgery services.

Differences in the incidence of complications could be largely influenced by the characteristics of the population, the types of interventions performed, or even the types of complications reported. Disparities have been noted in the occurrence across different racial groups and age categories, with a higher prevalence observed in patients aged 12 years or younger (19).

In this study, surgical site infections exhibited the highest incidence in the overall population, showing a pattern consistent with previous findings in general surgery. However, this incidence was slightly higher than that reported for appendectomy in the pediatric population (20, 21). Additionally, a lower frequency of reoperations was observed compared to what has been reported in the pediatric population with Crohn's disease (7).

Numerous studies have demonstrated a possible association between malnutrition and a higher risk of postoperative complications in adults (2, 7, 18). Previous study results cannot be directly extrapolated to the pediatric population, although evidence suggests that malnourished children with congenital heart disease (CHD) and those undergoing otolaryngological surgeries may experience significant deterioration in their nutritional status post-surgery (10, 22–24). While preoperative malnutrition assessed through anthropometric measures does not show a significant association with postoperative complications in elective pediatric surgeries (25), specific studies have found that parameters like mid-arm circumference z-scores and serum protein concentrations are useful in predicting certain short-term postoperative outcomes (26). Phase angle, a key indicator of body composition, has been shown to be a valuable predictor of complications in other populations (10, 14). Including phase angle in preoperative assessments could help identify patients who may benefit from appropriate perioperative nutritional interventions.

Based on the findings, our study recommends preoperative evaluations for all individuals scheduled for elective surgery. However, the use of PhA measurements may need to be tailored based on age.

Assessing nutritional status in the pediatric population presents a challenge in daily clinical practice due to the changes during this stage of life. Recently, the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines (9) recommend evaluating malnutrition in the pediatric population using the BMI-for-age *z*-score, which serves as a sensitive and useful tool to identify patients with malnutrition. Based on these guidelines, association between preoperative nutritional status and postoperative LOS has been reported (7, 27), consistent with findings from our study. Furthermore, a negative effect on intensive care unit LOS and the duration of mechanical ventilation has also been reported (24).

The BMI *z*-score alone does not fully capture the complexity of nutritional status and its impact on clinical outcomes, particularly in post-surgical processes.

PhA, on the other hand, measures cell membrane integrity and cell mass, reflecting tissue quality and overall nutritional and health status. Therefore, our study aligns with evidence showing that PhA can be a sensitive marker for malnutrition and inflammatory status, with the ability to predict complications and adverse outcomes across various populations (12, 28). PhA has been demonstrated to have a significant association with BMI and other nutritional indicators, suggesting that these two parameters could offer complementary insights into nutritional status (14).

PhA, by reflecting cellular mass integrity and body composition (29), offers a complementary perspective that may be more sensitive

TABLE 3 Nutritional and body composition characteristics according to complications.

Nutritional characteristics	All participants *n* = 391	Uncomplicated *n* = 340	Complications *n* = 51	*p*-value
Malnutrition by *Z*-score (yes) *n*, (%)	68 (17)	55 (16)	13 (26)	0.11
Preschoolers and schoolers *n*, (%)	45 (19)	31 (17)	10 (40)	0.013
Adolescents *n*, (%)	23 (15)	24 (15)	3 (12)	0.77
Nutritional status by BMI percentile, *n*, (%)				
Malnutrition	41 (10)	37 (11)	8 (16)	
Well nourished	226 (58)	195 (57)	31 (61)	0.08
Overweight	66 (17)	67 (20)	3 (6)	
Obesity	58 (15)	41 (12)	9 (18)	
Hand grip strength (kg), median (IQR)				
Preschoolers and schoolers				
Female	8.7 (5.8–11.4)	8.7 (6.4–11.1)	9.8 (2.4–12.4)	056
Male	7.9 (4.6–12.0)	8.1 (4.2–11.9)	7.7 (7.0–14.6)	0.72
Adolescents				
Female	19 (15.4–22.7)	18.9 (14.4–22.7)	19.8 (17.3–21.2)	0.93
Male	26.4 (19.2–33.6)	26.5 (19.8–34.2)	21.3 (13.1–30.3)	0.16
Bioelectrical impedance				
Phase angle (°), median (IQR)	5.08 (4.4–5.7)	5.1 (4.4–5.7)	5.2 (4.2–5.8)	0.67
Fat (kg), median (IQR)	12.0 (7–19.6)	11.9 (7–19.6)	15.1 (6.6–19.5)	0.38
Fat of total weight (%), mean ± SD	29.2 ± 9.9	29.3 ± 9.9	28.7 ± 10.3	0.73
FFM (kg), median (IQR)	29.7 (20.6–39.6)	28.8 (20.1–38.9)	33.4 (26.2–44.9)	0.037
SMM (kg), median (IQR)	12.4 (8.2–17.6)	11.8 (8–17.1)	14.2 (10.3–19.5)	0.087
Preschoolers and Schoolers, median (IQR)				
Female	8.4 (6.5–10.5)	8.2 (6.6–10.2)	9.2 (6.5–14.5)	0.48
Male	8.6 (6.5–11.4)	8.6 (6.5–11)	9.9 (6.7–13.1)	0.56
Adolescents, median (IQR)				
Female	15.1 (12.9–17.3)	15.1 (13.0–17.3)	13.7 (12.8–16.7)	0.97
Male	19.9 (16.0–25)	19.8 (16.0–25.2)	19.9 (17.9–22.5)	0.81
SMM of total weight (%), median (IQR)	29.0 (25.8–33.1)	28.9 (25.8–32.6)	30.4 (24.8–34.1)	0.54
SMM of FFM (%), median (IQR)	42.2 (39.1–45)	42.2 (38.8–44.9)	42.8 (40.2–45.7)	0.42
Total body water (L), median (IQR)	22.3 (16.1–28.7)	21.9 (16–27.9)	24.2 (19.4–32.4)	0.050

(Continued)

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TABLE 3 (Continued)

Nutritional characteristics	All participants $n = 391$	Uncomplicated $n = 340$	Complications $n = 51$	p-value
Intra-cellular water (L), median (IQR)	13.1 (10.8–16.7)	12.9 (10.7–16.3)	14.0 (12.4–18.9)	0.094
Extra-cellular water (L), median (IQR)	8.7 (5.6–12.2)	8.3 (5.5–12.1)	10.9 (6.7–13.6)	0.036
Dietary intake				
DEI (kcal/day), media (IQR)	1702 (1442–1899)	1,696 (1435–1913)	1723 (1549–1861)	0.50
Preschoolers and Schoolers	1,612 (1370–1831)	1,586 (1367–1825)	1,695 (1570–1856)	0.13
Adolescents	1790 (1583–1976)	1781 (1512–2004)	1783 (1549–1861)	0.44
Proteins (g/kg/day), median (IQR)	1.9 (1.27–2.84)	2.0 (1.3–2.8)	1.5 (1.2–3.1)	0.51
Preschoolers and Schoolers	2.6 (1.8–3.5)	2.7 (20–3.5)	3.0 (2.0–4.6)	0.38
Adolescents	1.3 (1.0–1.7)	1.3 (1.0–18)	1.2 (1.1–1.4)	0.28
Fat percentage, median (IQR)	33 (29–38)	33 (28.7–37.9)	33 (27–37.2)	0.58
Preschoolers and Schoolers	33.8 (29.3–38)	33.3 (29.4–38.0)	36 (31.7–40.0)	0.13
Adolescents	32.3 (27.5–37.4)	33 (28–37.5)	29 (24–35.4)	0.03

BMI, Body Mass Index; DEI, Dietary energy intake; FFM, Fat-Free Mass; SMM, Skeletal Muscle Mass.

to changes in muscle mass and hydration status (30), which are crucial for postoperative recovery (31). In younger children, the BMI *z*-score may not fully capture fluctuations in muscle mass and hydration that are important for postoperative recovery (32). PhA, by measuring body reactance, could provide a more accurate assessment of these factors (15).

It has been suggested that an important factor such as BMI has an impact on the duration of surgery, with each additional BMI point resulting in an increase of 58.0 s in surgical time (26, 33). However, the impact of dietary factors on these outcomes has been understudied. Our study observed that dietary fat intake in children aged 12 years or under is associated with prolonged duration of surgery. This could be explained by the influence of high fat intake in the diet, which increases the BMI of patients and affects both the preparation and the surgical procedure. It also contributes to difficulty in transferring the patient to the stretcher in the operating room and in proper management of the airways. Excess fat can interfere with intraoperative surgical exposure (25).

However, there is limited evidence evaluating the effect of preoperative malnutrition and PhA in the pediatric population (27). The PhA is determined by the resistance to the current and the capacitance of the cell membrane (reactance) (15). It has been used to quantify the integrity of cell membranes and the extent of their redistribution and can be negatively influenced by various clinical conditions, such as malnutrition (14).

In adults, associations between PhA, anthropometric measurements, and muscle strength, as well as postoperative infectious complications, have been reported (34). This confirms the notion that preoperative malnutrition can serve as an independent predictor of serious complications in patients undergoing major surgery (35, 36). In this study, PhA was associated with postoperative LOS across the entire population, consistent with findings from previous studies (18, 37–42), particularly when the PhA falls below 2.7 after 2 days of hospitalization (37).

The use of PhA as an indicator of malnutrition risk should be accompanied by a thorough assessment of hydration status, specifically extracellular water expansion. The behavior of extracellular water in patients scheduled for surgery is interesting, as it could be related to chronic inflammation or pre-existing metabolic stress (43, 44). A study in patients with cancer and sarcopenia suggests that increased ECW indicates an inflammatory state, which is associated with poorer clinical outcomes (45).

According to Lukaski et al. (46), PhA is a marker of cell membrane integrity and cellular health, but its reliability as a predictor of malnutrition is compromised by fluid shifts resulting from inflammation and disease-related malnutrition. Similarly, Bellido et al. (47) emphasize that standardizing PhA measurements and incorporating hydration assessments are crucial for accurate risk evaluation and monitoring of nutritional status. This consideration is particularly relevant in postoperative settings, where inflammation and fluid imbalance can significantly impact recovery and the risk of complications. Therefore, integrating hydration status into BIA evaluations can enhance the accuracy of predicting malnutrition and guide more effective patient management strategies.

For the analysis of nutritional status, it is important to use the PhA, which reflects changes in the cell membrane and alterations in the fluid balance. It has been observed that measuring the preoperative PhA helps in predicting the occurrence of postoperative infections

TABLE 4 Linear regression for association between surgery duration and hospital stay with nutritional characteristics.

	All participants		Preschoolers and schoolers		Adolescents	
	β. Coefficient (95% CI)	*p*-value	*β*. Coefficient (95% CI)	*p*-value	*β*. Coefficient (95% CI)	*p*-value
Duration of surgery (minutes)						
Malnutrition (yes)	7.28 (−13.55,28.44)	0.50	14.63 (−11.27,40.54)	0.27	−0.14 (−38.13,37.86)	0.99
Phase angle	1.44 (−6.19,9.06)	0.71	3.55 (−8.66,15.77)	0.57	−8.52 (−20.73,3.68)	0.37
Dietary fat/day (%)	−1.76 (−3.03, −0.49)	<0.01	−2.49 (−4.19, −7.44)	<0.01	−0.74 (−2.67, 1.19)	0.45
FFM	0.33 (−0.42, 1.07)	0.39	0.10 (−1.74, 1.94)	0.91	0.09 (−1.33, 1.51)	0.90
Hand grip strength	0.60 (−0.19–1.40)	0.14	0.95 (−0.98, 2.88)	0.33	−0.53 (−2.01, 0.95)	0.48
Hospital stay (days)						
Malnutrition (yes)	0.53 (−0.66, 1.72)	0.38	−0.49 (−1.94, 0.95)	0.50	2.37 (0.24, 4.50)	0.03
Phase angle	−0.85 (−1.26, −0.43)	<0.01	−1.18 (−0.18, −0.52)	<0.01	−1.09 (−1.77, −0.42)	<0.01
Dietary fat/day (%)	−0.05 (−0.12, 0.02)	0.19	−0.9 (−0.19, 0.01)	0.07	0.01 (−0.09, 0.12)	0.88
FFM	−0.02 (−0.06, 0.03)	0.445	−0.01 (−0.10,0.08)	0.82	−0.06 (−0.15, 0.02)	0.16
Hand grip strength	−0.01 (−0.06, 0.03)	0.59	0.01 (−0.11, 0.11)	0.98	−0.06 (−0.15, 0.02)	0.15

FFM, Fat-Free Mass. All models: Adjusted by gender, comorbidities, and dietary intake.

TABLE 5 Logistic regression for the association between perioperative complications and nutritional characteristics.

	All participants		Preschoolers and schoolers		Adolescents	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Surgical site infection						
Malnutrition (yes)	1.65 (0.75–3.62)	0.21	3.72 (1.42–9.69)	<0.01	0.29 (0.04–2.52)	0.27
Phase angle	0.89 (0.65–1.23)	0.49	1.24 (0.70–2.18)	0.46	0.69 (0.44–1.07)	0.10
Dietary fat/day (%)	0.98 (0.94–10.4)	0.61	1.02 (0.95–1.09)	0.57	0.94 (0.87–1.02)	0.14
FFM	1.01 (0.98–1.04)	0.48	1.01 (0.94–1.09)	0.37	1.01 (0.95–1.07)	0.82
Hand grip strength	0.99 (0.96–1.02)	0.56	1.03 (0.95–1.13)	0.53	0.95 (0.88–1.01)	0.10
Morbidity						
Malnutrition (yes)	3.63 (0.92–14.26)	0.06	14.95 (1.70–131)	0.01	1.15 (0.09–13.7)	0.91
Phase angle	0.66 (0.35–1.24)	0.19	1.05 (0.35–3.20)	0.93	0.35 (0.15–0.85)	0.02
Dietary fat/day (%)	0.96 (0.86–1.07)	0.42	1.01 (0.86–1.20)	0.83	0.91 (0.76–1.09)	0.30
FFM	1.03 (0.97–1.09)	0.30	0.83 (0.62–1.13)	0.23	1.02 (0.92–1.13)	0.72
Hand grip strength	1.03 (0.96–1.09)	0.41	0.99 (0.81–1.21)	0.94	0.98 (0.88–1.09)	0.76
General Complication						
Malnutrition (yes)	1.81 (0.89–3.67)	0.10	3.86 (1.61–9.27)	<0.01	0.51 (0.11–2.50)	0.41
Phase angle	0.84 (0.63–1.13)	0.25	1.01 (0.61–1.67)	0.97	0.63 (0.42–0.94)	0.02
Dietary fat/day (%)	0.97 (0.93–1.02)	0.22	1.01 (0.94–1.08)	0.75	0.93 (0.86–0.99)	0.04
FFM	1.02 (0.99–1.05)	0.11	1.01 (0.94–1.09)	0.71	1.01 (0.96–1.07)	0.58
Hand grip strength	1.00 (0.97–1.03)	0.99	1.00 (0.93–1.08)	0.95	0.96 (0.91–1.02)	0.23

FFM, Fat-Free Mass. All models: Adjusted by gender and comorbidities, and dietary intake.

(48), with a decrease noted in instances of disease, inflammation, or malnutrition (49) caused by microorganisms after major surgery (48). Malnutrition is a very important factor in immune dysfunction, affecting the body's ability to fight infections (48). It also influences wound healing; for instance, obesity can increase the risk of rupture or infectious complications, while a diet with low protein and energy intake can delay proper healing (33, 50). Because the PhA serves as a marker for both the quantity and quality of soft tissue mass, many authors consider it a useful marker of nutritional status and the strongest predictor of complications (14).

As part of the strengths of this study, the prospective design allows real-time data collection, which enhances data accuracy and minimizes retrospective biases. The inclusion of pediatric patients aged 3–17 provides a comprehensive insight into the association between nutritional status and postoperative complications across various developmental stages. Assessing nutritional status through

parameters such as BMI, *z*-score, muscle strength, and PhA offers a thorough evaluation of patients' physical condition. Considering clinical risk factors, such as neuromuscular disorders and central nervous system structural abnormalities, strengthens the validity of the results by accounting for significant variables that could influence postoperative complications. The limitations of the study include its sample size, which may potentially restrict the generalization of the findings to a broader population. Future research with larger cohorts could validate and strengthen the obtained results. Additionally, the 30-day follow-up post-surgery may not capture long-term complications. It is important to take these data with caution, it is necessary to do future studies with a specific analysis for those patients with neurological or muscular impairment.

All the findings in this study provide a comprehensive overview of the surgical landscape, patient demographics, and postoperative outcomes. Tailoring interventions based on age-specific risk factors and understanding the association between nutritional status and surgical outcomes are crucial for improving patient care and optimizing healthcare resources. Malnutrition is an important predictor of serious complications in patients undergoing major surgery. The PhA serves as a valuable tool for assessing the nutritional status of surgical patients and for predicting the risk of postoperative complications.

Conclusion

Malnutrition, as indicated by *z*-scores, is an important predictor of postoperative complications in preschoolers and school-age children who underwent surgery, whereas PhA proves useful in predicting complications in adolescents. PhA was a predictor of length of hospital stay in all the participants. Personalized nutritional and body composition assessments tailored to age are essential for improving outcomes for patients undergoing surgery. This research highlights the need for personalized assessment of nutrition and body composition based on age in pediatric patients undergoing surgery, which could significantly improve outcomes and patient recovery.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics committe from Instituto Nacional de Pediatria. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

MD-A: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. LR-A: Data curation, Formal analysis, Software, Writing – original draft, Writing – review & editing. JH-L: Investigation, Methodology, Writing – original draft, Writing – review & editing. BP-G: Conceptualization, Funding acquisition, Project administration, Resources, Writing – original draft, Writing – review & editing. KI-A: Methodology, Visualization, Writing – original draft, Writing – review & editing. SC-L: Conceptualization, Writing – original draft, Writing – review & editing. JG-Z: Conceptualization, Funding acquisition, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing. AG-O: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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EDITED BY
Luciane Bresciani Salaroli,
Federal University of Espirito Santo, Brazil

REVIEWED BY
Monica Cattafesta,
Federal University of Espirito Santo, Brazil
Camila Bruneli Do Prado,
Federal University of Espirito Santo, Brazil
Virginia Maria Muniz,
Secretaria de Estado da Saúde do Espírito Santo, Brazil

*CORRESPONDENCE
Kaiying Yang
yangkaiying1123@126.com

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Association between body roundness index and osteoarthritis: a cross-sectional analysis of NHANES 2011–2018

Huazheng Liang[1,2], Wenyue Si[3], Lin Li[4] and Kaiying Yang[1]*

[1]Department of Pediatric Surgery, Guangzhou Women and Children's Medical Center, National Children's Medical Center for South Central Region, Guangzhou Medical University, Guangzhou, China, [2]School of Pediatrics, Guangzhou Medical University, Guangzhou, China, [3]Department of Science Research and Education Management, Guangzhou Women and Children's Medical Center, National Children's Medical Center for South Central Region, Guangzhou Medical University, Guangzhou, China, [4]Department of Pediatric Surgery, Guangdong Provincial Key Laboratory of Research in Structural Birth Defect Disease, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangdong Provincial Clinical Research Center for Child Health, Guangzhou, China

Objective: The objective of this study was to investigate the potential association between body roundness index (BRI) and the risk of osteoarthritis (OA) in US adults.

Methods: A cross-sectional analysis consisting of 20,232 participants was conducted using data from the National Health and Nutrition Examination Survey (NHANES) from 2011 to 2018. Participants (≥20 years of age) were included and divided into OA and non-OA groups. Then, the demographics and characteristics of the participants were compared between the two groups. The relationship between BRI and OA was assessed using a multivariate logistic regression model with fitted smoothed curve techniques. Additionally, subgroup analyses on the correlation between BRI and OA were performed.

Results: The BRI scores in OA group were significantly higher than in the non-OA group (6.60 ± 2.62 vs. 5.46 ± 2.34, $p < 0.001$). Multivariate logistic analysis revealed that a significantly positive association between BRI and OA (OR = 1.12, 95% CI: 1.09–1.14, $p < 0.001$). In the subgroup analysis, only the race subgroup showed a significant difference between BRI and OA ($p < 0.001$).

Conclusion: Our findings highlight a significantly positive association between BRI and OA prevalence in the general US population.

KEYWORDS

osteoarthritis, body roundness index, obesity, cross-sectional study, National Health and Nutrition Examination Survey

1 Introduction

Osteoarthritis (OA), a common chronic joint disease, is characterized by the progressive deterioration of articular cartilage, the formation of secondary osteophytes, and adaptive changes in subchondral bone (1, 2). Recently, a study by Hunter et al. in 2020 reported that OA affects approximately 3.8% of the global population, equating to approximately 250 million people (3). The incidence and prevalence of OA are estimated to increase significantly in the coming decades, primarily due to an aging population, increasing obesity rates, and a high incidence of traumatic knee injuries (4). OA represents

a significant burden on global public health, causing widespread pain, severely limiting daily activities, and in some cases leading to disability, all of which significantly affect socioeconomic status and quality of life (5). Nevertheless, the etiology of OA remains unclear, and its risk factors are complex, including demographic-level factors such as age, sex, and obesity, as well as joint-level factors such as injury and malalignment (6). Therefore, determining modifiable risk factors may contribute to the development of strategies aimed at delaying OA progression and reducing its burden on public health.

Recently, an increasing number of scientific studies have indicated a strong association between obesity and the development of OA. Obesity may affect the development of OA by altering metabolism and inflammation in the body (7, 8). Obesity is a chronic and complex disease characterized by excessive fat deposition, which can lead to health damage. It can be diagnosed by measuring body mass index (BMI) or waist circumference (9, 10). However, the use of BMI and waist circumference to diagnose obesity has significant limitations. BMI does not account for the specifics of an individual's fat distribution and is subject to significant racial and individual differences, which may lead to misclassification of obesity (11, 12). While the waist circumference index reflects abdominal fat accumulation to some extent, it also fails to reveal the full extent of body fat distribution (13). In contrast, the body roundness index (BRI), as introduced by Thomas et al., is an emerging assessment tool that offers a more comprehensive evaluation of body fat distribution (14). By considering the ratio of body width to body height, the BRI provides a more detailed assessment of an individual's body shape, including the distribution of adiposity throughout the body, allowing it to more accurately reflect obesity status and its potential health risks (14).

To date, an increasing number of studies have indicated a correlation between the BRI and various health conditions, including cardiovascular disease, depression and diabetes (15–19). However, no studies have investigated the potential association between the BRI and OA. Therefore, the present study was conducted to explore the potential association between the BRI and OA among U.S. adults via data from the National Health and Nutrition Examination Survey (NHANES). In addition, our study elucidates the impact of obesity patterns on the risk of developing OA and facilitates the development of targeted prevention and treatment strategies.

2 Materials and methods

2.1 Data sources and study participants

The NHANES is a comprehensive, population-based survey research project sponsored by the National Center for Health Statistics (20, 21). The survey incorporates a detailed methodology involving interviews, physical examinations, and laboratory tests designed to assess the health and nutritional status of adults and children in the United States (22, 23). The data collection process for NHANES adheres to the highest ethical standards, with all study procedures approved by the National Research Ethics Board (1). Furthermore, informed consent was obtained from all participants. The detailed study design and data from NHANES are publicly available for review at: https://www.cdc.gov/nchs/nhanes/.

The data used in this study were derived from the NHANES database, which covers the results collected from four consecutive survey cycles between 2011 and 2018. A total of 39,156 participants were included in the study. Participants younger than 20 years of age ($n = 16{,}539$) were excluded. Additionally, those with missing OA ($n = 51$) or BRI ($n = 2{,}334$) data were also excluded. A total of 20,232 individuals participated in this study (Figure 1).

2.2 Assessment of OA and BRI

A previous study reported up to 81% agreement between self-reported and clinically validated outcomes of OA (24). In the NHANES database, OA status is primarily determined on the basis of a self-report questionnaire collected under the category of "medical conditions." Participants were first asked, "Has a doctor or other health professional ever told you that you had arthritis?." Those who answered "no" were excluded from further analysis in our study. If the response was positive, the participants were then asked the following question: "Which type of arthritis was it?." Those who self-reported "osteoarthritis" were defined as patients with OA, whereas those who reported having a different form of arthritis, including "rheumatoid arthritis and psoriatic arthritis," and their failure to answer the question were categorized as non-OA patients. Previous studies have supported the validity of self-reported OA concerns (25–28). Each NHANES participant was required to undergo a physical examination, which included measurements of height and waist circumference. The BRI formula, developed by Thomas et al., is calculated as $364.2 - 365.5 \times (1 - [(\text{waist circumference } (m)/2\pi)^2/(0.5 \times \text{height}(m))^2])^{1/2}$ (14).

2.3 Covariates

When exploring the association between the BRI and OA, it is important to consider the potential influence and moderating effects of multiple covariates on this relationship. Therefore, we included a total of 14 confounders in this study. The demographic data included age (≥20 years), sex (male vs. female), race (Mexican American, non-Hispanic white, non-Hispanic black, other Hispanic and other races including multiracial), education level (under high school, high school or equivalent, and above high school), marital status (married/cohabiting, widowed/divorced/separated, never married), and family income–poverty ratio (PIR), classified into three categories (< 1.3, 1.3–3.49, and ≥ 3.5), which are distinct segments rather than tertiles as determined by relevant NHANES studies (29, 30). The examination data included weight and BMI, which were classified as low to normal weight (<25), overweight (25–29.9), or obese (≥30) (31). The questionnaire section included questions concerning participation in moderate recreational activities (yes/no), diabetes (yes/no), hypertension (yes/no), cancer (yes/no), and alcohol use. Alcohol use and cigarette use were also assessed. Alcohol use was defined on the basis of the average daily consumption of alcoholic beverages in the past 12 months (32). Cigarette use was differentiated between nonsmokers (total lifetime number of cigarettes <100 cigarettes) and smokers (total lifetime number of cigarettes ≥100 cigarettes) on the basis of lifetime number of cigarettes smoked (33).

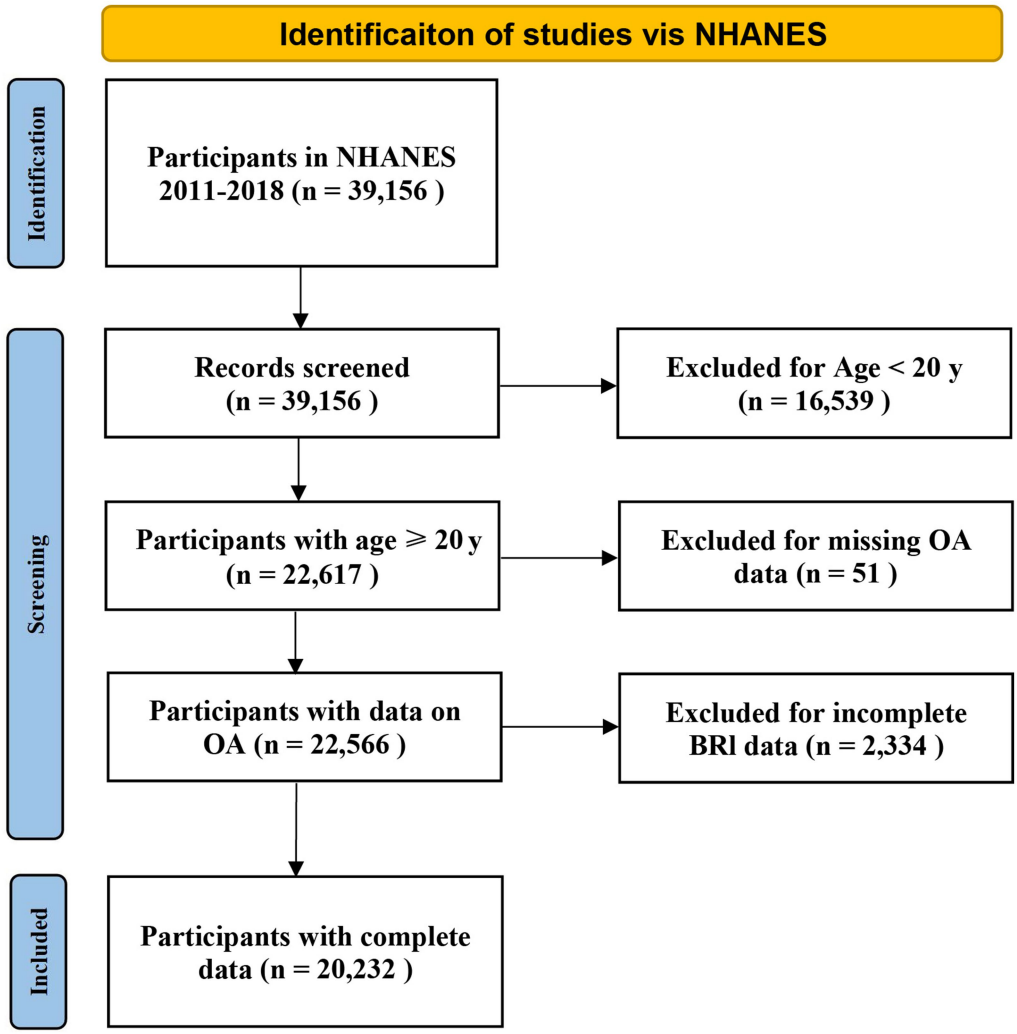

FIGURE 1
Flow chart demonstrating the exclusion and inclusion criteria for identifying OA patients from NHANES 2011-2018. NHANES, National Health and Nutrition Examination Survey.

2.4 Statistical analysis

Continuous variables are expressed as the means with standard deviations (SDs), whereas categorical variables are expressed as percentages. The Kruskal–Wallis test was employed for continuous variables, and the χ^2 test was used for categorical variables. In this study, multiple logistic regression analyses models were used to explore the correlation between the BRI scores and OA. The multiple logistic regression analysis was divided into three models: Model 1 was unadjusted; Model 2 was adjusted for age, sex, and race; and Model 3 was fully adjusted for age, sex, race, PIR, cigarette use, hypertension, education, diabetes, cancer, marital status, moderate recreational activities, and alcohol use. Furthermore, the smoothed curve fitting methods using a generalized additive model (GAM) were used to investigate the nonlinear association between the BRI index and OA. To further elucidate the potential influence of different subgroups on the correlation between BRI and OA, an interaction test was conducted to assess the impact of pertinent clinical confounders. All data analyses were conducted via Empower Stats software, version 2.0[1] (X&Y Solutions, Inc., Boston, MA). A two-sided p value of less than 0.05 was considered statistically significant.

3 Results

3.1 Baseline characteristics of the participants

The detailed baseline characteristics of the participants with and without OA are presented in Table 1. A total of 20,232 participants were enrolled in the present study, with a mean age of 49 years, of whom 48.75% were male and 51.25% were female. Of the 20,232 participants, 2,279 were reported to have OA. Age, sex, race, education, marital status, PIR, BMI, diabetes, cigarette use, alcohol

1 http://www.empowerstats.com

TABLE 1 The baseline characteristics of participants stratified by self-reported osteoarthritis (OA) among U.S. adults from the NHANES 2011–2018.

Characteristic	Total *N* = 20,232 (100%)	Non-OA *N* = 17,953 (88.74%)	OA *N* = 2,279 (11.26%)	*p*-value
Age (year)				< 0.001[a]
20 ~ 39	6,872 (3.97%)	6,728 (37.48%)	144 (6.32%)	
40 ~ 59	6,775 (33.49%)	6,117 (34.07%)	658 (28.87%)	
≥60	6,585 (32.55%)	5,108 (28.45%)	1,477 (64.81%)	
Sex, *n* (%)				< 0.001[a]
Male	9,863 (48.75%)	9,040 (50.35%)	823 (36.11%)	
Female	1,036 (51.25%)	8,913 (49.65%)	1,456 (63.89%)	
Race, *n* (%)				< 0.001[a]
Mexican American	2,740 (13.54%)	2,555 (14.23%)	185 (8.12%)	
Non-Hispanic White	7,449 (36.82%)	6,143 (34.22%)	1,306 (57.31%)	
Non-Hispanic Black	4,591 (22.69%)	4,202 (23.41%)	389 (17.07%)	
Other Hispanic	2,126 (10.51%)	1950 (10.86%)	176 (7.72%)	
Other race/multiracial	3,326 (16.44%)	3,103 (17.28%)	223 (9.78%)	
Education, *n* (%)				< 0.001[a]
Under high school	4,394 (21.72%)	3,969 (22.11%)	425 (18.65%)	
High School or equivalent	4,495 (22.22%)	3,992 (22.24%)	503 (22.07%)	
Above high school	11,343 (56.06%)	9,992 (55.66%)	1,351 (59.28%)	
Marital status, *n* (%)				< 0.001[a]
Married/cohabiting	3,925 (19.40%)	3,733 (20.79%)	192 (8.42%)	
Widowed/divorced/separated	12,000 (59.31%)	10,662 (59.39%)	1,338 (58.71%)	
Never married	4,307 (21.29%)	3,558 (19.82%)	749 (32.87%)	
Moderate recreational activities, *n* (%)				< 0.001[a]
Yes	8,459 (41.81%)	7,615 (42.42%)	844 (37.03%)	
No	11,773 (58.19%)	10,338 (57.58%)	1,435 (62.97%)	
PIR (%)				< 0.001[a]
<1.30	5,933 (29.32%)	5,351 (29.81%)	582 (25.54%)	
1.30 ~ 3.49	8,754 (43.27%)	7,755 (43.20%)	999 (43.84%)	
≥3.50	5,545 (27.41%)	4,847 (27.00%)	698 (30.63%)	
Alcohol use, *n* (%)	20,232 (3.79)	3.68 ± 23.12	4.70 ± 42.80	< 0.001[a]
Cigarette Use, *n* (%)				< 0.001[a]

(Continued)

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TABLE 1 (Continued)

Characteristic	Total *N* = 20,232 (100%)	Non-OA *N* = 17,953 (88.74%)	OA *N* = 2,279 (11.26%)	*p*-value
Smoked ≥ 100 cigarettes in life	8,631 (42.66%)	7,444 (41.46%)	1,187 (52.08%)	
Smoked < 100 cigarettes in life	11,601 (57.34%)	10,509 (58.54%)	1,092 (47.92%)	
Diabetes, *n* (%)				< 0.001[a]
Yes	2,731 (13.50%)	2,212 (12.32%)	519 (22.77%)	
No	17,501 (86.50%)	15,741 (87.68%)	1760 (77.23%)	
Hypertension, *n* (%)				< 0.001[a]
Yes	7,348 (36.32%)	5,945 (33.11%)	1,403 (61.56%)	
No	12,884 (63.68%)	12,008 (66.89%)	876 (38.44%)	
Cancer, *n* (%)				< 0.001[a]
Yes	1873 (9.26%)	1,407 (7.84%)	466 (20.45%)	
No	18,359 (90.74%)	16,546 (92.16%)	1813 (79.55%)	
Weight (kg)	20,232 (81.59)	81.12 ± 21.32	85.27 ± 23.35	<0.001[a]
Height (cm)	20,232 (166.81)	167.05 ± 10.10	164.94 ± 10.08	< 0.001[a]
BMI (%)				< 0.001[a]
<25	5,860 (28.96%)	5,399 (30.07%)	461 (20.23%)	
25 ~ 29.9	6,532 (32.29%)	5,864 (32.66%)	668 (29.31%)	
≥30	7,840 (38.75%)	6,690 (37.26%)	1,150 (50.46%)	
Waist circumference (cm)	20,232 (99.61)	98.85 ± 16.44	105.60 ± 17.06	< 0.001[b]
BRI	20,232 (5.59)	5.46 ± 2.34	6.60 ± 2.62	< 0.001[b]

Continuous variables are presented as the means ± standard deviations. Categorical variables are presented as *n* (%). [a]Chi-square test, [b]Kruskal–Wallis rank sum test. OA, osteoarthritis; Non-OA, nonosteoarthritis; BMI, body mass index; BRI, body roundness index; PIR, family income–poverty ratio.

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TABLE 2 Associations between BRI scores and its quartiles and the risk of OA in participants.

	OR (95% CI), *p*-value		
	Model 1 (*N* = 20,232)	Model 2 (*N* = 20,232)	Model 3 (*N* = 20,232)
BRI	1.19 (1.17, 1.20), < 0.001	1.14 (1.12, 1.16), < 0.001	1.12 (1.09, 1.14), < 0.001
Stratified by BRI quartiles			
Q1	Reference	Reference	Reference
Q2	1.90 (1.63, 2.21), < 0.001	1.32 (1.12, 1.55), < 0.001	1.24 (1.06, 1.46), 0.009
Q3	2.40 (2.07, 2.79), < 0.001	1.45 (1.24, 1.70), < 0.001	1.30 (1.11, 1.53), 0.001
Q4	3.80 (3.30, 4.38), < 0.001	2.18 (1.87, 2.54), < 0.001	1.86 (1.59, 2.18), < 0.001
P for trend	< 0.001	< 0.001	< 0.001

Model 1: adjusted for none. Model 2: adjusted for age (years), sex, and race. Model 3: adjusted for age (years), sex, race, PIR, cigarette use, hypertension, education, diabetes, cancer, marital status, moderate recreational activities, and alcohol use. BMI, body mass index; PIR, family income–poverty ratio; OR, odds ratio; CI, confidence interval.

use, hypertension, cancer, height, weight, waist circumference, and BRI were significantly different between the non-OA and OA groups. Compared with the non-OA group, the OA group had a greater proportion of women (51.25% vs. 48.75%), more never-married people (78.21% vs. 21.79%), and more people with a BMI of 25 or higher (71.04% vs. 28.96%). Moreover, OA is associated with higher levels of education, PIRs, and BRIs, among others.

3.2 Associations between the BRI and the risk of OA

To investigate the relationship between BRI and OA, a stepwise adjusted model using multivariate logistic regression was performed, as illustrated in Table 2. Our results revealed a positive correlation between the BRI and OA. The positive association remained in Model 3, even after adjusting for all relevant variables (OR = 1.12, 95% CI: 1.09–1.14), indicating that for each unit increase in the BRI, the odds of developing OA increased by 12%. For sensitivity analysis, the BRI was further transformed from a continuous variable into categorical quartiles (Table 2). The positive correlation between the BRI and OA remained consistent across all three adjusted models. According to the fully adjusted model, the increased odds of OA were significantly greater in the highest quartile than in the lowest quartile (OR = 1.86, 95% CI: 1.59–2.18).

3.3 Nonlinear relationship between the BRI and OA

In this study, the use of smoothed curve fitting facilitated the investigation of the nonlinear relationship between the BRI index and its tangent into quartiles and OA. The findings of the study indicated a nonlinear, positive correlation between BRI levels and OA (Figures 2, 3).

3.4 Subgroup analysis

In this study, a subgroup analysis was conducted to examine the stability of the nonlinear positive association between the BRI and OA across the identified subgroups (Table 3). The results of subgroup analyses revealed that a significant difference in the correlation between BRI and OA across different race groups (*P* for interaction <0.0001). For race subgroup, the OR (95%CI) of Mexican American, non-Hispanic White, non-Hispanic Black, other Hispanic and other races/multiracial were 1.13 (1.06, 1.20), 1.15 (1.07, 1.23), 1.07 (1.05, 1.10), 1.14 (1.10, 1.18), and 1.27 (1.19, 1.35), respectively. However, the association between the BRI and OA was not influenced by sex, education level, cigarette use, marital status, moderate recreational activities, PIR, hypertension, cancer, or diabetes mellitus (all *P* for interaction >0.05). This finding indicates that the nonlinear positive correlation between the BRI and OA remained robustly stable across all the cases except subgroup of race.

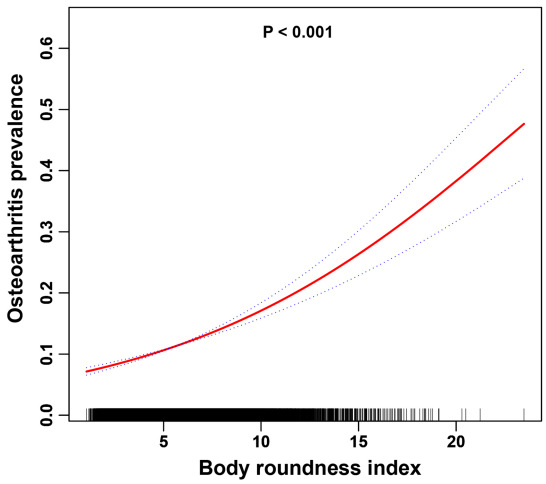

FIGURE 2
The association between the BRI index and OA is illustrated via smoothed curve fitting methods using a generalized additive model. Adjusted for age, sex, race, PIR, cigarette use, hypertension, education, diabetes, cancer, marital status, moderate recreational activities, and alcohol use. The solid red line depicts the smooth curve fit between the variables, whereas the blue bands represent the 95% confidence intervals derived from the fit.

4 Discussion

Obesity has been considered the key modifiable risk factor for OA (34). Recently, a considerable number of clinical studies have focused

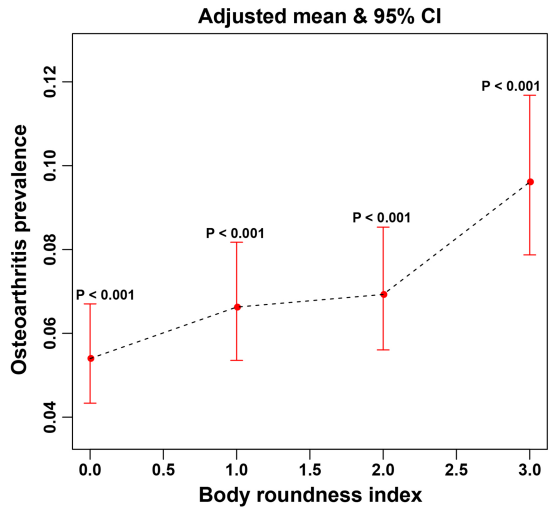

FIGURE 3
The associations between quartiles of BRI and OA were analyzed via smoothed curve fitting. The x-axis represents the quartiles of the BRI, which are categorized as Q1, Q2, Q3, and Q4, with the corresponding values indicated on the axis. The y-axis displays the adjusted mean prevalence of OA and the 95% confidence intervals for each BRI quartile. *P*-interaction was used to evaluate the interaction, with <0.05 indicating statistical significance.

on investigating the relationships between various indicators of obesity (such as BMI, waist circumference, and muscle mass) and the development and progression of OA (34–36). An observational study by Zhang et al. demonstrated that an increase in BMI, a traditional measure of obesity, is positively associated with the risk of OA, with the effect being particularly significant in patients with knee OA (35). In addition, a regional study in the U.S. revealed that an increase in waist circumference, a measure of abdominal obesity, is not only associated with an elevated risk of OA but also may predict a future decline in physical function (36). This highlights the importance of monitoring waist circumference alongside BMI in the clinical management of OA. Moreover, interest in the relationship between the loss of muscle mass, known as sarcopenia, and OA is increasing. Several studies have suggested that sarcopenia may increase the risk of OA by affecting the body's metabolic and functional status (37–39). These findings demonstrate the close association between obesity and OA. However, these traditional obesity indicators have their limitations. For instance, BMI does not account for individual fat distribution, and waist circumference only reflects abdominal obesity without capturing overall body fat distribution. Given these limitations, our study therefore explores the relationship between BRI and OA to provide a more comprehensive understanding of how visceral fat may influence OA development. This not only reinforces the link between obesity and OA but also provides a new direction for future research, highlighting the importance of body fat distribution in OA risk assessment.

Previously, substantial evidence indicated a significant correlation between the BRI and various diseases (18, 40–43). A cross-sectional study revealed that the BRI was associated with an estimated low glomerular filtration rate in a Chinese population, providing evidence that central obesity may play a role in the progression of chronic kidney disease (40). A retrospective study conducted in Japan demonstrated a positive and non-linear correlation between the BRI and diabetes mellitus incidence, indicating a threshold effect: when BRI exceeds 4.137 in females and 3.146 in males, a significant positive correlation with the incidence of type 2 diabetes mellitus is observed (41, 44). Additionally, a cross-sectional study using NHANES data indicated a strong, nonlinear relationship between BRI and metabolic syndrome (MetS), suggesting that the BRI may effectively identify individuals at risk for MetS (42). Furthermore, meta-analyses suggest a bidirectional association between MetS and OA, implying that OA can predict an increased risk of MetS, while MetS may also promote the development of OA (45). Moreover, BRI is shown to outperform traditional anthropometric indices, such as BMI, body shape index, and body adiposity index, in predicting MetS (46). In addition, BRI has been a positive association with hypertension and cardiovascular disease (47). Consequently, these studies implies that BRI may be associated with the OA risk through its association with MetS, thereby supporting its use as an indicator for assessing OA risk.

On the basis of the above research findings, we hypothesize that there may be an intrinsic association between the BRI and OA. To the best of our knowledge, this is the first cross-sectional study investigating the association between the BRI and OA. By analyzing cross-sectional data from 20,232 participants, we identified a significant and nonlinear positive association between the BRI and OA, providing compelling evidence for understanding the relationship between these two variables. Furthermore, through rigorous multivariate logistic regression analyses, we excluded the interference of other potential confounders and confirmed that a high BRI is an independent and significant risk factor for the development of OA. Subgroup analyses revealed that the associations between the BRI and OA were consistent across various factors, including sex, education level, cigarette use, marital status, moderate recreational activities, PIR, hypertension, cancer, and diabetes. Additionally, racial differences were found to partially affect the association between BRI and OA. Racial differences may influence the onset and manifestation of OA, potentially through a combination of biological and social factors, including genetic susceptibility, environmental factors, and lifestyle (48). Moreover, the significant differences in radiological, symptomatic, and clinical manifestations of hand OA between races highlight the potential role of race-specific biological mechanisms and environmental risk factors in the pathogenesis of osteoarthritis (49). These findings offer new insight into clinical risk prediction, suggesting that early identification of individuals with high BRI and targeted interventions could slow the progression of OA and improve patient quality of life.

The BRI, a recently developed indicator for assessing the degree of obesity in humans, may be associated with the development of OA through a variety of mechanisms. A review by Sampath et al. emphasized the strong correlation between obesity, metabolic syndrome, and OA (50). Specifically, obesity induces a chronic low-grade inflammatory state, which can accelerate cartilage degradation. This process is mediated by elevated levels of different mediators, especially those with proinflammatory qualities, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), thereby increasing the risk of developing OA. Moreover, individuals with obesity typically exhibit elevated levels of adipokines, which play pivotal roles in regulating energy metabolism, inflammation, and the immune response. Research by Xie and Chen investigated the potential of adipokines as novel therapeutic targets in osteoarthritis

TABLE 3 Subgroup analysis of the effect of the body roundness index on osteoarthritis (*N* = 20,232).

Subgroup	*N*	OR (95% CI)	*p*-value	*P* for interaction
Age (year)				0.075
20 ~ 39	6,872	1.14 (1.08, 1.20)	<0.001	
40 ~ 59	6,775	1.14 (1.10, 1.17)	<0.001	
≥60	6,585	1.09 (1.06, 1.12)	<0.001	
Sex				0.698
Male	9,863	1.12 (1.08, 1.16)	<0.001	
Female	10,369	1.11 (1.09, 1.14)	<0.001	
Race				< 0.001
Mexican American	2,740	1.13 (1.06, 1.20)	<0.001	
Non-Hispanic White	2,126	1.15 (1.07, 1.23)	<0.001	
Non-Hispanic Black	7,449	1.07 (1.05, 1.10)	<0.001	
Other Hispanic	4,591	1.14 (1.10, 1.18)	<0.001	
Other race/multiracial	3,326	1.27 (1.19, 1.35)	<0.001	
Education				0.675
Under high school	4,394	1.10 (1.05, 1.15)	<0.001	
High School or equivalent	4,495	1.11 (1.07, 1.16)	<0.001	
Above high school	11,343	1.12 (1.09, 1.15)	<0.001	
Marital status				0.281
Married/cohabiting	3,925	1.16 (1.10, 1.21)	<0.001	
Widowed/divorced/separated	12,000	1.11 (1.08, 1.14)	<0.001	
Never married	4,307	1.11 (1.07, 1.15)	<0.001	
Moderate recreational activities				0.394
Yes	8,459	1.10 (1.07, 1.14)	<0.001	
No	11,773	1.12 (1.10, 1.15)	<0.001	
PIR				0.863
<1.30	5,933	1.11 (1.07, 1.15)	<0.001	
1.30 ~ 3.49	8,754	1.12 (1.09, 1.15)	<0.001	
≥3.50	5,545	1.12 (1.08, 1.16)	<0.001	
Cigarette Use				0.131
Smoked ≥ 100 cigarettes in life	8,631	1.10 (1.07, 1.13)	<0.001	
Smoked < 100 cigarettes in life	11,601	1.13 (1.10, 1.16)	<0.001	
Diabetes				0.489
Yes	2,731	1.13 (1.08, 1.17)	<0.001	
No	17,501	1.11 (1.09, 1.14)	<0.001	
Hypertension				0.487
Yes	7,348	1.11 (1.08, 1.14)	<0.001	
No	12,884	1.12 (1.09, 1.16)	<0.001	
Cancer				0.513
Yes	1873	1.10 (1.05, 1.15)	<0.001	
No	18,359	1.12 (1.09, 1.14)	<0.001	

Age, sex, race, PIR, cigarette use, hypertension, education, diabetes status, cancer status, marital status, and moderate recreational activities were adjusted. *P* for interaction were used to evaluate whether the association between BRI and OA differed across various subgroups in the regression models, such as sex, education level, cigarette use, marital status, moderate recreational activities, PIR, hypertension, cancer, and diabetes mellitus. PIR, family income–poverty ratio.

(OA) (51). Specific adipokines, such as leptin, adiponectin, and resistin, are expressed at abnormal levels in the joint fluid and serum of patients with OA, indicating that they may play critical roles in the pathological process of OA. For example, leptin and resistin have been shown to exert proinflammatory effects and enhance the expression of proinflammatory cytokines such as IL-1β and TNF-α. This, in turn, contributes to an increased risk of developing OA. In addition, Zhu and colleagues demonstrated that increasing Sirt3 expression in mice

reduced OA lesions induced by a high-fat diet (52). These findings suggest that Sirt3 may play a role in protecting cartilage and slowing OA progression. Furthermore, the symptoms associated with decreased Sirt3 expression levels in individuals on high-fat diets could provide a potential mechanism for the observed positive correlation between BRI and OA. These studies suggest a potential mechanism by which the BRI may contribute to the development of OA.

This study has several strengths. First, this is an innovative study revealing the association between the BRI and OA. In the present study, the BRI, an emerging assessment tool, was used instead of traditional obesity measurement indicators such as BMI or waist circumference to evaluate individual body characteristics more comprehensively. Second, the reliability and representativeness of our study were significantly enhanced by the large sample size collected from the NHANES database and the precise covariate correction measures. Additionally, the sensitivity analysis enabled us to effectively minimize the probability of false-positive results. However, this study also has several limitations. Specifically, the cross-sectional study design limits our ability to explore causal relationships directly. Although self-reported OA data is commonly used in large epidemiological studies, it is important to acknowledge its limitations compared to clinically assessed OA. it is known that OA prevalence varies depending on the definition used, with radiographic OA being more frequent than symptomatic OA. However, within individual joint sites, the prevalence estimates for self-reported OA and symptomatic OA tend to be similar, providing a reasonable approximation for large-scale studies like ours (53, 54). Despite this, since the osteoarthritis data is self-reported, recall bias among participants may have affected the accuracy of the included variables. Future studies with large-scale prospective samples are needed to better elucidate the potential causal relationships.

5 Conclusion

The results of our study demonstrate a significantly positive correlation between BRI and OA. This finding highlights the necessity of early intervention in individuals with elevated BRI to prevent the onset of OA. However, the results of the current cross-sectional study are insufficient to establish a direct causal relationship. Further large-scale prospective studies are needed to validate our results.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Guangzhou Women and Children's Medical Center. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

HL: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft. WS: Data curation, Investigation, Software, Validation, Writing – review & editing. LL: Conceptualization, Supervision, Visualization, Writing – review & editing. KY: Supervision, Funding acquisition, Project administration, Software, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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EDITED BY
Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Virginia Maria Muniz,
Secretaria de Estado da Saúde do Espírito Santo, Brazil
Dafeng Liu,
Public Health and Clinical Center of Chengdu, China

*CORRESPONDENCE
Ying Zhou
✉ doczhy85302@126.com
Yuping Li
✉ wzliyp@163.com

†These authors have contributed equally to this work

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Comparative analysis of six nutritional scores in predicting prognosis of COVID-19 patients

Shangpu Zou[1†], Pengcheng Lin[1†], Xiaoyu Chen[2], Lijing Xia[1], Xiling Liu[1], Shanshan Su[1], Ying Zhou[1*] and Yuping Li[1*]

[1]The Key Laboratory of Interventional Pulmonology of Zhejiang Province, Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [2]Department of Respiratory and Critical Care Medicine, The Second Hospital of Yiwu, Yiwu, China

Background: Identifying nutritional risk in COVID-19 patients poses a challenge due to the unique qualities of every nutritional screening instrument. The objective was to assess the efficacy of six nutritional scores, including the Nutritional Risk Screening 2002 (NRS-2002) score, the NUTRIC (nutrition risk in the critically ill) score, the modified NUTRIC score, the prognostic nutritional index (PNI), controlling nutritional status (CONUT) score, TCB index (TCBI), predicting prognosis of COVID-19 patients.

Methods: Clinical data were collected from COVID-19 patients admitted to the First Affiliated Hospital of Wenzhou Medical University between December 2022 and February 2023. Participants in this research were divided into two groups: all patients and those specifically from the intensive care unit (ICU). Each group was further stratified into two groups: survivors and non-survivors.

Result: 506 COVID-19 patients and 190 COVID-19 patients in intensive care unit (ICU) were evaluated. In all COVID-19 patients, we found that NRS-2002 ($p < 0.001$) and TCBI ($p = 0.002$) were statistically significant independent predictors in multivariate analyses, while APACHE II score ($p = 0,048$) and the mNUTRIC score ($p = 0.025$) were statistically significant independent predictors in multivariate analyses in ICU patients. The NRS-2002 demonstrated a higher AUC value (0.687) than other nutritional scores in all patients, with an optimum cut-off value of 3, translating into a corresponding sensitivity of 66.2% and specificity of 68.7%. With an optimum cut-off value of 4, the mNUTRIC score demonstrated a higher AUC value (0.884) in ICU patients, resulting in a sensitivity of 88.4% and a specificity of 76.9%. By using the discrimination and clinical application (DCA) curve, NRS-2002 demonstrated the greatest net benefit in all patients, while NUTRIC score and mNUTRIC score offered the more significant overall advantage than other nutritional scores in ICU patients. Kaplan–Meier analyses showed lower survival rates in patients in low nutritional risk.

Conclusion: Malnutrition was common in COVID-19 patients. The mNUTRIC score and NRS-2002 were, respectively, more effctive scoring systems of prognosis in all COVID-19 patients and severe or critical COVID-19 patients of the intensive care unit (ICU).

KEYWORDS

nutritional scores, COVID-19, prognostic value, nutritional risk, nutritional assessment

1 Introduction

COVID-19 is a critical respiratory illness constituting a substantial threat to human life. There is a great deal of variation in the clinical manifestations of COVID-19, ranging from asymptomatic illness to severe pneumonia with potentially fatal consequences. Acute respiratory distress syndrome (ARDS), multiorgan failure, and sometimes lethal consequences are some of these problems (1–4). Individuals with severe illness had a greater frequency of comorbid diseases than individuals without it. These diseases often need treatment in an intensive care unit (ICU) and may potentially be fatal, thus placing a significant burden on healthcare facilities (5). Early identification of those who might have a serious disease is essential for effective allocation of medical resources and timely intervention to enhance their prognosis. Malnutrition is strongly linked to poor prognosis in various diseases, but is often ignored and modifiable (6–17). By identifying individuals who are at risk of malnutrition, we can offer them early nutritional support, which in turn improves their outcomes and extends their lifespan (9).

In most cases, malnutrition is studied through screening tools, which are usually applied by doctors, nutritionists or other healthcare professionals prior to conducting a comprehensive nutritional assessment. However, there is no golden standard for determining malnutrition (18, 19). There are a few screening tools for malnutrition, which associated with poor prognosis in COVID-19 (20–22). Two scoring systems are used to evaluate the nutritional risk in patients receiving intensive care unit (ICU) treatment: the NUTRIC (nutrition risk in the critically sick) score and the modified NUTRIC score. The sole distinction between the two lies in the examination of interleukin-6 (IL-6) levels (23, 24). The nutritional risk score (NRS-2002) is a commonly utilized nutritional screening tool in clinical settings (25). The prognostic nutritional index (PNI), controlling nutritional status (CONUT) score, and Triglycerides (TG) × Total Cholesterol (TC) × Body Weight (BW) Index (TCBI) are convenient, efficientive and practical nutritional scores that can be derived from readily available and cost-effective parameters (26–28). Nevertheless, determining which scoring system is better at predicting prognostic outcomes for COVID-19 patients still lacks clarity.

There is a dearth of research on how nutritional ratings compare to predict COVID-19 patient prognosis. As a result, we investigated the usefulness of nutrition scores utilizing the various above-mentioned scoring systems in determining the prognostic relevance of the nutritional status in COVID-19 patients.

2 Methods

2.1 Study population

This single-center, retrospective cohort research included information from 595 patients aged 18 years and above who were under follow-up at the First Affiliated Hospital of Wenzhou Medical University from December 2022 to February 2023.

Patients with positive results from thoracic CT scans or reverse transcriptase-polymerase chain reaction (RT-PCR), which showed features that indicated the disease, were included in the study. The cohort under observation in the ICU comprised individuals diagnosed with severe pneumonia and critically ill patients. The exclusion criteria included re-admissions, immunosuppressed state (treated with corticosteroids, immunosuppressive agents or cytotoxic agents for a duration exceeding 1 month), therapeutic limitations, individuals who are pregnant or whose data is insufficient.

The First Affiliated Hospital Ethics Committee of Wenzhou Medical University approved the research protocol.

2.2 Data collection

The baseline information, which includes immunosuppressive and glucocorticoid usage (previous use of immunosuppressive agents and corticosteroids, but for less than 1 month), anthropometric measurements, and demographic traits, history of smoking, chronic medical conditions, days in hospital preceding admission to the ICU, total length of stay in hospital, length of stay in ICU, Glasgow Coma Score (GCS), the requirement for vasopressors, the requirement for noninvasive oxygen treatments and the development of acute kidney damage, the length of invasive mechanical ventilation, the amount of urine produced, the need for renal replacement treatment, disease outcome (survival/non-survival) and laboratory parameters.

2.3 Assessment of nutritional status

The NUTRIC score and the mNUTRIC score for each patient were assessed based on six paraments: Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, age, quantity of comorbid conditions, duration of hospital stay prior to ICU admission and interleukin-6 (IL-6) levels (23, 24). NRS-2002 comprises the patient's declining eating capacity, the recent proportion of weight loss over the last 3 months, the current Body Mass Index (BMI), age and comorbidities (25). PNI was determined using the formula: $PNI = albumin\,(ALB)\,(g/L) + 0.005 \times lymphocyte\ count\,(/mm^3)$ (26). CONUT was assessed using lymphocyte count, total cholesterol (TC) and albumin (ALB) levels (27). TCBI was determined using the formula: $TCBI = \mathrm{TG}\,(\mathrm{mg/dL}) \times \mathrm{TC}\,(\mathrm{mg/dL}) \times \mathrm{BW}\,(\mathrm{kg})/1000$ (28).

Calculate the NUTRIC score and the mNUTRIC score for patients upon their admission to the ICU, within 24 h of ICU admission, the remaining nutritional scores were calculated within 48 h after the patient is admitted. For the purpose of comparison, instead of using established scoring definitions, we purposely classified patients into low nutritional risk and high nutritional risk based on the optimal cut-off value of the ROC curve for one of any nutritional scores.

2.4 Outcome

The rate of COVID-19-related in-hospital mortality was the study's major endpoint, while the 28-day all-cause mortality was its secondary objective.

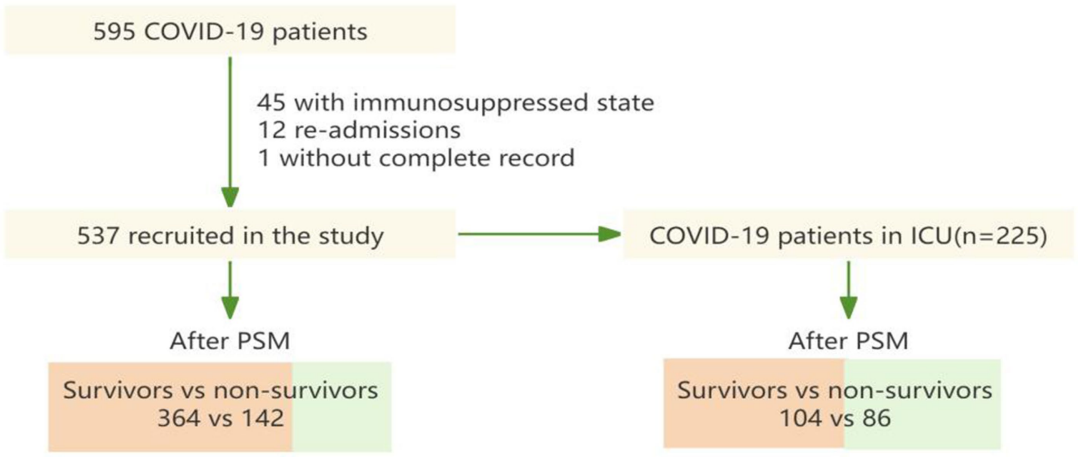


FIGURE 1
The flowchart showing the strategy of participant enrollment.

2.5 Statistical analysis

As a retrospective analysis, there was no prior statistical analysis plan. There was no calculation of statistical power. The missing values for each variable were estimated using multiple imputation (29).

In this study, patients were segregated into two distinct groups of study subjects, all patients and ICU patients. Each group was further categorized into survivors and non-survivors (Figure 1). The propensity score-matching (PSM) model is employed to mitigate baseline characteristic disparities among study subjects. For variables that have a normal distribution, the data are shown as mean ± standard deviation; for skewed variables, they are presented as median with interquartile range; and for categorical variables, as *n* (%). In testing, differences were compared using the Mann–Whitney U test for skewed data, the student's t-test for normally distributed variables, or the Chi-squared test for categorical variables. Spearman's correlation analysis is used to test the multicollinearity of variables.

The optimum cut-off values of nutritional scores and its area under the curve (AUC) for in-hospital mortality were assessed using receiver operating characteristic (ROC) curves (37). We employed sensitivity, specificity, and accuracy to assess the optimum cut-off values' diagnostic usefulness. The predictive model proposed here has a net therapeutic benefit that was evaluated using decision-curve analysis (DCA) (38).

Using Kaplan–Meier analyses to ascertain the influence of prognostic variables on patient survival, patients were divided into groups according to their nutritional risk: high and low, which based on the optimal cut-off value derived from the ROC curve of one of any nutritional scores. A significance threshold of $p < 0.05$ was used as the standard for statistical significance in all tests.

R statistical software[1] was utilized for data handing, statistical analyses, and the generation of graphical representations. The particular packages used were multipleROC, rmda, MatchIt, ggplot2, ggpubr, corrplot.

1 https://www.Rproject.org/

3 Results

3.1 Population characteristics

Figure 1 shows that a total of 595 COVID-19 patients were found in the course of the study. Following the exclusion of episodes related to re-admissions ($n = 12$), patients with immunosuppressed state ($n = 45$) and patients without complete record ($n = 1$), 537 patients were included in this study. For subjects enrolled in the propensity score-matching (PSM) model, 142 deceased patients were matched with 364 patients who were discharged. Meanwhile, after PSM, 86 patients in ICU from the dead group were matched to 104 patients in ICU from the discharged group.

Tables 1, 2 respectively described the baseline characteristics of all COVID-19 patients and COVID-19 patients in ICU before and after propensity score matching (PSM). In the respective study groups, the baseline characteristics were found to be comparable between the survivors and the non-survivors after propensity score matching (PSM).

Among the 537 selected patients, their median age ranged from 68.00 to 83.00 years, with 368 male and 169 female cases. Among them, 151 patients died, 386 patients were discharged, and 225 patients were admitted in ICU. The mortality rate inside hospitals was reported to be 28.1%, the ICU admission rate was 37.8%. The participants who died were older (77.0 versus 74.0 years of age, $p = 0.002$), had a greater percentage of men and had higher prevalence of chronic medical conditions, including chronic kidney diseases (14.57% versus 7.25%, $p = 0.009$), the history of stroke (14.57% versus 8.55%, $p = 0.039$) than those who were discharged.

The baseline characteristics of all COVID-19 patients and COVID-19 patients in ICU before and after propensity score matching were shown in Tables 1, 2.

3.2 Testing multicollinearity of variables

PNI and CONUT showed a strong negative association, according to Spearman's correlation study ($r = -0.88$) in all COVID-19 patients.

TABLE 1 Baseline characteristics of all COVID-19 patients before and after propensity score matching (PSM).

Variable	Unmatched		*p* value	Matched		*p* value
	Survivors (*n* = 386)	non-survivors (*n* = 151)		Survivors (*n* = 364)	non-survivors (*n* = 142)	
Weight, Mean ± SD	64.49 ± 11.78	63.20 ± 11.66	0.252	64.56 ± 11.74	63.05 ± 11.71	0.195
BMI, Mean ± SD	23.78 ± 3.78	23.07 ± 3.79	0.051	23.75 ± 3.77	23.05 ± 3.80	0.062
Age, M (Q_1, Q_3)	74.00 (65.00, 82.00)	77.00 (71.00, 84.00)	0.002*	75.00 (67.00, 83.00)	77.00 (71.00, 84.00)	0.065
Height, M (Q_1, Q_3)	165.00 (158.00, 170.00)	165.00 (160.00, 170.00)	0.275	165.00 (158.75, 170.00)	165.00 (160.00, 170.00)	0.558
Male gender, *n* (%)	255 (66.06)	113 (74.83)	0.049*	253 (69.51)	105 (73.94)	0.324
Smoker, *n* (%)	105 (27.20)	43 (28.48)	0.766	103 (28.30)	41 (28.87)	0.897
Glucocorticoid, *n* (%)	38 (9.84)	20 (13.25)	0.254	37 (10.16)	19 (13.38)	0.3
Immunodepressant, *n* (%)	3 (0.78)	0 (0.00)	0.563	3 (0.82)	0 (0.00)	0.563
chronic medical conditions						
Diabetes, *n* (%)	137 (35.49)	58 (38.41)	0.527	133 (36.54)	54 (38.03)	0.755
Hypertension, *n* (%)	217 (56.22)	95 (62.91)	0.157	214 (58.79)	88 (61.97)	0.512
Transplantation, *n* (%)	5 (1.30)	2 (1.32)	1	3 (0.82)	2 (1.41)	0.923
Solid malignancies, *n* (%)	61 (15.80)	19 (12.58)	0.346	58 (15.93)	18 (12.68)	0.357
Hematologic malignancies, *n* (%)	10 (2.59)	8 (5.30)	0.117	8 (2.20)	8 (5.63)	0.089
Cirrhosis, *n* (%)	4 (1.04)	2 (1.32)	1	4 (1.10)	2 (1.41)	1
Hepatitis, *n* (%)	7 (1.81)	1 (0.66)	0.553	5 (1.37)	1 (0.70)	0.867
Heart Failure, *n* (%)	3 (0.78)	4 (2.65)	0.195	3 (0.82)	3 (2.11)	0.456
Nephropathy, *n* (%)	28 (7.25)	22 (14.57)	0.009*	27 (7.42)	13 (9.15)	0.515
Stroke, *n* (%)	33 (8.55)	22 (14.57)	0.039*	33 (9.07)	18 (12.68)	0.226
COPD, *n* (%)	10 (2.59)	5 (3.31)	0.869	10 (2.75)	4 (2.82)	1
Bronchiectasis, *n* (%)	1 (0.26)	0 (0.00)	1	1 (0.27)	0 (0.00)	1
Asthma, *n* (%)	1 (0.26)	1 (0.66)	0.484	1 (0.27)	1 (0.70)	0.483
The history of Pneumonia, *n* (%)	15 (3.89)	2 (1.32)	0.211	15 (4.12)	2 (1.41)	0.212
Interstitial lung disease, *n* (%)	2 (0.52)	2 (1.32)	0.675	2 (0.55)	2 (1.41)	0.673

BMI, body mass index; COPD, chronic obstructive pulmonary disease.
Data are shown as *n* (%), mean ± standard deviation (SD) or median with interquartile range. In testing, differences were compared using the Mann–Whitney U test for skewed data, the student's *t*-test for normally distributed variables, or the Chi-squared test for categorical variables. *p* value < 0.05 is statistically significant. *Indicates *p* value < 0.05.

In COVID-19 patients in ICU, apart from the mNUTRIC score and the NUTRIC score exhibited a strong correlation, the mNUTRIC score and its components showed a strong positive correlation, PNI and CONUT showed a strong negative association, according to spearman's correlation study ($r = -0.83$) (Figure 2).

3.3 Comparison of predictive accuracy and predictors for in-hospital mortality

Univariable and multivariable analyses of in-hospital death in all patients and ICU patients are detailed in Tables 3, 4, respectively.

Table 3 indicated, that in all COVID-19 patients, NRS-2002($p < 0.001$), CONUT ($p < 0.001$), PNI ($p < 0.001$), LOS ($p = 0.047$) were significantly elevated in non-survivors compared to survivors, PNI ($p < 0.001$) was much greater in survivors than in non-survivors. However, TCBI although was an independent predictor in multivariate analyses that was statistically significant, but its Beta was 0. We also found that NRS-2002 ($p < 0.001$) and TCBI ($p = 0.002$) were statistically significant independent predictors in multivariate analyses.

Table 4 indicated that among patients in ICU, APACHE II score ($p < 0.001$), SOFA score ($p < 0.001$), the NUTRIC score ($p < 0.001$), the mNUTRIC score ($p < 0.001$), NRS-2002 ($p = 0.007$) were much greater in non-survivors than in survivors. The mNUTRIC score ($p = 0.025$) and the APACHE II score ($p = 0.048$) were both shown to be statistically significant independent predictors in multivariate analyses.

Employing the ROC approach, curves were generated to ascertain the optimal cut-off points for forecasting mortality inside hospitals. The optimum cut-off value for the CONUT score was 6, which produced an AUC of 0.625, 73.9% sensitivity, and 46.2% specificity for all patients. With the optimum cut-off value set at 3, the NRS-2002 score demonstrated a higher AUC value of 0.687, surpassing the

TABLE 2 Baseline characteristics of COVID-19 patients in ICU before and after propensity score matching (PSM).

Variable	Unmatched		*p* value	Matched		*p* value
	Survivors (*n* = 112)	Non-survivors (*n* = 113)		Survivors (*n* = 104)	Non-survivors (*n* = 86)	
Weight, Mean ± SD	65.21 ± 11.00	63.55 ± 12.17	0.283	64.60 ± 10.66	63.49 ± 12.29	0.505
BMI, Mean ± SD	23.71 ± 3.58	23.20 ± 3.95	0.308	23.61 ± 3.58	23.26 ± 3.94	0.522
Age, M (Q_1, Q_3)	75.00 (66.00,81.00)	77.00 (71.00, 84.00)	0.031*	76.00 (68.00, 82.25)	76.50 (71.00, 82.00)	0.481
Height, M (Q_1, Q_3)	167.00 (160.00, 170.00)	166.00 (160.00, 170.00)	0.738	167.00 (160.00, 170.00)	165.00 (160.00, 170.00)	0.779
Male gender, *n* (%)	73 (65.18)	84 (74.34)	0.135	68 (65.38)	60 (69.77)	0.521
Smoker, *n* (%)	26 (23.21)	32 (28.32)	0.381	25 (24.04)	21 (24.42)	0.951
Glucocorticoid, *n* (%)	12 (10.71)	14 (12.39)	0.694	11 (10.58)	12 (13.95)	0.478
Immunodepressant, *n* (%)	1 (0.89)	0 (0.00)	0.498	1 (0.96)	0 (0.00)	1
chronic medical conditions						
Diabetes, *n* (%)	42 (37.50)	45 (39.82)	0.721	40 (38.46)	38 (44.19)	0.425
Hypertension, *n* (%)	63 (56.25)	67 (59.29)	0.644	61 (58.65)	49 (56.98)	0.816
Transplantation, *n* (%)	1 (0.89)	2 (1.77)	1	1 (0.96)	1 (1.16)	1
Solid malignancies, *n* (%)	19 (16.96)	13 (11.50)	0.241	19 (18.27)	10 (11.63)	0.205
Hematologic malignancies, *n* (%)	0 (0.00)	7 (6.19)	0.022*	0 (0.00)	0 (0.00)	–
Cirrhosis, *n* (%)	1 (0.89)	2 (1.77)	1	1 (0.96)	2 (2.33)	0.868
Hepatitis, *n* (%)	3 (2.68)	1 (0.88)	0.608	2 (1.92)	1 (1.16)	1
Heart Failure, *n* (%)	1 (0.89)	2 (1.77)	1	1 (0.96)	2 (2.33)	0.868
Nephropathy, n (%)	11 (9.82)	13 (11.50)	0.683	10 (9.62)	12 (13.95)	0.352
Stroke, *n* (%)	16 (14.29)	17 (15.04)	0.872	16 (15.38)	12 (13.95)	0.782
COPD, *n* (%)	6 (5.36)	4 (3.54)	0.735	6 (5.77)	4 (4.65)	0.986
Bronchiectasis, *n* (%)	1 (0.89)	0 (0.00)	0.498	1 (0.96)	0 (0.00)	1
Asthma, *n* (%)	2 (1.79)	0 (0.00)	0.247	1 (0.96)	0 (0.00)	1
The history of Pneumonia, *n* (%)	5 (4.46)	0 (0.00)	0.069	5 (4.81)	0 (0.00)	0.108
Interstitial lung disease, *n* (%)	2 (1.79)	2 (1.77)	1	2 (1.92)	2 (2.33)	1

BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.
Data are shown as *n* (%), mean ± standard deviation (SD) or median with interquartile range. In testing, differences were compared using the Mann–Whitney U test for skewed data, the student's *t*-test for normally distributed variables, or the Chi-squared test for categorical variables. *p* value < 0.05 is statistically significant. *Indicates *p* value < 0.05.

CONUT score and yielding a sensitivity and specificity of 66.2 and 68.7%, respectively. The sensitivity and specificity of the APACHE II score in ICU patients were 41.9 and 83.7%, respectively, with an optimum cut-off value of 13 and an AUC of 0.65. With an optimum cut-off value of 4, the mNUTRIC score and the NUTRIC score showed surperior AUC values of 0.884 and 0.878, respectively, outperforming the APACHE II score (Figure 3).

Statistical significance calculated by De-long's test, the outcomes are shown in Table 5.

3.4 Comparison of clinical application value

The Discrimination and Clinical Application (DCA) curve was shown in Figure 4. In all patients, through a comparison of NRS-2002 with PNI, CONUT score, TCBI, and length of hospital (LOS), it was evident that NRS-2002 demonstrated the greatest net benefit. In ICU patients, upon evaluating the NUTRIC score, the mNUTRIC score, APACHE 2 score, SOFA score, NRS-2002, PNI, TCBI, and CONUT scores, LOS, LOS in ICU, it becomed apparent that NUTRIC score and mNUTRIC score offered the more significant overall advantage than other nutritional scores.

3.5 Kaplan–Meier analyses showed lower survival rates in patients in low nutritional risk

In all COVID-19 patients, 208 individuals had high nutritional risk (41.1%), which assessed by NRS-2002. In COVID-19 patients in ICU, 94 individuals had high nutritional risk (49.5%). Figure 5 shows the Kaplane

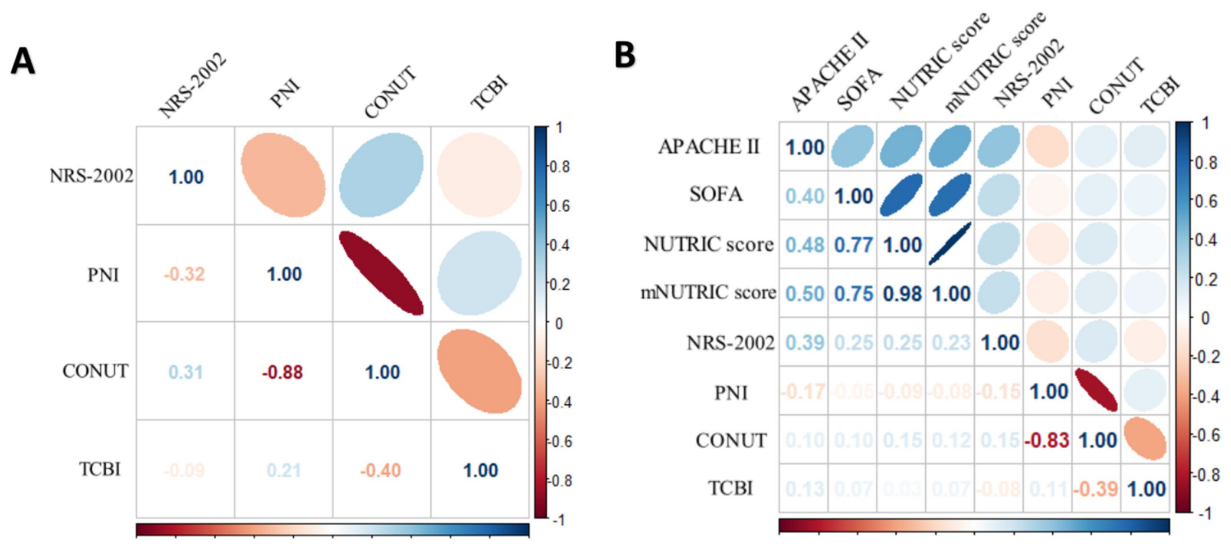


FIGURE 2
(A) Spearman correlation analysis of NRS-2002, PNI CONUT and TCBI for all COVID-19 patients. **(B)** Spearman correlation analysis of the NUTRIC score, mNUTRIC score and its components, NRS-2002, PNI, CONUT, TCBI for all COVID-19 patients.

TABLE 3 Univariable and multivariable analysis of in-hospital death in all COVID-19 patients.

	Univariable analysis					Multivariable analysis				
Variables	Beta	SE	*Z*	OR (95%CI)	*p* value	aBeta	aSE	aZ	aOR (95%CI)	a*p* value
NRS-2002	0.44	0.07	6.34	1.55 (1.35–1.77)	<0.001*	0.39	0.07	5.19	1.47 (1.27–1.70)	<0.001*
PNI	−0.07	0.02	−4.24	0.93 (0.90–0.96)	<0.001*	0.01	0.04	0.26	1.01 (0.94–1.08)	0.796
CONUT	0.17	0.04	4.13	1.18 (1.09–1.28)	<0.001*	0.18	0.09	1.95	1.19 (1.00–1.42)	0.051
TCBI	0	0	2.09	1.01 (1.01–1.01)	0.037*	0	0	3.14	1.01 (1.01–1.01)	0.002*
LOS	0.02	0.01	1.99	1.02 (1.01–1.04)	0.047*	0	0.01	−0.07	1.00 (0.98–1.02)	0.944

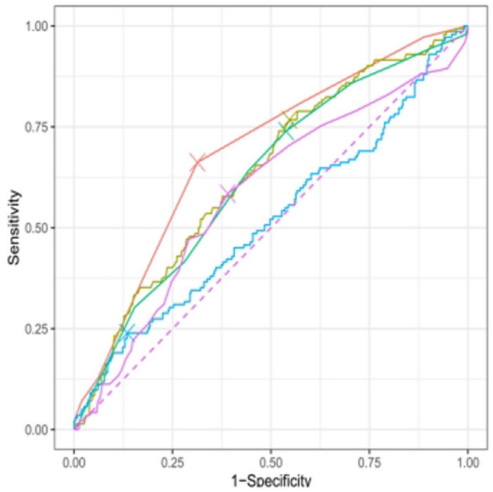
SE, standard error; OR, odds ration; CI, confidence interval; NRS-2002, the Nutritional Risk Screening 2002; PNI, the prognostic nutritional index; CONUT, controlling nutritional status; TCBI, Triglycerides × Total Cholesterol × Body Weight Index; LOS, length of hospital.
In testing, differences were compared using the Binary Logistic Regression Analysis. *p* value < 0.05 is statistically significant. *Indicates *p* value < 0.05.

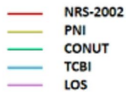
TABLE 4 Univariable and multivariable analysis of in-hospital death in COVID-19 patients in ICU.

	Univariable analysis					Multivariable analysis				
Variables	Beta	SE	*Z*	OR (95%CI)	*p* value	aBeta	aSE	aZ	aOR (95%CI)	a*p* value
APACHE II	0.14	0.04	3.69	1.15(1.07–1.25)	<0.001	−0.13	0.07	−1.98	0.88 (0.77–0.99)	0.048
SOFA	0.36	0.06	5.92	1.43(1.27–1.61)	<0.001	−0.06	0.09	−0.69	0.94 (0.80–1.12)	0.489
NUTRIC score	1.33	0.19	7.08	3.78 (2.61–5.46)	<0.001	0.27	0.6	0.44	1.31 (0.40–4.23)	0.656
mNUTRIC score	1.47	0.21	6.99	4.36(2.89–6.59)	<0.001	1.47	0.66	2.24	4.36 (1.20–15.77)	0.025
NRS-2002	0.26	0.1	2.71	1.30 (1.08–1.58)	0.007	0.19	0.15	1.27	1.20 (0.90–1.60)	0.203
PNI	−0.01	0.03	−0.28	0.99 (0.94–1.04)	0.78					
CONUT	0.03	0.06	0.51	1.03(0.91–1.17)	0.609					
TCBI	0	0	1.8	1.00(1.00–1.00)	0.073					
LOS	−0.01	0.01	−1.2	0.99 (0.97–1.01)	0.231					
LOS in ICU	0	0.01	−0.36	1.00 (0.97–1.02)	0.722					

SE, standard error; OR, odds ration; CI, confidence interval; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ Failure assessment; NUTRIC score, the nutrition risk in the critically ill score; mNUTRIC score, the modified nutrition risk in the critically ill score; NRS-2002, the Nutritional Risk Screening 2002; PNI, the prognostic nutritional index; CONUT, controlling nutritional status; TCBI, Triglycerides × Total Cholesterol × Body Weight Index; LOS, length of hospital; ICU, intensive care unit.
In testing, differences were compared using the Binary Logistic Regression Analysis. *p* value < 0.05 is statistically significant. *Indicates *p* value < 0.05.

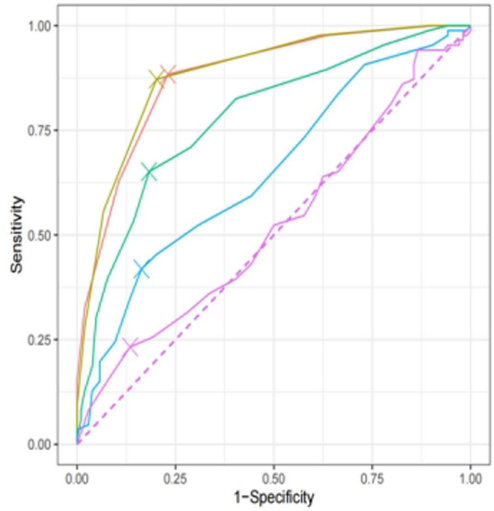
A

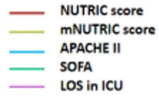




	Cut-Off	AUC	95% CI	Sensitivity	Specificity	p Value
NRS-2002	3	0.687	0.637-0.737	66.2%	68.7%	<0.001
PNI	36.05	0.636	0.583-0.689	76.8%	45.3%	<0.001
CONUT	6	0.625	0.572-0.679	73.9%	46.2%	<0.001
TCBI	2312.57	0.518	0.460-0.577	23.0%	86.5%	<0.001
LOS	12	0.583	0.527-0.640	58.5%	61.0%	<0.001

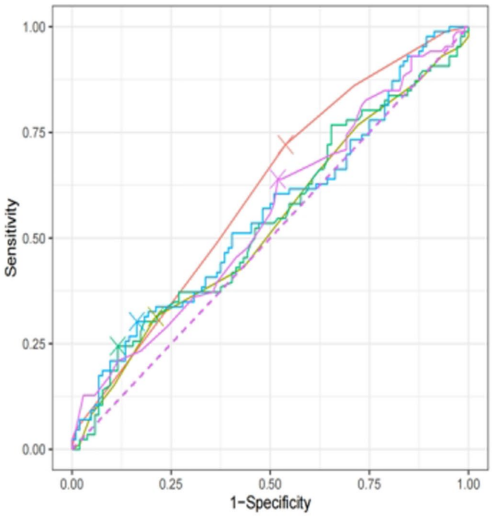
B

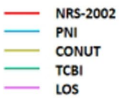




	Cut-Off	AUC	95% CI	Sensitivity	Specificity	p Value
NUTRIC score	4	0.878	0.831-0.925	88.4%	76.9%	<0.001
mNUTRIC score	4	0.884	0.837-0.930	87.2%	79.8%	<0.001
APACHE II	13	0.650	0.572-0.728	41.9%	83.7%	<0.001
SOFA	10	0.781	0.715-0.847	65.1%	81.7%	<0.001
LOS in ICU	3	0.524	0.440-0.607	23.3%	86.5%	<0.001

C





	Cut-Off	AUC	95% CI	Sensitivity	Specificity	p Value
NRS-2002	3	0.607	0.529-0.685	72.1%	46.2%	<0.001
PNI	28.55	0.539	0.455-0.622	24.4%	88.5%	<0.001
CONUT	9	0.531	0.448-0.631	31.4%	78.8%	<0.001
TCBI	2041.27	0.556	0.474-0.639	30.2%	83.7%	<0.001
LOS	17	0.554	0.472-0.636	64.0%	48.1%	<0.001

FIGURE 3
(A) The ROC curves of NRS-2002, PNI, CONUT, TCBI and hospital length of stay (LOS) for the prediction of in-hospital mortality of all COVID-19 patients. **(B)** The ROC curves of the NUTRIC score, the mNUTRIC score and its components, hospital length of stay (LOS) in ICU for the prediction of in-hospital mortality of COVID-19 patients in ICU. **(C)** The ROC curves of NRS-2002, PNI, CONUT, TCBI, hospital length of stay (LOS) for the prediction of in-hospital mortality of COVID-19 patients in ICU.

TABLE 5 De-long's test of AUC of nutritional scores in all COVID-19 patients and COVID-19 patients in ICU.

All COVID-19 patients				COVID-19 patients in ICU			
Variables	AUC	95% CI	*p*-value	Variables	AUC	95% CI	*p*-value
NRS-2002	0.687	0.637–0.737	Ref.	mNUTRIC score	0.884	0.837–0.930	Ref.
PNI	0.636	0.583–0.689	0.125	NUTRIC score	0.878	0.831–0.925	0.456
CONUT	0.625	0.572–0.679	0.066	APACHE II	0.650	0.572–0.728	<0.001*
TCBI	0.518	0.460–0.577	<0.001*	SOFA	0.781	0.715–0.847	<0.001*
LOS	0.583	0.527–0.640	0.002*	NRS-2002	0.607	0.529–0.685	<0.001*
				PNI	0.539	0.455–0.622	<0.001*
				CONUT	0.531	0.448–0.631	<0.001*
				TCBI	0.556	0.474–0.639	<0.001*
				LOS	0.554	0.472–0.636	<0.001*
				LOS in ICU	0.524	0.440–0.607	<0.001*

AUC, area under curve; CI, confidence interval; ICU, intensive care unit; NRS-2002, the Nutritional Risk Screening 2002; PNI, the prognostic nutritional index; CONUT, controlling nutritional status; TCBI, Triglycerides × Total Cholesterol × Body Weight Index; LOS, length of hospital; mNUTRIC score, the modified nutrition risk in the critically ill score; NUTRIC score, the nutrition risk in the critically ill score; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ Failure assessment.
In testing, differences were compared using the De-long's test. p value < 0.05 is statistically significant. *Indicates p value < 0.05.

Meier curve for 28-day all-cause mortality stratified by nutritional risk, as evaluated using NRS-2002 in all COVID-19 patients, as well as the NUTRIC score and the mNUTRIC score among COVID-19 patients in ICU. Patients with a high risk of malnutrition exhibit a significantly poorer prognosis than those at low nutritional risk, with the statistical significance of the observed discrepancies ($p < 0.001$).

4 Discussion

The COVID-19 pandemic has brought about various challenges and posed threats to both healthcare and economic infrastructures (5, 30). A few studies have demonstrated the importance of nutritional scores to forecast the prognosis of COVID-19 patients, highlighting its ability to promptly detect malnutrition (20–22). Currently, the incidence of malnutrition may vary depending on the nutritional screening methods used, and there is no widely agreed set of criteria for identifying malnutrition (18, 19). To the extent of our understanding, this study represents the initial investigation into the prognostic significance of six nutritional scores among patients diagnosed with COVID-19. The current investigation suggested that patients identified as having a high nutritional risk based on any of the six objective nutritional scores (the NUTRIC score, the mNUTRIC score, NRS-2002, PNI, TCBI, and CONUT score), demonstrated lower overall survival rates. Furthermore, NRS-2002 and TCBI were connected with significant in-hospital mortality in each patient in an independent manner, APACHE 2 score and mNUTRIC score were independently correlated with high in-hospital mortality in ICU patients, even after controlling for irrelevant factors through binary logistic regression analysis, the conclusion remains valid. As an independent predictor in multivariate analyses, TCBI was statistically significant in all COVID-19 patients, but its Beta was 0. The reason maybe was the insufficient sample size.

In ICU patients, the AUC values of both the mNUTRIC score and the NUTRIC score were significantly higher than those of other nutritional scores, indicating superior predictive accuracy. In all COVID-19 patients, the NRS-2002 score exhibited a higher AUC value compared to other nutritional scores, despite not showing significant differences from them. Evaluating the clinical application value of various nutritional scores through DCA Curves, NRS-2002 showed the greatest net benefit in all patients, the NUTRIC score and the mNUTRIC score were offer significant advantage over other nutritional indices in ICU patients. The results above indicated that the mNUTRIC score and the NUTRIC score exhibited more effective prognostic assessment capabilities among all COVID-19 patients, while NRS-2002 score exhibited more effective prognostic assessment capability in COVID-19 patients of ICU. Further Kaplan–Meier analyses for these three factors reaffirmed their predictive significance for patient prognosis.

Several potential factors may contribute to the risk of malnutrition among COVID-19 patients. The development of malnutrition is mainly influenced by multiple factors, including diminished dietary intake, elevated requirements for energy and protein, augmented losses, and inflammation (31). Elsa Dent noted that aging, inadequate supply of food, socioeconomic and psychological factors, and modifiable risk factors such as low physical function, low appetite, eating dependency, poor self-perceived health, a previous hospital stay, marital status, and poor oral health. These elements collectively contribute significantly to the occurrence of malnutrition (32).

In 2016, the American Society for Parenteral and Enteral Nutrition (ASPEN) endorsed the utilization of both NRS-2002 and the NUTRIC score for evaluating the nutritional status of critically ill patients (33). The NUTRIC score considers inflammation and nutritional factors, including age, BMI, organ dysfunction, diagnosis, inflammatory markers and nutritional therapy requirements. On the other hand, NRS-2002 takes into account the patient's nutritional status, age, BMI, nature and severity of the disease and treatment modalities. Both of them share the APACHE II score as a common variable, which can be used to forecast the severity of diseases and assist researchers in evaluating the effectiveness of new or alternative treatments (33). Neeraj Kumar observed a mortality rate of 92.8% in COVID-19 patients with elevated NUTRIC score, contrasting sharply with a 38% mortality rate in patients with low NUTRIC score, while using 3.5 as the cut-off value (34).

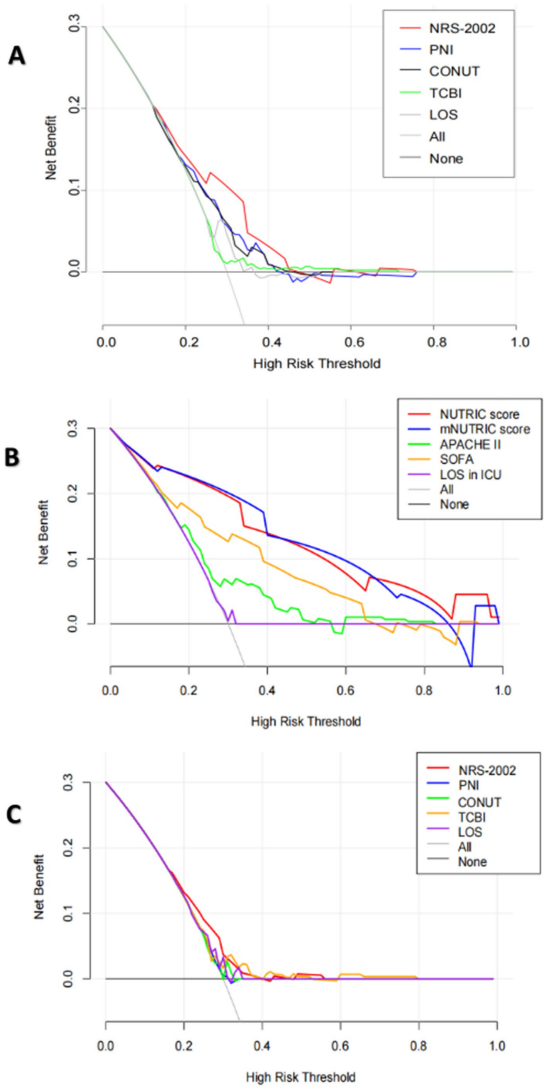


FIGURE 4
(A) The DCA curves of NRS-2002, PNI, CONUT, TCBI and hospital length of stay (LOS) for the prediction of in-hospital mortality of all COVID-19 patients. **(B)** The DCA curves of the NUTRIC score, the mNUTRIC score and its components, LOS in ICU for the prediction of in-hospital mortality of COVID-19 patients in ICU. **(C)** The DCA curves of NRS-2002, PNI, CONUT, TCBI, hospital length of stay (LOS), LOS in ICU for the prediction of in-hospital mortality of COVID-19 patients in ICU.

Berkay Kucuk reported that, in addition to the APACHE II and SOFA scores, the NUTRIC score and the mNUTRIC score were both effective in predicting death in COVID-19 patients in the intensive care unit, which is consistent with our research (22). Considering its easier accessibility, the mNUTRIC score may be preferred in comparison to the NUTRIC score. The research conducted by Matteo Luigi Giuseppe Leoni indicates that the prevalence of malnutrition is high among critically ill COVID-19 patients admitted to the ICU, and that mNUTRIC and CRP levels are independently associated with 28-day mortality in critically ill COVID-19 patients (35). In our presented study, we determined that the mNUTRIC score cut-off value of 4 for predicting in-hospital mortality in COVID-19 patients was much lower than the previously established cut-off of 5. This suggested an increased importance of nutrition in COVID-19 patients relative to those unaffected by the SARS-CoV-2, necessitating a paramount focus on this aspect.

Ghalia Shamlan observed that COVID-19 patients with an infection duration of 6 months or longer, those who had been vaccinated, obese patients, and those without cardiovascular disease were less likely to experience malnutrition when assessed using the NRS-2002 as a tool for evaluating nutritional risk (36). Ghadamieh Fatemeh et al. reported that patients exhibiting elevated NRS-2002 scores experienced increased in-hospital mortality rates, prolonged hospital stays, and higher rates of ICU admission (20). Among all COVID-19 patients, we found that the NRS-2002 demonstrated superior predictive efficacy for in-hospital mortality compared to other nutritional assessment scores, which also served as a stand-alone predictor of death inside a hospital. The NRS-2002 was not specifically intended for the assessment of critically ill patients. In COVID-19 patients of ICU, the NUTRIC and mNUTRIC scores have much more prediction power for in-hospital mortality than the NRS-2002 score. Interestingly, Audrey Machado dos Reis also demonstrated that the

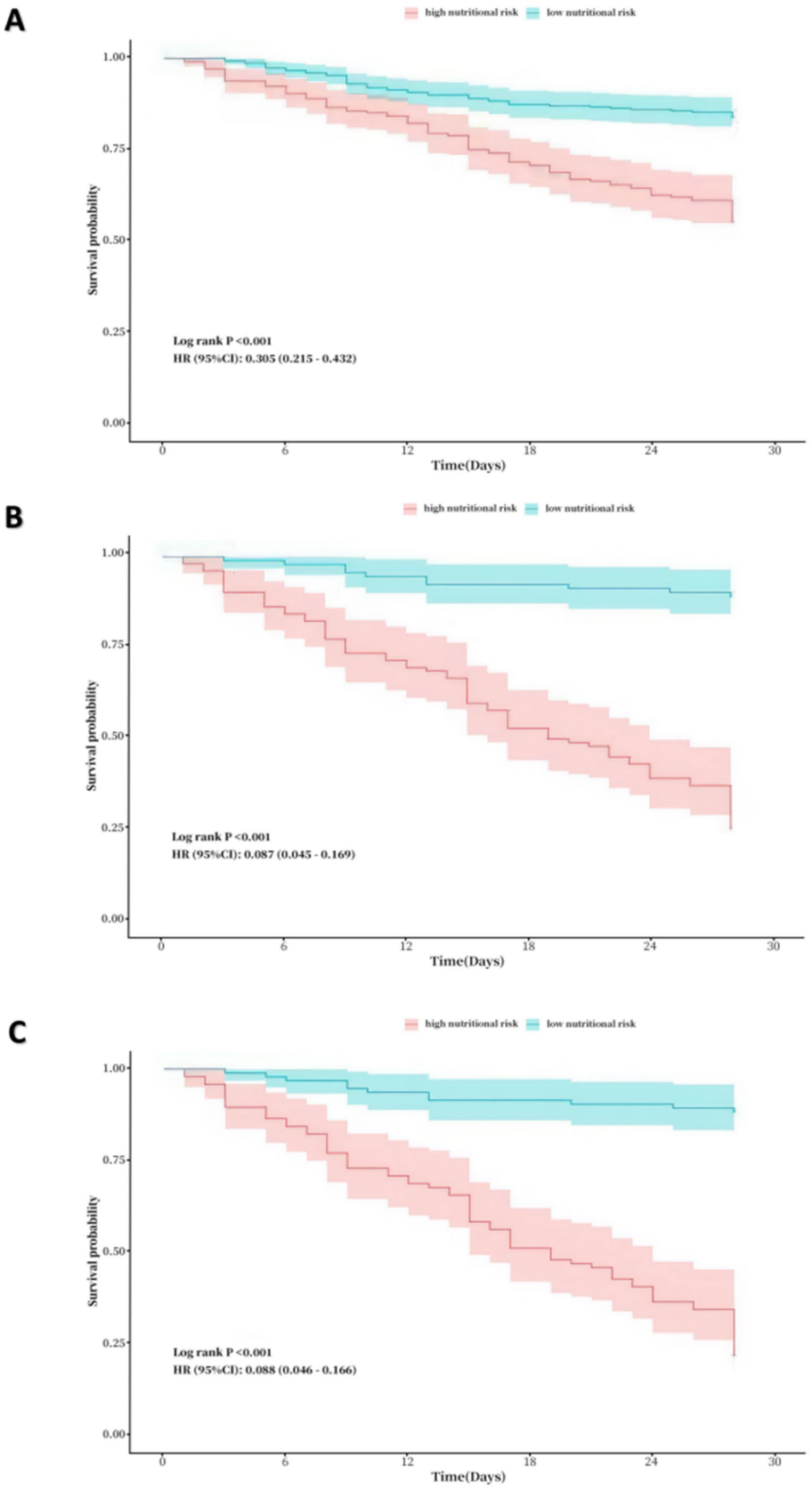


FIGURE 5
(A) Kaplane-Meier curve for 28-day all-cause mortality by nutritional risk in all patients. (assessed by NRS-2002, where low nutrional risk: NRS-2002<3 vs. high nutritional risk: NRS-200≥3). **(B)** Kaplane-Meier curve for 28-day all-cause mortality by nutritional risk in ICU patients (assessed by the NUTRIC score, where low nutrional risk: the NUTRIC score<4 vs. high nutritional risk: the NUTRIC score≥4). **(C)** Kaplane-Meier curve for 28-day all-cause mortality by nutritional risk in ICU patients (assessed by the mNUTRIC score, where low nutrional risk: the NUTRIC score<4 vs. high nutritional risk: the NUTRIC score≥4).

mNUTRIC exhibited superior discriminatory performance in calculating the critical illness patients' chance of dying in the hospital (8).

Our investigation is constrained by specific limitations. First, all score data were gathered exclusively by a single trained investigator. Second, this research is a retrospective study, hence susceptible to inherent limitations common in such studies. Objective data like laboratory values may be underrepresented due to reliance on historical medical records predating the study. Third, this study, conducted at a single center, presents both benefits and limitations inherent to its design. Enrolling numerous consecutive patients and ensuring uniform criteria and assessments are simpler in a single center. Conversely, variations in patients and procedures, along with potential enrollment challenges, might compromise the epidemiological representativeness of multicenter studies compared to a well-executed single-center study. Our study has several innovative aspects. First, following PSM based on baseline characteristics, we reduced selection bias and enhancing the credibility of causal inference. Furthermore, we divided the study population into all patients and ICU patients, comparing more comprehensively the predictive abilities of prognosis of various nutritional scores. On the other hand, it is underscored that this study represents the inaugural evaluation of the performance of six nutritional scores to date, to predict prognosis of COVID-19 patients that could be implemented to improve prognosis in this population.

5 Conclusion

This study revealed that malnutrition is prevalent among COVID-19 patients. The mNUTRIC score and NRS-2002 were, respectively, more effctive scoring systems of prognosis in all COVID-19 patients and COVID-19 patients of ICU. Early application of the aforementioned nutritional scores in clinical practice to evaluate nutritional risk in COVID-19 patients, it may be possible to identify the risk of malnutrition earlier and implement nutritional interventions, thereby reducing mortality rates and alleviating the socioeconomic burden. It is anticipated that this study will be expanded to include a larger population.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by Ethics Committee in Clinical Research of the First Affiliated Hospital of Wenzhou Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. The human samples used in this study were acquired from a by- product of routine care or industry. Written informed consent for participation was not required from the participants or the participants' legal guardians/ next of kin in accordance with the national legislation and institutional requirements.

Author contributions

SZ: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. PL: Writing – original draft, Writing – review & editing. XC: Writing – original draft, Writing – review & editing. LX: Writing – original draft, Writing – review & editing. XL: Writing – original draft, Writing – review & editing. SS: Writing – original draft, Writing – review & editing. YZ: Writing – original draft, Writing – review & editing. YL: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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EDITED BY
Luciane Bresciani Salaroli,
Federal University of Espirito Santo, Brazil

REVIEWED BY
Danilo Ferreira de Sousa,
Federal University of Ceara, Brazil
Virginia Maria Muniz,
Secretaria de Estado da Saúde do Espírito Santo, Brazil

*CORRESPONDENCE
Bin Wang
✉ wangbin@gdiist.cn
Yaomin Hu
✉ amin99@163.com

†These authors have contributed equally to this work

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Development and validation of a predicative model for identifying sarcopenia in Chinese adults using nutrition indicators (AHLC)

Xin Zhao[1†], Pengdong Yan[2†], Ningxin Chen[1], Tingting Han[1], Bin Wang[2*] and Yaomin Hu[1*]

[1]Department of Geriatrics, Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [2]Guangdong Institute of Intelligence Science and Technology, Hengqin, Zhuhai, China

Background: Sarcopenia, a condition characterized by low muscle mass, plays a critical role in the health of older adults. Early identification of individuals at risk is essential to prevent sarcopenia-related complications. This study aimed to develop a predictive model using readily available clinical nutrition indicators to facilitate early detection.

Methods: A total of 1,002 participants were categorized into two groups: 819 with normal skeletal muscle mass (SMM) and 183 with low muscle mass (sarcopenia). A predictive model was developed for sarcopenia risk via multivariate logistic regression, and its performance was assessed using four analyses: receiver operating characteristic (ROC) curve analysis, decision curve analysis (DCA), a nomogram chart, and external validation. These methods were used to evaluate the model's discriminative ability and clinical applicability.

Results: In the low-SMM group, more females (55.73% vs. 40.42%) and older individuals (median 61 vs. 55 years) were observed. These patients had lower albumin (41.00 vs. 42.50 g/L) and lymphocyte levels (1.60 vs. 2.02 × 10^9/L) but higher HDL (1.45 vs. 1.16 mmol/L) and calcium levels (2.24 vs. 2.20 mmol/L) (all $p < 0.001$). Using LASSO regression, we developed a nutritional AHLC (albumin + HDL cholesterol + lymphocytes + calcium) model for sarcopenia risk prediction. AUROC and DCA analyses, as well as nomogram charts and external validation, confirmed the robustness and clinical relevance of the AHLC model for predicting sarcopenia.

Conclusion: Our study employs serum nutrition indicators to aid clinicians in promoting healthier aging. The AHLC model stands out for weight-independent evaluations. This novel approach could assess sarcopenia risk in the Chinese population, thereby enhancing aging and quality of life.

KEYWORDS

sarcopenia, nutrition indicators, AHLC, predicative model, sarcopenia risk

Introduction

As the global aging issue intensifies, age-related health challenges like sarcopenia and malnutrition have increasingly attracted extensive attention in the field of gerontology (1). Sarcopenia is defined as a disease, the root causes of which include factors such as old age, decreased physical activity, insufficient nutrition, chronic diseases, malignant tumors and

physical cachexia, leading to gradual weakening of skeletal muscle mass, strength and function (2–5). Malnutrition or undernutrition, on the other hand, could be defined as a condition in which changes in body composition (but not including loss of fat mass), a decrease in the number of body cells, resulting in a decline in physical and mental function, and a deterioration in clinical outcomes, primarily due to insufficient intake or absorption of nutrients (6).

Malnutrition is a common but underrecognized comorbidity among hospitalized older adults, and its prevalence typically varies between 30 and 55%, depending on the study population and the assessment tools used (7). Multiple studies have confirmed that malnutrition significantly increases the risk of sarcopenia in older adults. For example, a follow-up study conducted by Beaudart et al. found that older adults who were malnourished had a four-fold higher risk of developing sarcopenia (8), which indicates that sarcopenia is strongly associated with insufficient protein or nutrient intake (9). Previous study showed that insufficient protein intake destroys the balance of protein catabolism and stimulates the occurrence of skeletal muscle atrophy and impaired muscle growth, resulting in decreased muscle mass and physical function in the elderly (10).

Despite numerous studies suggesting a potential connection between malnutrition and sarcopenia (8, 9), this area remains relatively underexplored. Timely screening for sarcopenia through nutritional assessment and inclusion in personalized nutrition and exercise interventions could enhance management and improve physical and mental well-being, as well as quality of life (11).

Over the years, various predictive tools, such as the simple five-item questionnaire (SARC-F), have been developed to identify individuals at risk of sarcopenia (12). While tools like SARC-F provide valuable insights, they often rely on subjective measures that may not be universally accessible in resource-limited settings. Moreover, indices such as the Prognostic Nutrition Index (PNI) (13), Nutritional Risk Index (NRI) (14), Geriatric Nutritional Risk Index (GNRI) (15), Controlling Nutritional Status (CONUT) score (16), and Body Mass Index (BMI) (17) are commonly used for quantifying nutritional risk, but they lack specificity of nutritional indicators for sarcopenia diagnosis.

To address these gaps, this study aimed to conduct a cross-sectional investigation and develop a risk prediction model for sarcopenia diagnosis (low skeletal muscle mass) using objective clinical nutritional indicators in a Chinese population aged 18 years and older. The results were compared with established indices, including PNI, NRI, GNRI, CONUT score, and BMI. By leveraging readily accessible nutritional biomarkers, this study seeks to enhance the accuracy and applicability of sarcopenia risk prediction, providing robust theoretical backing and practical guidance for advancing healthy aging initiatives.

Methods

Study design and population

This retrospective cross-sectional study was conducted in the Department of Geriatrics, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University from December 2020 to August 2023. In accordance with the Declaration of Helsinki, this study has been approved by the Ethics Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University (No. KY2021-071-B). Prior to inclusion in the study, all participants had signed informed consent for the use of their health examination data. Study participants were required to meet the following criteria: have undergone regular health checkups and bioelectrical impedance analysis (BIA), and be at least 18 years of age. Exclusion criteria include: (1) severe systemic disease, such as severe infection, malignancy or multiple organ failure (including liver, kidney, respiratory system or heart); (2) have been diagnosed with a neuromuscular disease; (3) have peripheral edema or have received diuretic treatment in the past month; (4) Oral, inhalation or nasal use of glucocorticoids; (5) Received nutritional support, such as gastric tube or nasal feeding enteral nutrition or peripheral deep vein parenteral nutrition; and (6) There is incomplete data. Additionally, a total of 460 participants were included for external validation. These participants were enrolled from Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University between September 2023 and June 2024.

Data collection

After obtaining consent from the participants, trained staff measured their height and weight. We collected information about their medical history, including chronic conditions such as hypertension, type 2 diabetes, coronary heart disease, hyperlipidemia, cerebral infarction, as well as their history of alcohol and tobacco use using questionnaires.

All participants fasted for 8 h following their dinner on the evening prior to the physical examination. Fasting venous blood samples were collected and treated with heparin for anticoagulation. The collected blood samples were stored at a temperature of −20°C and sent to the laboratory at Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University for analysis. A wide range of biochemical markers were measured, including blood routine parameters (hemoglobin, lymphocyte count, C-reactive protein), blood biochemistry (albumin, aspartate aminotransferase, alanine aminotransferase, urea nitrogen, creatinine, uric acid, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, fasting blood glucose, glycated hemoglobin, calcium, phosphorus, magnesium), serum ferritin, 25(OH) vitamin D, and thyroid function tests (FT3, FT4, TSH).

All these assays underwent rigorous quality control procedures, conducted by trained laboratory personnel, and were tested using Hitachi 7,600–110 and Hitachi 7,020 automatic analyzers (Hitachi, Tokyo, Japan). Reagents used for these assays were provided by the respective companies.

Nutritional assessments

Contents and characteristics of the five nutritional indexes are shown in Supplementary Tables S1, S2. PNI is calculated as serum albumin (g/L) + 5 × total lymphocyte count ($\times 10^9$/L) (13); NRI is calculated according to the following formula: NRI = (1.519 × serum albumin) (g/L) +41.7 × (present weight/ideal body weight), which is suitable for patients under 60 years old (14); GNRI is calculated as follows: GNRI = (1.489 × serum albumin) (g/L) + 41.7 × (present weight/ideal body weight), which is suitable for patients aged 60 years and above; The ideal weight is calculated using the Lorentz equation

(15); CONUT score is calculated based on levels of serum albumin, total lymphocyte count and total cholesterol (16); BMI = weight (kg)/height^2 (m^2) (17).

Muscle mass measurement

Limb skeletal muscle mass (SMM) was measured using Bioelectrical Impedance Analysis (BIA) with the InBody770 device (InBody, Seoul, Korea). Before the examination, participants were instructed to fast, empty their bladders, and rest for at least 15 min. Limb BIA measurement evaluates limb body composition by positioning four electrodes (two on the wrists and two on the ankles) on the participant's limbs. We utilized the square of height to adjust for SMM and calculate the Limb Skeletal Muscle Mass Index (SMI), defined as SMM (Kg)/height (m^2). According to the SMI value, women <5.7 kg/m^2 and men <7.0 kg/m^2 were diagnosed with sarcopenia (4).

Statistical analysis

Continuous variables were expressed as medians (range), while categorical variables were expressed as the number of patients (percentage, %). The Wilcoxon test (Mann–Whitney U test) was employed to compare differences among continuous variables, and the $\chi 2$ test was used to assess differences among categorical variables. Subsequently, we conducted Pearson correlation analysis to explore the relationship between SMI and relevant variables. Lasso regression was applied for variable selection. Univariate and multivariate logistic regression analyses were performed to predict the potential risk of sarcopenia. We evaluated the predictive performance of different models using calibration curve analysis, AUROC analysis, and DCA analysis. In the AUROC analysis, we determined the optimal classification threshold by maximizing the Youden's index (18), which effectively balances the sensitivity and specificity of the predictive model. Model calibration analysis was conducted to mitigate the impact of confounding factors. A nomogram was utilized to visualize the relationships between variables in the prediction model.

All statistical analyses were carried out using R software (version 4.2.3, https://www.r-project.org/). Statistical significance was considered when double-tailed p values were < 0.05.

Results

Basic characteristics of the study population

During the study period, a total of 1,213 subjects who visited the Geriatric Department, including individuals under 59 years of age receiving specialized care, were enrolled. Subsequently, 166 patients were excluded from the analysis, and an additional 45 patients were found to have missing nutritional data. Ultimately, our analysis focused on the data of 1,002 eligible patients (Figure 1). We measured SMI values via BIA and classified these patients according to the criteria proposed by the Asian Sarcopenia Working Group (AWGS) (19).

A total of 183 participants (18.3%) were classified as having low skeletal muscle mass (SMM), while 819 participants (81.7%) were classified as having normal SMM based on SMI values obtained via BIA (Table 1). Significant differences were observed between the low SMM and normal SMM groups in gender, age, BMI, and most nutrition-related biochemical markers (all $p < 0.05$). The low SMM group comprised a higher proportion of women, older individuals, and participants with lower BMI. Additionally, lymphocyte count, hemoglobin, albumin, triglyceride, ferritin, creatinine, and uric acid levels were significantly lower, while HDL and calcium levels were significantly higher in the low SMM group. Nutritional indices such as NRI and GNRI were also decreased, whereas PNI and CONUT scores were increased in the low SMM group. No significant differences were observed in AST, cholesterol, LDL, FT4, TSH, or phosphorus levels between the two groups (Table 1).

The Pearson correlation analysis indicated strong positive correlations ($R > 0.6$, $p < 0.001$) between SMI and weight-related parameters, including weight (R = 0.89), height (R = 0.73), BMI (R = 0.73), NRI (R = 0.62), GNRI (R = 0.62), PNI (R = 0.33). In terms of clinical biochemical markers, SMI demonstrated significant positive correlations ($R \geq 0.3$, $p < 0.001$) with hemoglobin (R = 0.57), albumin (R = 0.30), uric acid (R = 0.52), creatinine (R = 0.50), ferritin (R = 0.41) and triglyceride (R = 0.37), while it exhibits a significant negative correlation ($R = -0.47$, $p < 0.001$) with HDL. Other correlations with different indicators appear comparatively weaker (all absolute $R < 0.30$) (Supplementary Figure S1).

Development and comparative performance of a predictive model for sarcopenia

We initially attempted to construct a new assessment model by incorporating variables that exhibited significant differences in baseline comparisons and demonstrated significant associations with SMI values in Lasso regression analyses. However, when weight-related indicators were present, the importance of weight and gender variables overshadowed that of other indicators (e.g., lambda decreased, the coefficients of weight and sex increased, while the coefficients of other indicators approached 0) (Supplementary Figure S2A). This made it challenging to discern the relative importance of non-weight-related measures.

To address this issue, we performed a modified Lasso regression analysis, excluding weight-related variables. In the weight-independent model (Supplementary Figure S2B), when lambda is relatively low at exp.(−6), the absolute values of the coefficients for the Albumin, Age stage, Calcium, HDL, and Lymphocytes indicators rank among the top five, with values of (−0.748, 0.741, 0.654, 0.567, −0.442), respectively. As lambda increases to exp.(−3), only these five variables still have significant coefficients (HDL = 0.411, Age stage = 0.254, Albumin = −0.178, Lymphocytes = −0.140, Calcium = 0.085), while the others are excluded (Supplementary Figure S2B). Consequently, we identified these five prominent variables subsequent modeling, aiming to distinguish between the two population groups.

Following variable selection process, we proceeded with additional univariate and multivariate Logistic regression analyses

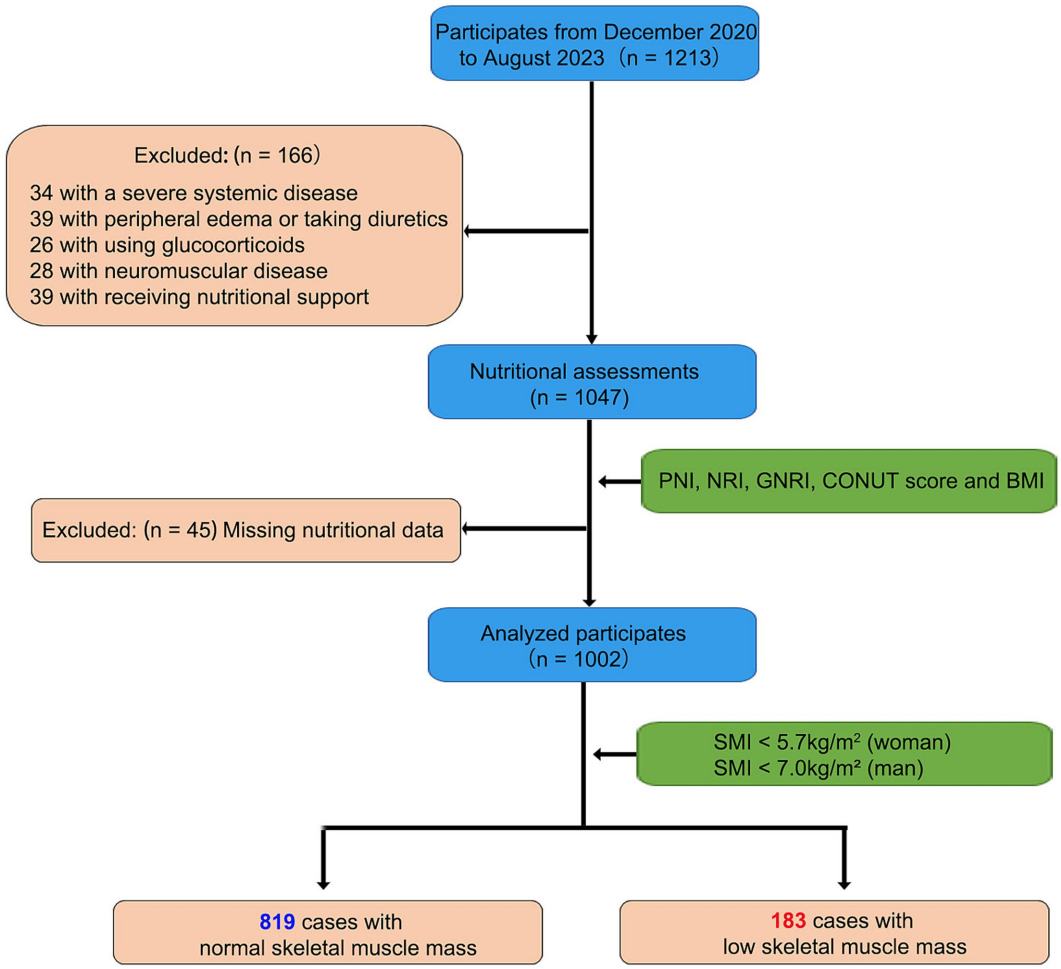

FIGURE 1
The flow diagram of study population. Initially, 1,213 subjects were enrolled from the Geriatric Department. Of these, 166 patients were excluded due to severe disease or medication issues, and 45 patients were excluded due to missing nutritional data. The final analysis included 1,002 eligible subjects: 819 with normal skeletal muscle mass and 183 with low skeletal muscle mass. This diagram provides an overview of the inclusion and exclusion criteria, detailing the final study sample size and data availability.

(Supplementary Table S3) and constructed several models. The model related to weight was named WS: Weight + Sex. In contrast, models independent of body weight were named as AHL: Albumin + HDL + Lymphocytes, AHLC: Albumin + HDL + Lymphocytes + Calcium, and AHLCA: Albumin + HDL + Lymphocytes + Calcium + Age stage. The results demonstrated that the selected variables (Weight, Sex, Age stage, Calcium, HDL, Lymphocytes, and Albumin) were all statistically significant in univariate Logistic regression analysis (all $p < 0.001$). Additionally, models WS (AUC = 0.935), AHL (AUC = 0.780), AHLC (AUC = 0.805), and AHLCA (AUC = 0.812) constructed using these variables, all exhibited strong predictive performance (AUC $\geq$ 0.78, all $p < 0.01$).

To assess the robustness of these four models' predictive capabilities, we conducted calibration curve analysis. After 1,000 bootstrap replicates, the original and calibrated prediction curves for these four models including WS (mean absolute error = 0.006), AHLC (mean absolute error = 0.011), AHL (mean absolute error = 0.009) and AHLCA (mean absolute error = 0.009) closely matched the ideal curve (Supplementary Figures S2C–F).

The combination of AUROC and DCA analysis confirms the robustness and clinical relevance of the AHLC model

To comprehensively assess the performance of our newly developed models, we conducted a series of comparisons, including established indices such as NRI, GNRI, BMI, PNI, and CONUT score, which are currently recognized to quantify nutritional risk. Additionally, we included univariate models associated with these parameters for validation and comparison. We randomly divided our dataset and employed 10-fold cross-validation with 10 repetitions for both validation (Supplementary Table S4) and training set.

The results of validation set revealed that the WS model (AUC = 0.934, Accuracy = 0.877 and Youden index = 0.773) exhibited the highest performance, which was superior to the univariate model focused solely on weight (AUC = 0.885, Accuracy = 0.800 and Youden index = 0.654) (Supplementary Table S4). In the category of models independent of weight, both AHLCA (AUC = 0.806, Accuracy = 0.758 and Youden index = 0.547) and AHLC (AUC = 0.802, Accuracy = 0.781 and Youden index = 0.544) exhibited robust

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TABLE 1 Clinical characteristics of participants with normal and low skeletal muscle mass (SMM).

Characteristics	All subjects	Normal SMM	Low SMM (sarcopenia)
N (%)	1,002	819 (81.7%)	183 (18.3%)
Sex (%)			
Female	433 (43.21)	331 (40.42)	102 (55.74) ***
Male	569 (56.79)	488 (59.59)	81 (44.26) ***
Age stage (%)			
<60 (age)	636 (63.47)	557 (68.01)	79 (43.17) ***
[60, 80]	320 (31.94)	235 (28.69)	85 (46.45)
≥80 (age)	46 (4.59)	27 (3.30)	19 (10.38)
Age	56 [47, 65]	55 [47, 63]	61 [49, 72] ***
Height (m)	1.68 [1.60, 1.73]	1.69 [1.62, 1.74]	1.62 [1.57, 1.68] ***
BMI (Kg/m^2)	23.50 [21.29, 25.85]	24.29 [22.30, 26.33]	19.86 [18.50, 21.02] ***
Weight (Kg)	65.95 [56.23, 74.98]	68.70 [60.30, 77.05]	51.50 [47.40, 57.45] ***
SMI (Kg/m^2)	7.10 [6.20, 7.90]	7.40 [6.50, 8.10]	5.60 [5.30, 6.60] ***
Lymphocytes (×10^9/L)	1.96 [1.58, 2.43]	2.02 [1.67, 2.48]	1.60 [1.32, 2.13] ***
Hemoglobin (g/L)	136.00 [125.00, 147.00]	138.00 [127.00, 148.00]	129.00 [120.00, 140.00] ***
ALT (U/L)	18.00 [13.00, 25.00]	18.00 [13.00, 26.00]	15.00 [12.00, 21.00] ***
AST (U/L)	18.00 [15.00, 22.00]	18.00 [15.00, 22.00]	19.00 [16.00, 22.00]
Albumin (g/L)	42.30 [40.30, 44.70]	42.50 [40.70, 44.85]	41.00 [38.15, 44.05] ***
Triglyceride (mmol/L)	1.30 [0.92, 1.86]	1.35 [0.99, 1.96]	1.01 [0.68, 1.43] ***
Cholesterol (mmol/L)	185.76 [162.15, 211.30]	185.76 [161.38, 211.30]	185.37 [165.06, 216.14]
HDL (mmol/L)	1.19 [1.00, 1.46]	1.16 [0.97, 1.38]	1.45 [1.18, 1.76] ***
LDL (mmol/L)	2.82 [2.29, 3.40]	2.83 [2.30, 3.43]	2.74 [2.23, 3.26]
Creatinine (mmol/L)	61.00 [50.00, 72.00]	62.00 [51.00, 72.00]	57.00 [46.50, 69.00] ***
Urea nitrogen (μmol/L)	5.10 [4.40, 5.90]	5.00 [4.30, 5.80]	5.40 [4.40, 6.30] *
Uric acid (μmol/L)	325.00 [269.25, 384.00]	335.00 [278.50, 391.00]	293.00 [245.00, 348.00] ***
FT3 (pmol/L)	4.67 [4.31, 5.11]	4.72 [4.34, 5.14]	4.56 [4.14, 4.89] ***
FT4 (pmol/L)	15.90 [14.63, 17.40]	15.90 [14.70, 17.40]	15.80 [14.40, 17.90]
TSH (mIU/L)	2.09 [1.43, 3.02]	2.10 [1.450 3.02]	2.08 [1.330, 3.00]
Calcium (mmol/L)	2.21 [2.14, 2.28]	2.20 [2.14, 2.27]	2.24 [2.16, 2.32] ***
Phosphorus (mmol/L)	1.15 [1.05, 1.26]	1.15 [1.06, 1.26]	1.16 [1.05, 1.31]
Magnesium (mmol/L)	0.91 [0.87, 0.95]	0.91 [0.87, 0.95]	0.93 [0.88, 0.97] *
CRP (mg/l)	0.67 [0.37, 1.42]	0.77 [0.38, 1.44]	0.47 [0.35, 1.26] ***
Fasting blood sugar (mmol/L)	4.70 [4.20, 5.39]	4.68 [4.19, 5.34]	4.83 [4.25, 5.50]
Glycated hemoglobin (%)	5.60 [5.30, 6.00]	5.60 [5.30, 6.00]	5.50 [5.20, 5.80] *
Serum total 25 (OH)D (ng/ml)	19.99 [16.27, 23.96]	20.08 [16.43, 23.81]	18.58 [15.28, 24.67]
Ferritin (μg/L)	112.45 [58.40, 210.23]	118.70 [59.45, 215.90]	93.20 [54.45, 161.20] *
NRI	109.25 [103.23, 115.29]	111.40 [105.53, 116.58]	100.39 [95.53, 104.79] ***
GNRI	107.99 [102.02, 113.92]	110.12 [104.28, 115.30]	99.10 [94.34, 103.55] ***
PNI	52.70 [49.51, 55.59]	53.25 [50.25, 56.00]	50.00 [46.23, 52.93] ***
CONUT	1 [0, 1]	1 [0, 1]	1 [0, 2] ***

Data presented as median (interquartile range, IQR). Statistical significance determined by $p < 0.05$. *, $p < 0.05$; ***, $p < 0.001$. BMI, Body Mass Index; SMI, Muscle Mass Index; ALT, alanine transaminase; AST, aspartate aminotransferase; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; FT3, free Triiodothyronine; FT4, free Thyroxine; TSH, thyroid-stimulating hormone; CRP, C-reactive protein; NRI, nutritional risk index; GNRI, geriatric nutritional risk index; PNI, prognostic nutritional index; CONUT, controlling nutritional status.

performance, with minimal performance differences between them (Supplementary Table S4).

Furthermore, we carried out an analysis of the area under the receiver operating characteristic curve (AUROC) and decision curve analysis (DCA) to compare the effectiveness of different models. Among models independent of weight, AHLCA (AUC = 0.812) and AHLC (AUC = 0.805) emerged as top performers (Figures 2A–D). In accordance with the Occam's razor principle (20), when model performance was comparable, we choose the AHLC model, characterized by fewer variables.

To further evaluate the discriminative ability and clinical applicability, we conducted external validation with a total of 460 participants enrolled from Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, the same hospital where the primary study population

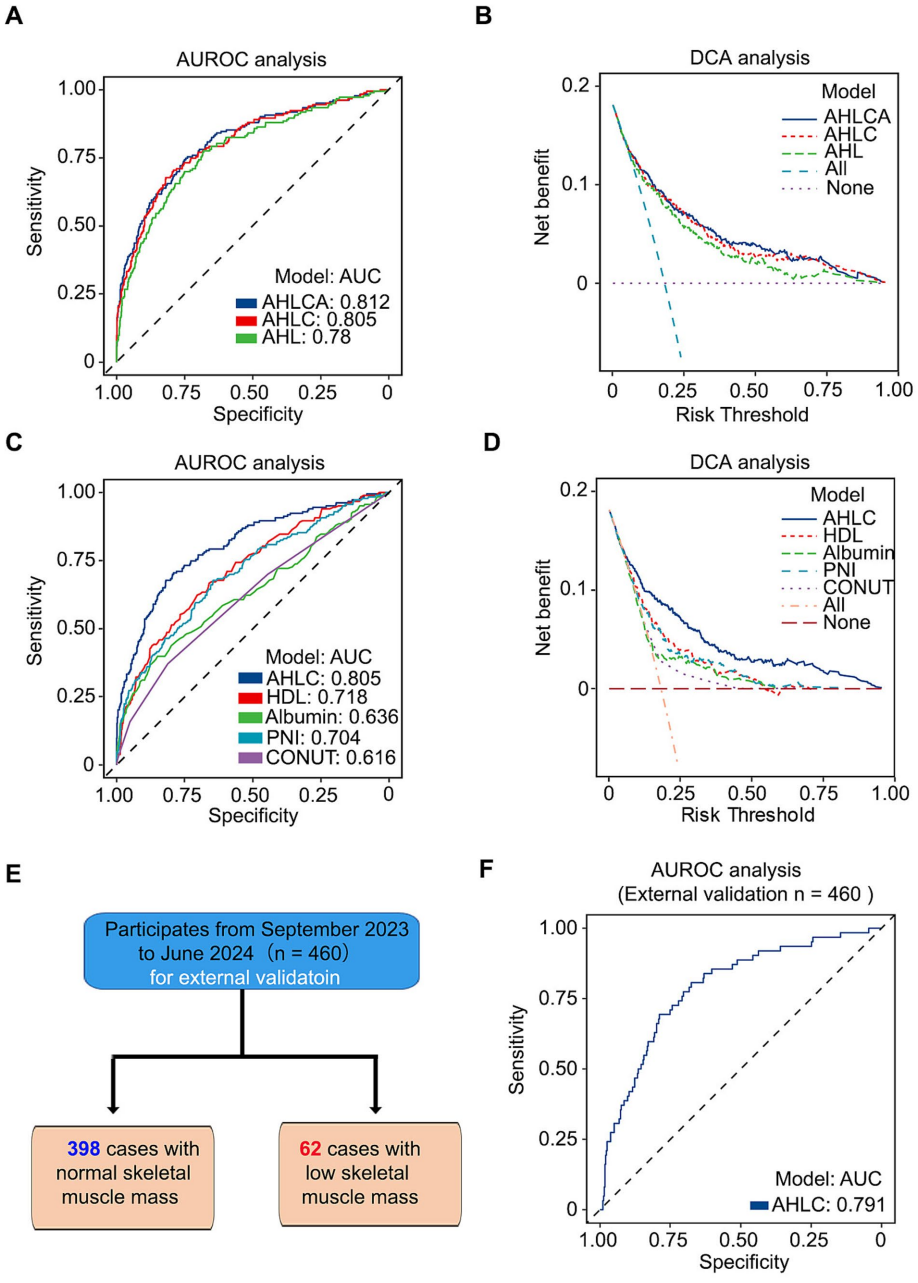

FIGURE 2
The combination of AUROC and DCA analysis confirms the robustness and clinical relevance of the AHLC model. **(A)** AUROC analysis of three weight-independent models, illustrating their predictive performance. **(B)** DCA analysis of the same three models, highlighting their clinical utility. **(C)** AUROC analysis comparing the AHLC model with other weight-independent models. **(D)** DCA analysis comparing the AHLC model with other weight-independent models, assessing clinical relevance. **(E)** Flow diagram of the study population for external validation, detailing the enrollment and analysis process with 460 subjects, including 398 with normal skeletal muscle mass and 62 with low skeletal muscle mass. **(F)** AUROC analysis of the AHLC model in the external validation dataset, confirming its predictive accuracy in a different cohort. AUROC (Area Under the Receiver Operating Characteristic Curve) and DCA (Decision Curve Analysis) values are used to assess model performance and clinical utility. AUROC, area under the receiver operating characteristic curve; DCA, decision curve analysis; AHLC, Albumin + HDL + Lymphocytes + Calcium.

TABLE 2 Validation of the AHLC model through internal and external validation methods in the study population.

Models	AUC	Sensitivity	Specificity	Accuracy	Positive predicting value	Negative predicting value	Positive likelihood ratio	Negative likelihood ratio	Youden Index
AHLC (Training set, n = 902)	0.805	0.699	0.800	0.782	0.440	0.923	3.531	0.376	0.499
AHLC (Internal validation set, n = 100)	0.802	0.759	0.786	0.781	0.469	0.938	4.354	0.299	0.544
AHLC (External validation set, n = 460)	0.791	0.694	0.789	0.776	0.339	0.943	3.286	0.388	0.482

Data presented as individual values of statistical metrics. AUROC (area under the receiver operating characteristic curve), DCA (decision curve analysis); AHL (Albumin + HDL + Lymphocytes); AHLC (Albumin + HDL + Lymphocytes + Calcium); AHLCA (Albumin + HDL + Lymphocytes + Calcium + Age Stage); PNI (prognostic nutritional index); RNI (nutritional risk index); GNRI (geriatric nutritional risk index); CONUT (controlling nutritional status); BMI (Body Mass Index); AHLC (Albumin + HDL + Lymphocytes + Calcium).

was recruited (Figure 2E; Supplementary Table S5). The AUC for the external validation of the AHLC model was 0.791 (Figure 2E; Table 2). Overall, both internal and external validation (Table 2) demonstrated that the AHLC model has strong screening ability, indicating its potential clinical application value.

After finalizing the model, we conducted variable adjustment to alleviate the potential influence of confounding variables. The results emphasized that AHLC model maintained significant predictive capability (all $p < 0.001$) even after variable adjustment (Supplementary Table S6).

In summary, when considering predictors associated with weight or weight-related indicators, the WS model proves to be the most appropriate choice for predicting muscle mass deficiency. Conversely, when utilizing measures unrelated to body weight for predictions, the AHLC model stands out as the optimal choice.

Nomograms for sarcopenia using AHLC score

To visualize AHLC models, we generated a nomogram using an explicit formula (Figure 3A) that provides a graphical representation. Each variable corresponds to a specific value and is assigned an associated score, initially located in the first row (Figure 3B). Subsequently, by summing the scores for each variable and identifying the total score on the respective scale, the nomogram facilitates the calculation of the probability of sarcopenia development. In the AHLC model (with a sensitivity of 0.759 and specificity of 0.786, as shown in Table 2), it signifies a higher predicted risk of sarcopenia for the individual. When the risk value, which is precisely calculated by the formula, surpasses 0.222 in the AHLC model (Figure 3C).

Discussion

Sarcopenia is a common health problem in the elderly, which seriously affects the quality of life and overall health status (21). In this study, we introduced the AHLC model, which integrates albumin, HDL cholesterol, lymphocytes, and calcium as key predictors of sarcopenia risk. Our results confirmed the model's accuracy and clinical utility, as validated by AUROC, DCA, and nomogram analyses. This novel approach offers a simple, nutrition-based method for identifying individuals at risk of sarcopenia, providing an accessible and practical tool for early intervention and promoting healthy aging, especially in the Chinese adult's population.

Construction of weight-related WS model and the weight-independent AHLC model

Previous studies have consistently demonstrated a strong association between malnutrition and sarcopenia (22). In a two-center prospective cohort study that included 350 hospitalized older adults (mean age: 77.2 ± 7.6 years, 56% of whom were women), 98 participants (28%) tragically died during 2 years of follow-up. The study found that participants with malnutrition-sarcopenia syndrome had the highest risk ratio (HR: 19.8) (23). Additionally, the EFFORT study highlighted the significance of early intensive nutritional therapy, reducing mortality by 35% and improving clinical outcomes, including a 21% reduction in intensive care unit admissions, major complications, readmissions, and decreased function (24). These findings highlight the pivotal role of nutrition in the development of sarcopenia and provide important background support for our study.

In this study, we conducted a cross-sectional analysis involving 1,002 participants who underwent health checkups and bioelectrical impedance analysis (BIA). Results indicated that 18.3% of the participants were classified as having low skeletal muscle mass (sarcopenia). Statistically significant differences in nutritional status (e.g., NRI, GNRI, PNI, CONUT score, BMI, etc.) were observed between individuals with low skeletal muscle mass and those with normal skeletal muscle mass ($p < 0.001$). Furthermore, individuals with low skeletal muscle mass were predominantly female and of older age, consistent with previous research findings (1, 25, 26).

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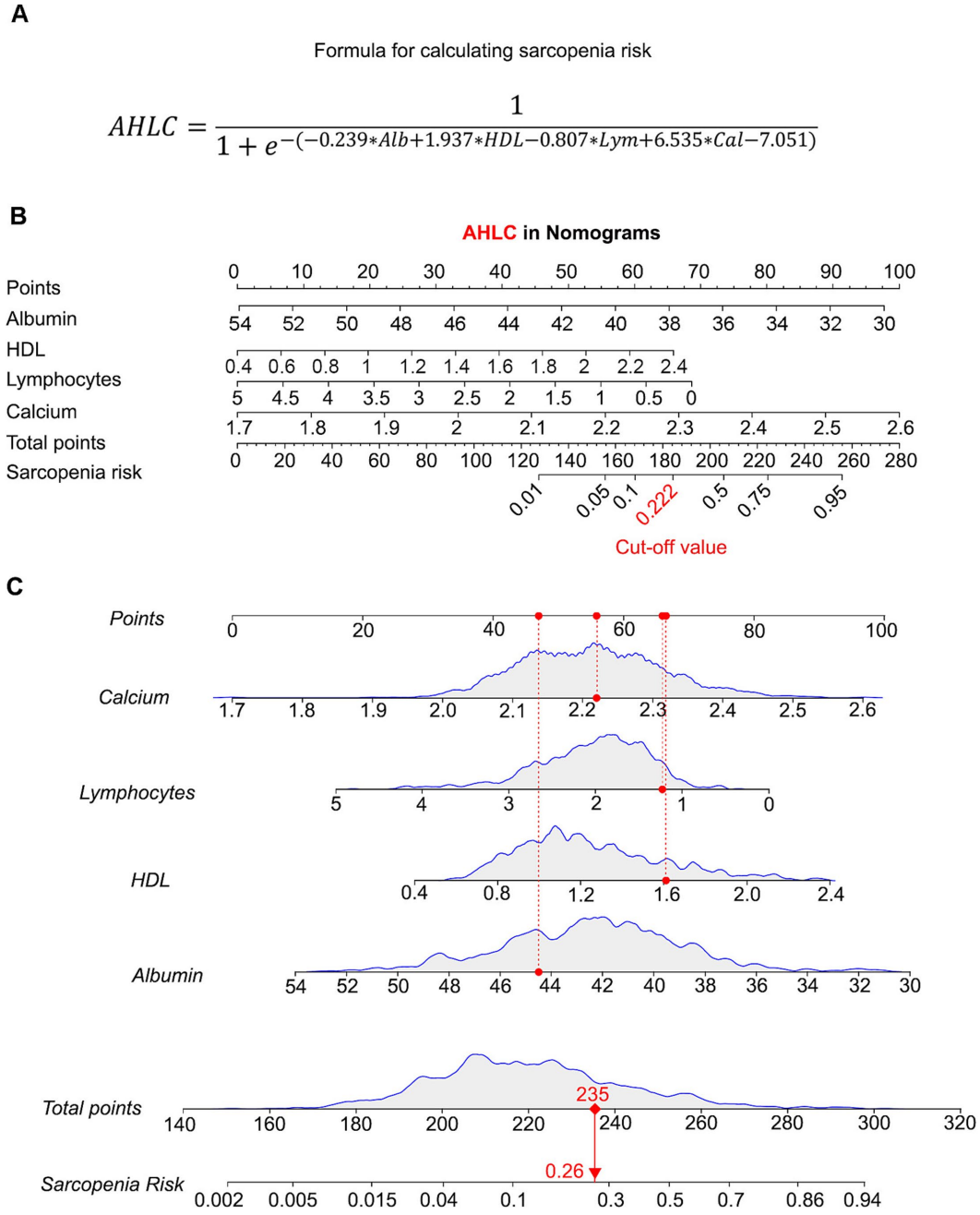

FIGURE 3
Predictive validity of AHLC models using nomograms. **(A)** A formula for sarcopenia risk calculation of AHLC model. **(B)** Nomogram for the AHLC model, showing how each variable contributes to the total risk score. The corresponding risk value cut-off for the AHLC model, set at 0.222, used to classify the risk of sarcopenia. Nomograms are used to visualize the predictive power of the AHLC model, with the cut-off value indicating the threshold for risk classification. **(C)** Individual Risk Evaluation with the AHLC nomogram for Sarcopenia Assessment. Each line represents an individual biological indicator. The curve above each line shows the statistical distribution of that indicator, with the red dot indicating the specific measurement value for an example individual. The red dashed line shows the position of this value within the distribution. The total score is calculated based on these indicators, which is used to estimate the risk of sarcopenia. Calcium: Red dot corresponds to 2.22 mmol/L. Lymphocytes: Red dot corresponds to 1.23 × 10^9/L. HDL: Red dot corresponds to 1.61 mmol/L. Albumin: Red dot corresponds to 44.5 g/L. Total points: Sum of the weighted scores for each biological indicator, resulting in a total score of 235 points. The sarcopenia risk, estimated based on the total score, is indicated by the red dot on the risk curve, which shows a risk value of 0.26. The red arrow connects the total score to the corresponding sarcopenia risk on the curve, indicating the risk probability. AHLC, Albumin + HDL + Lymphocytes + Calcium; HDL, high-density lipoprotein.

In the construction of potential sarcopenia risk prediction models, we initially employed Lasso regression analysis for variable selection. Notably, weight and gender exhibited such high importance that other indicators were overshadowed. Consequently, we developed two distinct models: the weight-related WS model and the weight-independent AHLC model. Both models demonstrated strong performance in predicting sarcopenia risk and provided clinicians with valuable assessment tools in different clinical contexts. When compared to widely

recognized quantitative nutritional risk indicators (e.g., NRI, GNRI, PNI, CONUT score, BMI), the WS model performed the best (AUC = 0.935) among weight-related models (NRI, GNRI, BMI, WS), while among weight-independent models (PNI, CONUT score, AHLC), the AHLC model exhibited the most favorable performance (AUC = 0.805).

Our findings consistently highlight the critical roles of weight and gender in predicting the risk of sarcopenia, which is consistent with previous findings (27–29). Importantly, it is worth noting that among individuals with sarcopenia, there are those with sarcopenic obesity (SO) (30), and SO is associated with multiple adverse health outcomes, including frailty, falls, disability, increased morbidity, and mortality (31). In such cases, body weight alone does not serve as an independent predictor.

Clinical serum nutritional AHLC model in predicting sarcopenia risk

Thus, we further developed the clinical serum nutritional AHLC model to provide a more objective indicator of potential sarcopenia risk in the absence of weight effects. This model incorporates four serological indicators: albumin, high-density lipoprotein (HDL), blood calcium, and lymphocyte counts, providing a comprehensive assessment of nutritional status, lipid metabolism, skeletal muscle health, and immune function—factors that play pivotal roles in the onset and progression of sarcopenia (21).

Secondary data analysis from our China Health and Retirement Longitudinal Study indicated that higher serum triglyceride to HDL cholesterol ratios in elderly diabetic patients were associated with better muscle status (32). Furthermore, mounting evidence suggests a high co-occurrence rate of sarcopenia and osteoporosis (33), with shared biological pathways including aging, inflammation, hormonal imbalances, and nutritional deficiencies (34–37). Consequently, some researchers advocate for considering osteoporosis and sarcopenia as a unified entity: osteosarcopenia (38–40). This revelation underscores the importance of addressing bone and muscle health in an integrated manner when managing the health of the elderly, rather than addressing these issues in isolation.

To facilitate comprehension of sarcopenia risk among clinicians, caregivers, and older adults, we developed a nomogram for predicting the potential risk of sarcopenia. This nomogram can visually show the individual's risk value (41). When the Value at Risk (VAR) of the AHLC score exceeds 0.222, an individual may face a heightened risk of potential sarcopenia. This tool holds promise for the early identification of sarcopenic individuals, allowing for interventions to enhance quality of life and prevent the onset of decreased muscle function and related complications.

Nevertheless, it is essential to acknowledge the limitations of this study. Firstly, the relatively small sample size may introduce selective bias. We were only able to gather data on muscle mass, and unfortunately, we lacked information on muscle strength or functionality. Future research should encompass larger, multi-center studies to validate and refine the application of AHLC scoring. Another potential limitation of our study is the single-center design, which may limit the generalizability of the AHLC model to other populations. However, recent evidence suggests a strong association between elevated HDL-C levels and an increased risk of sarcopenia and reduced grip strength in older adults (42). These findings align with our model, where HDL-C emerged as a significant predictor of sarcopenia risk, reinforcing the biological relevance of this marker. To further validate the AHLC model and ensure its applicability across diverse populations, future studies will leverage external datasets from varied regions and demographic groups. This approach will help establish the model's robustness and expand its utility in global clinical settings. In addition, while acute inflammatory conditions were accounted for using CRP levels, chronic inflammatory diseases or long-term medication use may also influence biomarkers such as lymphocytes and albumin. Future studies should incorporate additional adjustments or sensitivity analyses to account for these potential confounders.

While the biomarkers used in our model (such as albumin and lymphocytes) are commonly available in hospital settings, we acknowledge that they may not be as easily accessible in low-resource environments. In such cases, other simple and widely used methods for diagnosing sarcopenia, such as grip strength and calf circumference, could be incorporated into the model as alternatives. In future studies, we plan to explore how the model can be applied in these settings, and whether including additional simple measures like grip strength and calf circumference would enhance the model's effectiveness in low-resource environments. Additionally, our current studies are focusing on interventions and treatments for sarcopenia. Early-stage tools for identifying sarcopenia risk are crucial for selecting appropriate interventions. By improving nutrition, increasing exercise, and maintaining a healthy weight, we could help older adults reduce their risk of sarcopenia and maintain optimal muscle mass and function (43, 44). Achieving a healthier and more vibrant aging society necessitates collaboration among the healthcare sector, healthcare institutions, and the community to collectively enhance the overall health of older individuals.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

In accordance with the Declaration of Helsinki, this study has been approved by the Ethics Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University (No. KY2021-071-B). Prior to inclusion in the study, all participants had signed informed consent for the use of their health examination data.

Author contributions

XZ: Funding acquisition, Data curation, Writing – original draft, Conceptualization. PY: Software, Methodology, Writing – original draft, Data curation. NC: Writing – original draft, Methodology, Data curation. TH: Software, Investigation, Writing – original draft. BW: Writing – review & editing, Supervision, Conceptualization, Writing – original draft. YH: Writing – review & editing, Writing – original draft, Conceptualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1505655/full#supplementary-material

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Glossary

SMM	skeletal muscle mass
BIA	bioelectrical impedance analysis
ROC	receiver operating characteristic
DCA	decision curve analysis
BMI	body mass index
SMI	muscle mass index
ALT	alanine transaminase
AST	aspartate aminotransferase
HDL	high-density lipoprotein cholesterol
LDL	low-density lipoprotein cholesterol
FT3	free triiodothyronine
FT4	free thyroxine
TSH	thyroid-stimulating hormone
CRP	C-reactive protein
NRI	nutritional risk index
GNRI	geriatric nutritional risk index
PNI	prognostic nutritional index
CONUT	controlling nutritional status
AHL	Albumin + HDL + Lymphocytes
AHLC	Albumin + HDL + Lymphocytes + Calcium
AHLCA	Albumin + HDL + Lymphocytes + Calcium + Age
WS	Weight + Sex

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EDITED BY
Juliana Vaz,
Federal University of Pelotas, Brazil

REVIEWED BY
Virginia Maria Muniz,
Secretaria de Estado da Saúde do Espírito Santo, Brazil
Nkereuwem Ekerette,
University of Uyo, Nigeria

*CORRESPONDENCE
Gudina Egata
✉ gudina_egata@yahoo.com

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Mid-upper-arm circumference: a surrogate measure for BMI for age z-score to identify thinness among adolescent girls in Addis Ababa, Ethiopia

Solome Zebene[1], Gudina Egata[1]* and Demewoz Haile[2]

[1]Department of Nutrition and Dietetics, School of Public Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia, [2]Institute for Health Metrics and Evaluation (IHME), Seattle, WA, United States

Background: The mid-upper arm circumference (MUAC) is an anthropometric screening tool used to assess the nutritional status of individuals, offering a practical and feasible option in low-resource settings. However, the potential of MUAC as a screening tool for identifying thinness among adolescents remains underexplored.

Objective: This study aimed to evaluate the accuracy of MUAC in identifying all forms of thinness among adolescent girls enrolled in selected schools in Addis Ababa, Ethiopia.

Methods and materials: A representative sample of 913 female adolescent students was selected using a stratified sampling technique in a cross-sectional study. Socio-demographic data were collected via interviewer-administered questionnaires. Anthropometric measurements, including height, weight, and MUAC, were collected using a portable stadiometer, a battery-powered digital scale, and a non-stretchable MUAC tape, respectively. The Pearson correlation coefficient (r) assessed the relationship between MUAC, age, and body mass index for age (BAZ). The Receiver Operating Characteristic (ROC) curve was used to evaluate MUAC's ability to classify those with or without thinness. The optimal threshold for adolescents aged 10–14 years was determined using Youden's index.

Results: A strong, significant positive correlation (r = 0.80) was observed between MUAC and BAZ. MUAC demonstrated good accuracy in detecting thinness and severe thinness (AUC = 0.86). Based on the highest Youden's index values, MUAC cut-offs of 20.1 cm and 19.7 cm were identified to detect thinness and severe thinness, respectively. MUAC exhibited 92.1% sensitivity and 67.3% specificity in identifying moderate thinness and 95.9% sensitivity and 68.5% specificity for severe thinness among adolescent girls.

Conclusion: MUAC showed good accuracy in predicting thinness and severe thinness, with comparable sensitivity but lower specificity than BAZ. Incorporating MUAC as a screening criterion for identifying thinness and severe thinness among female adolescents could be particularly beneficial in resource-limited settings such as Ethiopia.

KEYWORDS

mid-upper arm circumference, body mass index for age z-score, thinness, adolescent, Ethiopia

1 Introduction

According to the World Health Organization (WHO), adolescence is defined as the age group between 10 and 19 years (1). This stage of life is characterized by increased demands for macronutrients and micronutrients to support accelerated physical and mental growth, development, and reproductive maturity. Poor nutritional status during adolescence can have long-lasting effects, exposing individuals and future generations to adverse health outcomes. Malnutrition often begins in the uterus and can persist across generations (2). As a result, malnourished female adolescents are more likely to become malnourished adults and give birth to low birth-weight infants. If those infants are girls, they are at greater risk of continuing the cycle by becoming stunted adults (3, 4).

For the assessment of the nutritional status of individuals, body mass index (BMI) is often used as a proxy measure to estimate body mass. However, it must also be taken into account that in practice, especially in many poor and middle-income countries, inadequate measuring devices such as a stadiometer make measuring height problematic, and skilled human resources are required to compute BMI in a population context (5). Hence, it would be important to consider the necessity for a surrogate marker that gives good results while also being easy to assess in a population setting.

The concept of using the arm circumference as the public health index for protein-calorie malnutrition (PCM) in the community was first employed in a nationwide survey in the Republic of Haiti in 1958, and since then, it has been applied in different study settings under different scenarios (6). Middle upper arm circumference (MUAC) is increasingly being used as an alternative tool to screen for undernutrition in adolescents and adults in low-resource settings, particularly among pregnant women and people living with HIV who are eligible for antiretroviral therapy (ART). This is because MUAC is easier and more convenient, requires less expertise, is simple and relatively inexpensive, and can be measured in both community and facility settings (7–9).

Recent studies have revealed that MUAC can be used to accurately identify moderate and severe forms of thinness in adolescents (10–14). More specifically, some studies revealed that the sensitivity and specificity tests proved the relationship between BMI and MUAC and that MUAC represents adolescent nutritional status with considerable efficiency and recommended further research to more establish that MUAC is a better and promising measure of adolescent nutrition, having the advantage of needing fewer resources for data collection (15, 16). Despite the evidence of a strong association, global MUAC cut-offs for adolescent thinness classification are yet to be established.

Different countries use different MAUC cut-offs for categorizing adolescent nutritional status for their respective programs due to differences in body size and body fat distribution across populations (17). Therefore, establishing standardized MUAC cut-offs for identifying cases of thinness among female adolescents would be of great help in reaching out to a larger community and strengthening and harmonizing programming in adolescent nutrition programs. However, little is known about the potential for MUAC to be utilized as a screening tool for determining thinness in adolescents. The present study evaluates the use of MUAC as an alternative tool for BMI z-score to detect all forms of thinness among adolescent girls.

2 Methods and materials

2.1 Study setting, design, and participants

A school-based cross-sectional study design was used among 913 randomly selected female adolescent students aged 10 to 14 years living in Addis Ababa, the capital city of the Federal Government of Ethiopia, which is located at 9°1′48″N latitude and 38°44′24″E and covers a total area of 540 km^2. The city is subdivided into 11 sub-cities. The sub-cities are also divided into districts, and there are 126 districts in the city administration. According to the 2007 Census conducted by the Central Statistical Agency of Ethiopia (CSA), the city has a total population of 3,384,569, making nearly 4% of the country's total, of whom 635,903 were adolescents, which is 23.2% of the total population (18). This study was conducted from April to June 2021 in selected governmental and non-governmental schools in Addis Ababa. Adolescents with visible physical deformities that can affect anthropometric measurements were excluded from the study.

2.2 Sample size determination

The diagnostic accuracy test sample size formula was used to calculate the required sample size (19) with the following assumptions.

The sample size required for sensitivity:

$$N1 = z\alpha/2^2 * SN(1-SN) / \left(L^2 * P\right)$$

The sample size required for specificity is as follows:

$$N2 = z\alpha/2^2 * SP(1-SP) / \left(L^2 * (1-P)\right),$$

where n is the larger sample size between N1 and N2. Z $\alpha/2$: Z value corresponding to a 95% level of significance = 1.96. P: Assumed prevalence. SN: Anticipated sensitivity. SP: Anticipated specificity. L: maximum clinically acceptable width or precision of the 95% confidence level.

Hence, assuming an anticipated sensitivity of 94.0% and specificity of 79.0% (12), using a prevalence of 21.3% (20), absolute precision of 5%, taking a design effect of 2, and a non-response rate of 10%, a maximum feasible sample size of 913 adolescents was used.

2.3 Sampling procedures

A stratified multistage sampling procedure was used to obtain a representative sample. The schools were first stratified by ownership into governmental (232 schools) and non-governmental (553 schools) categories. A simple random sampling was used to select 15 schools, of whom 10 belonged to private and 5 to governmental institutions, respectively. Then, the sample size was proportionally allocated to each selected school based on the number of students. One section from each grade level in selected schools was randomly chosen. Sampling frames (lists of students) were obtained from each school's administrators. After proportionally allocating the number of study participants to each selected section, participants were randomly

selected from these lists. Room teachers (i.e., those responsible for supervision of students) assisted in identifying the study participants (Figure 1).

2.4 Data collection

2.4.1 Information on socio-economic, demographic, and environmental conditions

The data collection tool included socio-economic, demographic, environmental conditions, and anthropometry. Data were collected by eight trained data collectors and supervised by two supervisors who had previous exposure to research data collection and supervision, respectively.

Data on socioeconomic, demographic, and environmental conditions were collected using pretested, pretested, and structured questionnaires administered by the interviewer. All data were collected electronically using Kobo Collect software (an open-source Android app for collecting survey data), which is available at https://www.kobotoolbox.org/.

2.4.2 Anthropometric measurements

All anthropometric measurements were taken twice, and the average was used for the analysis. Height measurement was carried out using a portable stadiometer with a sliding headpiece. Participants stood straight on a leveled surface without shoes, with heels together, arms hanging freely by the sides, palms facing forward, and fingers pointing downwards. The head, shoulder blades, buttocks, and heels touched the board's wall. The measurement was taken from the sole of the feet to the vertex of the head and recorded to the nearest 0.1 cm. Weight was measured using a portable battery-powered digital scale without shoes and with minimum clothes (inner wear that does not affect the precision of measurements and can be adjusted for after measurement) and recorded to the nearest 0.1 kg. The MUAC was measured by a non-stretchable measuring tape on the non-dominant bare arm. This was determined by marking the mid-point between the tip of the lateral border of acromion and olecranon, then applying the tape measure to its middle point with the non-dominant arm hanging and relaxed. The tape was placed firmly but gently on the arm to avoid compression of soft tissue, and MUAC was recorded to the nearest 0·1 cm (21).

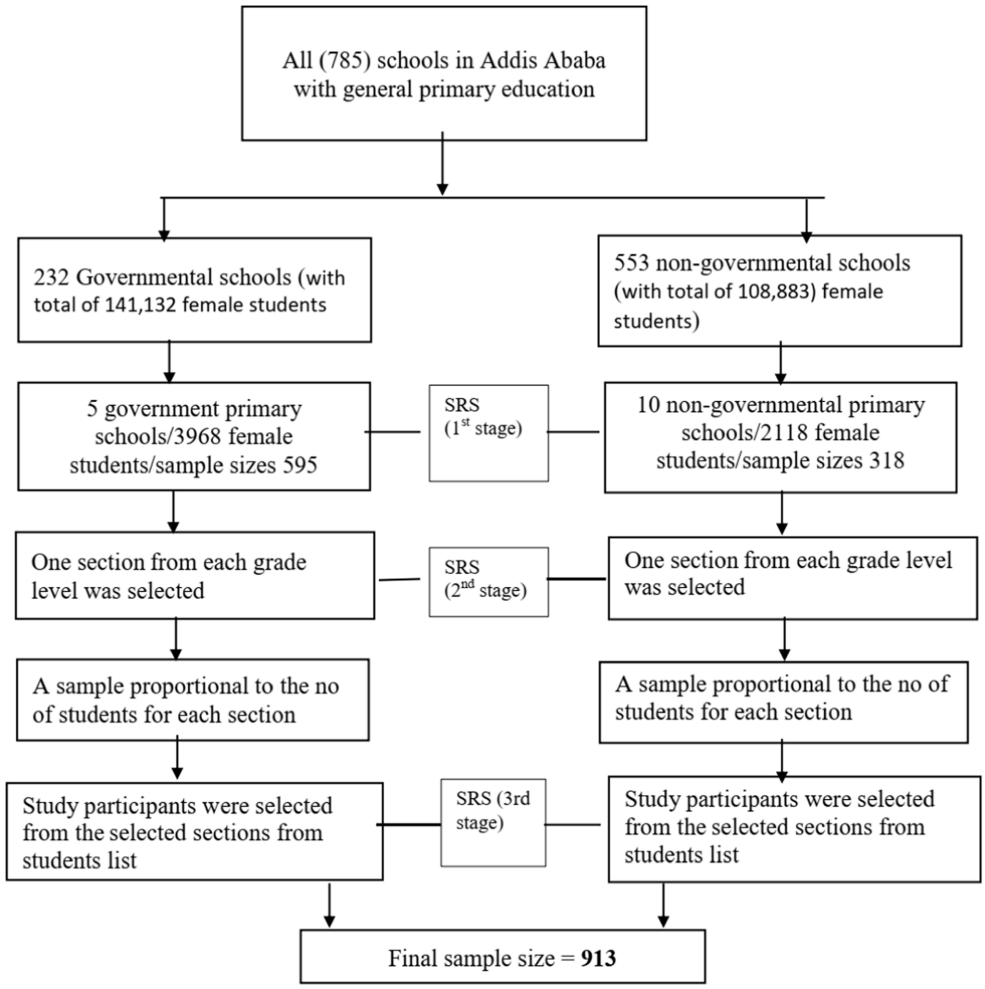

FIGURE 1
Sampling procedures of the study, 2022.

2.4.3 Age determination

Although the grades of the students were used as proxies for age estimation, age was estimated by asking participants for their date of birth, followed by the month and year. The exact age was calculated as the difference between the interview date and the date of birth.

In this study, adolescents refer to individuals aged 10–14 years, which is consistent with the WHO definition of early adolescence (22). The 2007 WHO growth reference was used to classify adolescents with or without thinness/severe thinness using WHO Anthro Plus version 1.0.4 software. Adolescents with BAZ values corresponding to < -3 z-scores and < -2 to ≥ -3 z-scores were classified as severely thin and thin, respectively. Those with BAZ corresponding to ≥ 2 to $< +1$ z-scores and $\geq +2$ z-scores were classified as overweight and obese, respectively (23).

2.5 Data quality assurance

The questionnaire was prepared in English, translated into the local language, and then translated back into English by another expert to ensure consistency and contextualization. Three days of training were provided to data collectors and supervisors about the study's objective, measurement procedures, data collection, interviewing, and ethical issues. Practical exercises were performed on data collection techniques and procedures, as well as height, weight, and MUAC measurements, to ensure the quality of the field operation. The questionnaire was pretested on 46 school-going adolescents from non-selected schools in the city before the actual data collection. Amendments were made to the questionnaires as needed. Supervisors and investigators checked the collected data daily for completeness and consistency, providing feedback every morning before the next day's activities. Measurement scales were carefully handled and calibrated every day before data collection. During weight measurement, the scales were carefully handled and periodically calibrated by placing the standard calibration weight of a 5 kg iron bar on the scale before use to ascertain accuracy. The data collector checked whether the scale reads 0.00 before weighing each participant. To improve the quality of the anthropometric data, an anthropometric standardization exercise was conducted. Based on the standardization exercise, technical error of measurement (TEM) was calculated among 10 adolescent girls. The intra-observer TEM for height ranged from 14.8–28.1%, for weight from 11.6–23.0%, and for MUAC from 8.9 to 26.07%. The inter-observer TEM was 12.5% for height, 23.6% for weight, and 35.7% for MUAC. In all cases, the computed TEM was within the acceptable range (24).

2.6 Statistical analysis

All statistical analysis was performed using STATA version 16.0 (25). Pearson correlation coefficient (r) was used to assess the relationship of MUAC with BAZ and age. It was interpreted according to Cohen's criteria for r = 0.1–0.3 as weak, r = 0.3–0.5 as medium, and r = 0.5–1.0 as strong correlation (26). A paired t-test was used to analyze test–retest reliability for the 1st and 2nd mid-upper arm circumference measurements. For the variable MUAC, a Receiver Operating Characteristic (ROC) curve was plotted with the aim of obtaining a global measure of the accuracy of the test for the combination of all the possible cut-off points. The area under the curve (AUC) and its 95% confidence interval (CI) were calculated. An AUC of 1 indicates the ability to perfectly distinguish between those participants with and without thinness/severe thinness (perfect test), whereas an AUC of 0.5 suggests that these results were obtained just by chance (worthless test). The categories used to summarize the accuracy of AUC in ROC analysis were as follows: excellent (0.9–1), good (0.8–0.9), fair (0.7–0.8), poor (0.6–0.7), and fail (0.5–0.6) (27). Based on the curve coordinates, a cut-off point was selected for the variable MUAC. The optimal threshold for all age groups was determined from Youden's index, which is the maximum value of J: j = sensitivity + specificity − 1. For a perfect diagnostic test, J = 1, whereas for a poor diagnostic test, J equals 0. Sensitivity, specificity, likelihood ratios (positive and negative), and positive and negative predictive values of MUAC were calculated for the proposed cutoff points for all age groups (28).

Positive likelihood ratios were calculated by dividing sensitivity by 1 − specificity, indicating the increased odds of a positive test result. Negative likelihood ratios were calculated by dividing 1 − sensitivity by specificity, indicating the odds of a case when a test is negative.

3 Results

3.1 Socio-demographic characteristics of study participants

Out of the sampled 913 adolescent students, a total of 884 participated in this study, making the overall response rate 96.8%. The majority (66.6%) of the respondents were from governmental schools, while the remaining 301 (33.4%) were from non-governmental schools. The majority of the study participants (58.8%) were in the age range of 10–12 years. The participants' mean (±SD) age was 12.07 (±1.433) years. Over three-quarters (77.6%) of respondents were Orthodox Christian, followed by Muslim (10.9%), Protestant (9.8%), and Catholic (1.7%). Regarding the family size, the majority (61.43%) had a family size of five or more. Most of the respondents (40.9%) are self-employed fathers, while the proportion (30.6%) is less self-employed mothers. Similarly, 69.1% of the respondents belong to fathers and 50.4% to mothers whose educational status was secondary school and above, respectively (Table 1).

3.2 Nutritional status of adolescents

The overall mean (± SD) weight, height, and MUAC among respondents in this study were 38.5 (±9.3) kg, 150 (±0.1) cm, and 20.7 (± 2.5) cm, respectively. On the other hand, the mean (± SD) BAZ was −0.84 (±1.30) (Table 2). The body mass index for age (BAZ) measurement of the study participants revealed that a quarter of the study participants had normal body weight. The overall magnitude of thinness was 18.0%. The magnitude of thinness, including severe thinness, was relatively higher (27.0%) among girls aged 11 years compared with other age groups in the early adolescent period. The

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TABLE 1 Socio-demographic characteristics of the study participants Addis Ababa, Ethiopia, 2022 (n = 884).

Variables	Frequency	Percent
Age in years		
10–12	520	58.8
13–14	364	41.21
Mean age(±SD) years	12.07 (±1.433)	
Religion		
Orthodox Christian	686	77.6
Catholic	15	1.7
Protestant	87	9.8
Muslim	96	10.9
Family size		
≥5	543	61.43
<5	341	38.57
Paternal educational status		
Have no formal education	110	12.4
Primary school	163	18.4
Secondary school (grades 9–12 and above)	611	69.1
Paternal occupation		
Government/private employee	313	35.4
Self-employed	331	37.4
Daily labourer	59	6.7
Unemployed	46	5.2
Others	135	15.3
Mother's educational status		
Have no formal education	202	22.9
Primary school (grades 1–8)	236	26.7
Secondary school (grade 9–12 and above)	446	50.4
Mother's occupation		
Government/private employee	225	25.68
Self-employed	268	30.59
Daily labourer	48	5.48
Unemployed	316	36.07
Others	27	3.05
School enrolment		
Governmental	598	66.52
Non-governmental	301	33.48

magnitude of overweight and obesity (combined) was 7.0% in the total sample and relatively higher among adolescents aged 14 years (Figure 2).

3.3 Test–retest reliability of MUAC

A perfect agreement was reached between the first and second MUAC measurements in all age groups (Table 3).

3.4 Relationship between MUAC and other anthropometric characteristics

The correlation between MUAC with BAZ and age revealed that MUAC had a strong, significant positive correlation with BAZ in all the subjects studied. Meanwhile, MUAC and age were moderately correlated (Table 4). Moreover, the results of the MUAC correlation coefficient with BAZ by the age of the study participants revealed that MUAC showed a strong correlation with BMI z-score across all age groups (Table 5).

TABLE 2 Mean of weight, height, mid-upper arm circumference (MUAC), and BMI for age (BAZ) of female adolescents Addis Ababa, 2022.

Age(years)	Weight (kg)	Height (cm)	MUAC (cm)	BAZ
	Mean (± SD)	Mean (± SD)	Mean (± SD)	Mean (± SD)
10	31.7 (−6.7)	142 (−0.1)	19.1 (−2.2)	−0.85 (−1.29)
11	34 (−7.0)	147 (−0.1)	19.8 (−2.1)	−1.18 (−1.26)
12	38.7 (−7.7)	151 (−0.1)	20.4 (−2.2)	−0.83 (−1.29)
13	41.8 (−9.5)	154 (−0.1)	21.3 (−2.0)	−0.93 (−1.36)
14	46 (−7.3)	155 (−0.1)	22.7 (−2.0)	−0.45 (−1.20)
Oct-14	38.5 (−9.3)	150 (−0.1)	20.7 (−2.5)	−0.84 (−1.30)

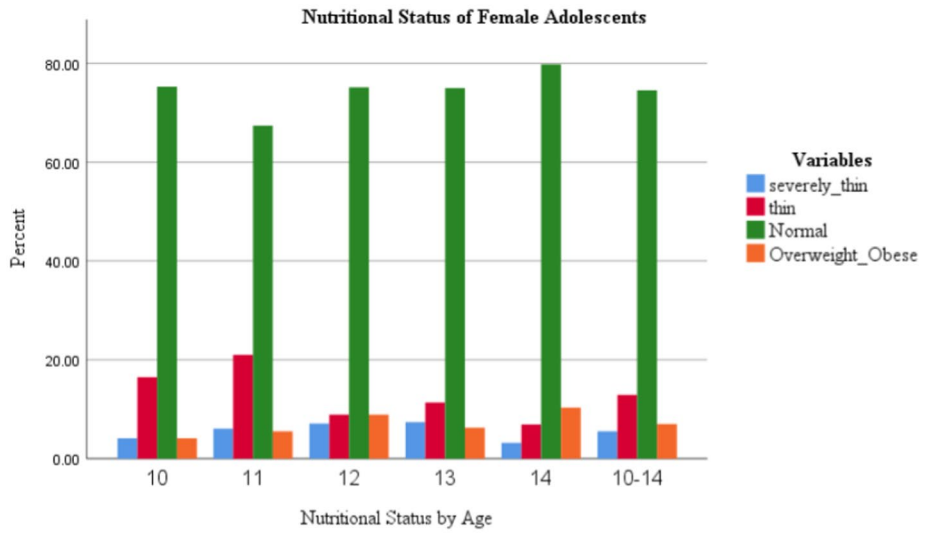


FIGURE 2
Age-wise distribution of adolescent school girls by their BAZ categories in Addis Ababa, Ethiopia, 2022.

TABLE 3 Analysis of the reliability of MUAC among primary school adolescent girls, Addis Ababa, Ethiopia, 2022.

Age in years	MUAC 1st Mean (± SD)	MUAC 2nd Mean (±SD)	*p*-values	*t*-values
10	19.1 (2.2)	19.1 (2.2)	0.9975	−2.8439
11	19.7 (2.1)	19.8 (2.1)	0.9717	−1.9181
12	20.4 (2.2)	20.4 (2.3)	0.6660	−0.4297
13	21.2 (2.0)	21.3 (2.0)	0.9942	−2.5512
14	22.6 (2.0)	22.7 (2.0)	0.8179	−0.9097
Total	20.7 (2.4)	20.7 (2.5)	0.9972	−2.7750

MUAC, Mid-Upper Arm Circumference.

TABLE 4 Results of overall Pearson correlation coefficient between MUAC with BMI for age *z*-score and age in years among adolescent girls in Addis Ababa, Ethiopia, 2022.

Characteristic	Mid-upper arm circumference	
	r	95% CI
Age in years	0.50	0.447–0.546
BMI *z*-score	0.80	0.775–0.822

TABLE 5 Results of Pearson correlation coefficient between MUAC and BMI for age *z*-score by different age groups among adolescent girls in Addis Ababa, Ethiopia, 2022.

Mid-upper arm circumference					
Age	10 years	11 years	12 years	13 years	14 years
Index	r(95% CI)	r(95% CI)	r(95% CI)	r(95% CI)	r(95% CI)
BMI *z*-score	0.88 (0.84–0.91)	0.89 (0.85–0.91)	0.81 (0.75–0.86)	0.92 (0.89–0.94)	0.82 (0.76–0.86)

3.5 Performance of MUAC to detect thinness, including severe thinness among female adolescents (BAZ of < −2)

The AUC for MUAC to correctly identify thinness/severe thinness in girls during early adolescence against the reference based on BAZ ranged between 0.87 and 0.97. The performance of MUAC in detecting thinness, including severe thinness, was excellent in all age categories and 'good' for girls aged 10 years (Figure 3).

The MUAC value of ≤19.8 cm was the best optimal cut-off point to distinguish those adolescents with and without thinness/severe thinness with a higher Youden's index of 0.67. The diagnostic accuracy measures, sensitivity, specificity, and negative predictive value (PPN) at this cut-off point were higher, while positive likelihood ratio (LR+), negative likelihood ratio (LR-), and positive predictive value (PPV) values were lower (Table 6).

3.6 The ability of MUAC to detect thinness among female adolescents

The ROC curves comparing MUAC's prediction of thinness in female adolescents throughout early adolescence to the gold standard/reference based on BMI z-score demonstrated that MUAC correctly detected thinness (AUC = 0.86). MUAC accurately predicted thinness in adolescents aged 12 to 14 years (Figure 4).

The proposed potential optimal MUAC cut-off to identify thinness was ≤20.1 cm. These cut-off points provide a sensitivity of 92.1, 95% CI: (85.5, 96.3%), and a specificity of 67.3, 95%CI: (63.7, 70.5%). Sensitivity and specificity were generally high for the optimal age-specific cut-points (73–100%). After stratification by age, higher optimal MUAC cutoffs were observed in the older age group (Table 7).

3.7 Diagnostic accuracy of MUAC cut-offs for thinness and severe thinness

The accuracy of MUAC in diagnosing severe thinness among early female adolescents was good (0.87). Except for the age group of 10 years, the performance of MUAC in detecting severe thinness was excellent in adolescents of all ages (Figure 5).

The optimal MUAC cutoffs for the prediction of severe thinness were ≤ 19.7 cm. Notably, the MUAC cut-offs for severe thinness showed high sensitivity (95.9%), and the specificity was 68.5%. Furthermore, almost all sensitivities and specificities were high (>79.8%) after stratification for age. The percentage of individuals correctly classified using the proposed cut-off points ranged from 80.0 to 93.1% across age groups (Table 8).

3.8 The ability of MUAC to classify overweight, including obesity, among female adolescents aged 10–14 years

The ROC curve, which was generated based on BAZ > +1SD, revealed that the area under the receiver operating curve (AUC) of MUAC for adolescent girls (0.95) was high (Figure 6).

The MUAC value of 23.1 cm was found to be the suitable cut-off point for detecting overweight, including obesity, as it possessed the highest Youden index of 0.78. A sensitivity of 87.1% and specificity of 90.4% were found at this MUAC cut-off point (Table 8).

4 Discussion

Nutritional issues have been identified as significant public health concerns in Ethiopia. Many studies have been conducted to determine the extent and impact of malnutrition in various population groups (13, 29–33). Accordingly, adolescents are considered the vulnerable segments of the population who have not received adequate care to meet their nutritional demands. This study will be crucial in determining the nutritional status of "future mothers."

The findings of this study indicated that the majority of subjects in the early adolescent (10–14 years) category have normal weight. The overall magnitude of thinness in this age category was 18.0%.

The magnitude of thinness observed in this study is consistent with a study conducted in the province of El Jadida in Morocco, which found that 18.8% of adolescents were underweight (34). This finding was lower than the results from studies conducted among adolescent girls in Adama City and Northern Ethiopia, which reported rates of 21.3 and 21.2%, respectively (20, 31). Nonetheless, the findings from the present study were higher than the report from a study in five rural districts of Amhara National Regional State, Ethiopia, which found that 13.6% of adolescent girls were underweight (33). Geographic, socio-economic, and behavioral variations of factors across these different settings may account for the difference.

The present study showed that MUAC had a significantly high positive correlation with BMI for age (MUAC versus BAZ: r = 0.80) but only moderately correlated with age (r = 0.5). This strong correlation is supported by findings from a study conducted on female adolescents in India, which found a positive correlation of 0.63 between BMI z-score and MUAC (11). Similar correlations of MUAC with BMI z-score were observed in studies conducted on adolescents in India and Ethiopia (r = 78, r = 0.81), respectively (12, 13). In contrast, a study from a rural area of Paschim Medinipur, India, reported a moderate correlation (r = 0.35) of MUAC with BMI among adolescent girls (14). Thus, MUAC may be a feasible nutritional screening tool in both clinical and field settings, especially where frontline professions (e.g., health extension workers) do not routinely use nutritional indicators like weight, height, and BMI z-score.

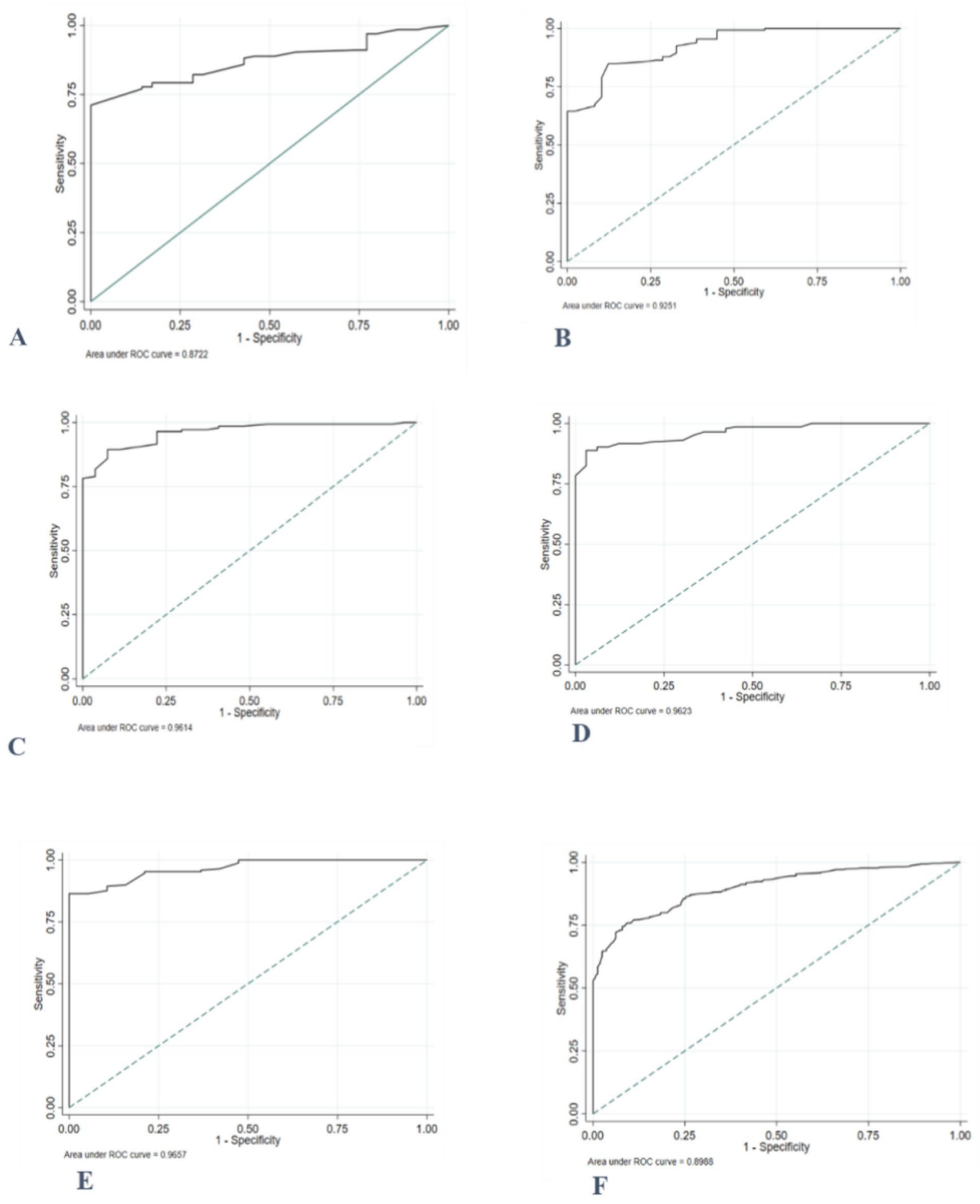


FIGURE 3
ROC curve depicting the ability of MUAC to classify thinness, including severe thinness among adolescent girls **(A)** 10 years old; **(B)** 11 years old; **(C)** 12 years old; **(D)** 13 years old; **(E)** 14 years old, and **(F)** 10–14 years old.

In this study, AUC values between 0.83 and 0.99 in various age groups showed that MUAC has accurate discriminatory performance among adolescents in identifying those with or without lower BMI-for-age z-scores. The results of this study are consistent with previous investigations. A study done in India reported an AUC ranging from 0.77–0.86 for adolescent girls aged between 10–14 years (MUAC vs. thinness/severe thinness) (11). Similarly, another study in the same country found AUC values ranging between 0·85 and 0·86, (p = 0·001) 0.93 and 0.98 for MUAC predicting thinness/severe thinness in a sample of Indian adolescent girls aged 10–19 years (12). These findings suggest that MUAC can serve as a complementary tool to BMI for age z-score in identifying thinness.

TABLE 6 Diagnostic test accuracy measures for varying cut-offs of mid-upper arm circumference (MUAC) at different ages for predicting thinness, including severe thinness among primary school adolescent girls, Addis Ababa, 2022.

Age in years	10 years	11 years	12 years	13 years	14 years	10–14 years
SN (%) (95% CI)	85.7 (69.7–95.2)	87.8 (75.2–95.4)	92.6 (75.7–99.1)	90.3 (84.2–99.9)	94.7 (74.0–99.9)	90.8 (85.3–94.8)
SP (%) (95% CI)	77.0 (69.0–83.8)	84.8 (77.6–90.5)	89.4 (83.2–94.0)	88.8 (82.5–93.5)	86.4 (80.3–91.2)	75.9 (72.6–78.9)
PLR (%) (95% CI)	3.73 (2.66–5.23)	5.79 (3.82–8.79)	8.77 (5.37–14.3)	8.67 (5.44–13.8)	6.96 (4.69–10.33)	3.76 (3.28–4.32)
NLR (%) (95% CI)	0.19 (0.08–0.42)	0.14 (0.07–0.31)	0.08 (0.02–0.31)	0.03 (0.00–0.24)	0.06 (0.01–0.41)	0.12 (0.07–0.20)
PPV (%) (95% CI)	49.2 (40.9–57.6)	68.3 (58.6–76.5)	62.8 (50.5–73.1)	66.7 (55.7–76.1)	43.9 (34.5–53.7)	46.0 (42.6–49.4)
NPV (%) (95% CI)	95.4 (90.2–97.9)	94.9 (89.8–97.5)	98.4 (94.4–99.6)	99.2 (94.8–99.9)	99.3 (95.6–99.9)	97.3 (95.7–98.3)
Correctly classified	87.1	82.6	84.8	89.1	85.1	78.5
YI	0.71	0.73	0.82	0.86	0.86	0.67
MUAC cut off point (cm)	≤17.8	≤18.8	≤18.8	≤20.0	≤21.1	≤19.8

SN, sensitivity; SP, specificity; PLR, Positive Likelihood Ratio, NLR, Negative Likelihood Ratio, YI, Youden's index; PPV, positive predictive value; NPV, negative predictive value.

The present study proposed new MUAC cut-offs for diagnosing thinness, including severe thinness among school-going early adolescent girls. The optimal MUAC cut-offs to assess thinness and severe thinness in female adolescents were MUAC<20.1 cm and MUAC<19.7 cm, respectively. In comparison, a study from two eastern Indian states found MUAC cut-offs of 19.4 cm and 18.9 cm to be acceptable for identifying thinness and severe thinness among female adolescents (12). Another study among female adolescents in the rural and urban parts of India also showed that 19.4 cm and 18.3 cm were the best MUAC cut-off values to distinguish those with thinness and severe thinness, respectively (11). These variations in cut-off values might be attributed to differences in body composition among different ethnic groups (35).

Furthermore, when calculated for each age, cut-off values of MUAC to identify adolescents with or without thinness were between 17.5–20.9 cm and 17.0–20.0 cm for those with severe thinness in specific age groups. It was found that MUAC slightly increases as the age of adolescents increases. These findings suggested higher cutoff points than previous studies' findings (11, 12). Because of significant physiologic age-related variations in body composition, the adoption of the same thinness/severe thinness cut-off point across different age groups and populations has been widely questioned (5). Therefore, the present study brought new evidence to shed some light on this controversy as it provides single age-specific MUAC cut-offs in addition to age-group-specific MUAC cut-offs to detect thinness and severe thinness among early female adolescents.

The performance analysis of the proposed cut-off points for MUAC carried out in this study revealed a good to excellent level of accuracy with sensitivity ranging from 92.1 to 95.9% and specificity from 67.3 to 68.5%. This specificity suggests that only a few adolescents at risk for thinness would be misclassified as normal. Given the greater health risks associated with thinness, it is more important to accurately classify those who are truly thin. Adolescents who are diagnosed as thin or severely thin using BMI z-score were also diagnosed as being thin or severely thin using MUAC. However, we feel that the optimal cutoff should not be established solely by an equation but rather with consideration of the context in which it will be applied. Selecting a cutoff requires a careful compromise between not missing any thin or severely thin adolescents (high sensitivity) and not misidentifying adolescents who do not need nutritional assistance (high specificity). In low-resource settings, using a cutoff with low specificity could further burden already overstretched health systems.

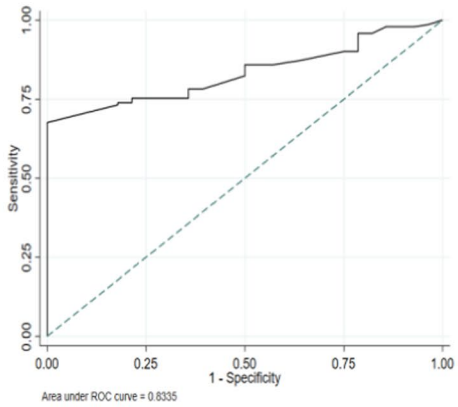
The accuracy of MUAC was also evaluated for all age groups. Sensitivity and specificity were in the range of 82.1 –100.0% and 72.1–92.9%, respectively, across stratified ages. These findings align with evidence from India, which showed high sensitivity and specificity for MUAC in predicting thinness/severe thinness in a sample of female adolescents aged 10–14 years (11, 12). In contrast, a study from Tanzania showed low sensitivity (40.0%) and high specificity (92.5%) for MUAC in predicting thinness/severe thinness in a sample of female adolescents aged 10–14 years (36). Similarly, a study among female adolescents in India further reported a 28.7% sensitivity and 96.46% specificity at the optimal MUAC cut-off point (10). This difference may be attributed to the varying reference values used in these studies.

This study has several important implications. First, it demonstrates that the anthropometric parameter MUAC is valid compared to the BMI z-score. Secondly, MUAC, as an alternative anthropometric measure, is a weightless tool that makes assessment more user-friendly, quick, and easy to use in the field. Additionally, this marker can be measured even in lying-down positions, making it suitable for individuals with disabilities. Therefore, this study demonstrates the potential of MUAC as a viable alternative anthropometric measurement in community-based screening and primary care settings.

The study also found that more than 78.5% of undernourished adolescents had thinness/severe thinness based on MUAC measurements. Since most Ethiopian adolescents have limited access to health facilities, relying solely on facility-based assessments may be insufficient to reach everyone. Screening in the community could be another way to reach out to the unreached group of the population.

The strengths of this study lie in its potential to provide a foundation for the utilization of MUAC as a screening tool for thinness and severe thinness among school-going female adolescents. Additionally, an anthropometric standardization exercise was conducted to enhance the quality of the anthropometric data. The TEM calculated from this exercise was within acceptable range in all cases (24). This reduces anthropometric measurement errors and ensures accurate and precise measurements.

Nevertheless, the findings of this study should be interpreted in light of its expected limitations. The use of MUAC in this particular study exclusively examined only on school-going



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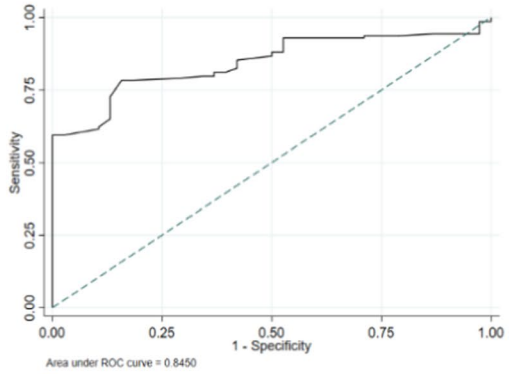

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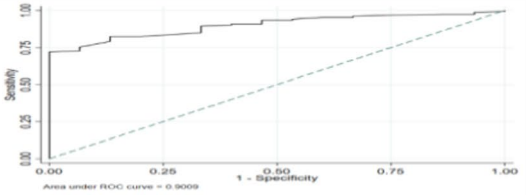

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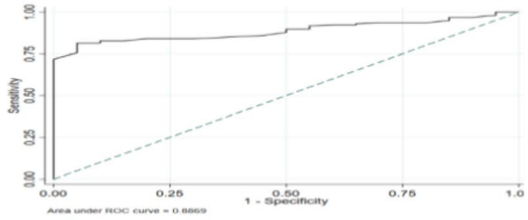

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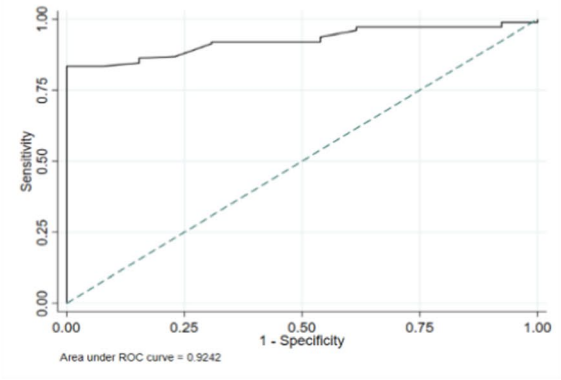

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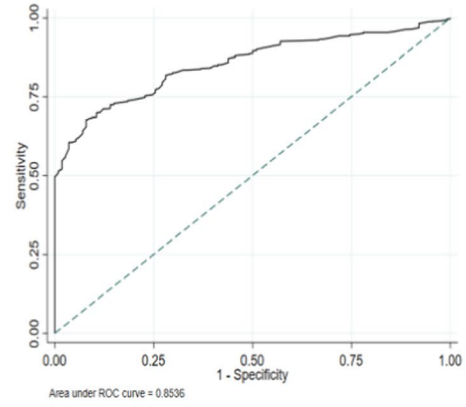

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FIGURE 4
ROC curve depicting performance of mid-upper arm circumference for identifying thinness among adolescent girls **(A)** 10 years old; **(B)** 11 years old; **(C)** 12 years old; **(D)** 13 years old; **(E)** 14 years old, and **(F)** 10–14 years old.

female adolescents, which may not represent male adolescents. Therefore, the optimal MUAC cut-off values need to be cross validated with other community groups to establish its utility as a screening tool for thinness/severe thinness among all adolescents. Moreover, as the study was limited to one city, the findings may not be representative of the broader Ethiopian adolescent population.

5 Conclusion

The study authenticates the use of MUAC measurement, which is simple, inexpensive, easy to use, and non-invasive, as a prospective surrogate for BMI z-score to accurately identify thinness among female adolescents. The study also revealed that MUAC cut-off points were age-specific, with 19.7 cm for severe thinness and

TABLE 7 Diagnostic test accuracy measures for varying cut-offs of mid-upper arm circumference (MUAC) at different ages for predicting thinness among primary school adolescent girls, Addis Ababa, 2022.

Age in years	10 years	11 years	12 years	13 years	14 years	10–14 years
SN (%) (95% CI)	82.1 (63.1–93.9)	84.2 (68.7–4.0)	100.0 (78.2–100)	95.0 (75.1–99.9)	84.6 (54.6–98.1)	92.1 (85.5–96.3)
SP (%) (95% CI)	73.2 (65.2–80.3)	78.3 (70.7–84.8)	72.1 (64.3–79.0)	81.4 (74.4–87.2)	86.3 (80.3–91.0)	67.3% (63.8–70.6)
PLR (%) (95%CI)	3.07 (2.22–4.24)	3.88 (2.76–5.46)	3.38 (2.78–4.62)	5.11 (3.62–7.20)	6.17 (3.98–9.56)	2.81 (2.51–3.16)
NLR (%) (95% CI)	0.24 (0.11–0.54)	0.20 (0.10–0.42)	0.00 (−)	0.06 (0.01–0.42)	0.18 (0.05–0.64)	0.12 (0.06–0.22)
PPV (%) (95% CI)	37.7 (30.5–45.5)	50.8 (42.3–59.2)	25.9 (21.3–31.0)	39.6 (31.7–48.0)	31.4 (22.8–41.5)	29.4% (27.1–31.9)
NPV (%) (95% CI)	95.4 (90.3–97.9)	94.9 (89.9–97.5)	100.0 (−)	99.2 (94.9–99.9)	98.7 (95.5–99.6)	98.3% (96.8–99.1)
Correctly classified (%)	74.7	79.6	74.6	65.1	84.1	70.8
YI	0.68	0.63	0.72	0.76	0.83	0.60
MUAC cut off point (cm)	≤17.8	≤18.9	≤19.6	≤20.0	≤21.1	≤20.1

SN, sensitivity; SP, specificity; PLR, Positive Likelihood Ratio; NLR, Negative Likelihood Ratio; YI, Youden's index; PPV, positive predictive value; NPV, negative predictive value.

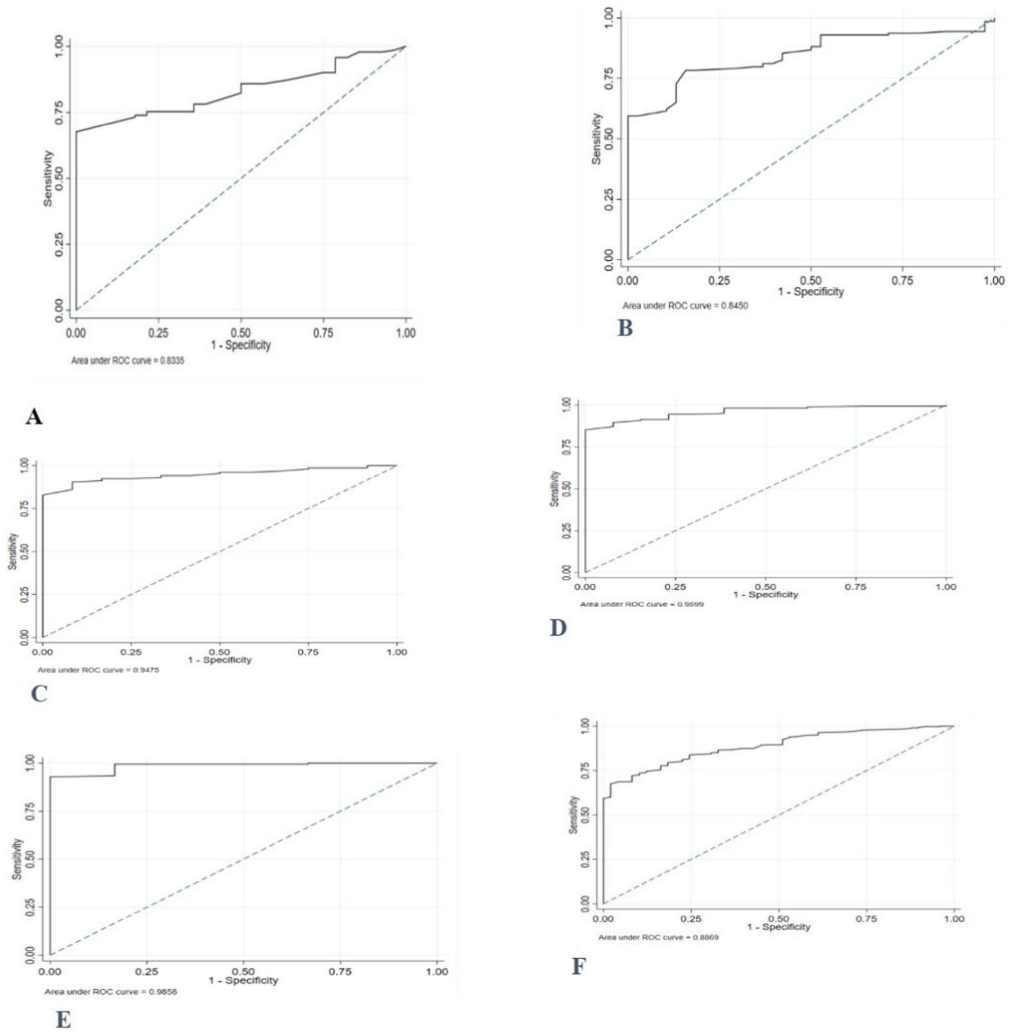

FIGURE 5
Receiver operating characteristics curve, depicting the performance of MUAC for identifying severe thinness among adolescent girls **(A)** 10 years old; **(B)** 11 years old; **(C)** 12 years old; **(D)** 13 years old; **(E)** 14 years old, and **(F)** 10–14 years old.

TABLE 8 Diagnostic test accuracy measures for varying cut-offs of mid-upper arm circumference (MUAC) at different ages for predicting severe thinness among primary school adolescent girls, Addis Ababa, 2022.

Age in years	10 years	11 years	12 years	13 years	14 years	10–14 years
SN (%) (95% CI)	85.7 (42.1–99.6)	100.0 (71.5–100)	91.7 (61.5–99.8)	92.3 (64.0–99.8)	100.0 (54.1–100.0)	95.9 (86.0–99.5)
SP (%) (95% CI)	79.8 (72.8–85.6)	85.9 (79.7–90.7)	86.0 (79.6–91.0)	87.1 (81.0–91.8)	92.9 (88.1–96.1)	68.5 (65.2–71.6)
PLR (%) (95% CI)	4.23 (2.76–6.50)	7.08 (4.9–10.3)	6.54 (4.28–9.99)	7.16 (4.67–11.0)	14.00 (8.29–23.64)	3.05 (2.71–3.42)
NLR (%) (95% CI)	0.18 (0.03–1.10)	0.00 (0.00–0.00)	0.10 (0.01–0.63)	0.09 (0.01–0.58)	0.00 (–)	0.06 (0.02–0.23)
PPV (%), (95% CI)	15.4 (10.6–21.8)	31.4 (24.0–39.9)	33.3 (24.7–43.3)	36.4 (27.1–46.8)	31.6 (21.5–43.8)	15.2 (13.7–16.7)
NPV (%) (95% CI)	99.2 (95.5–99.9)	100.0 (–)	99.3 (95.4–99.9)	99.3 (95.6–99.9)	100.0 (–)	99.7 (98.7–99.9)
Correctly classified (%)	80.0	85.6	86.4	87.5	93.1	70.02
YI	0.75	0.86	0.83	0.54	0.93	0.66
MUAC cut off point (cm)	≤17.3	≤17.7	≤18.7	≤19.4	≤20.3	≤19.7

SN, sensitivity; SP, specificity; PLR, Positive Likelihood Ratio; NLR, Negative Likelihood Ratio; YI, Youden's index; PPV, positive predictive value; NPV, negative predictive value.

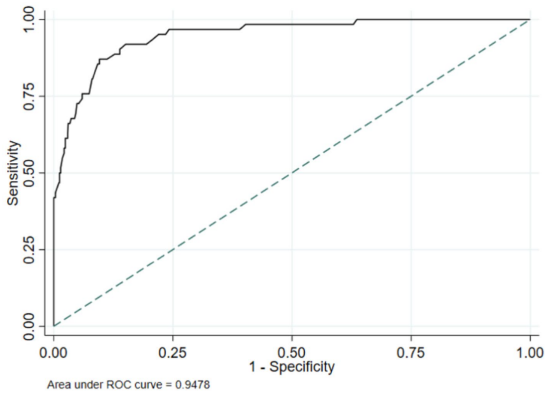

FIGURE 6
ROC curve depicting the ability of MUAC to classify overweight, including obesity, in 10- to 14-year-old female adolescents.

20.1 cm for thinness as optimal values, independent of age. This anthropometric measurement showed good accuracy in predicting thinness and severe thinness with a comparable level of sensitivity and a lower specificity compared with the BMI z-score. Hence, the investigators believe that the introduction of MUAC as a criterion for easy and quick identification of thinness and severe thinness among female adolescents would be ideal in low-resource settings.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Research and Ethics Committee (REC) of the School of Public Health, College of Health Sciences, Addis Ababa University, and the Research Ethics Committee of Addis Ababa City Health Bureau. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SZ: Conceptualization, Formal analysis, Investigation, Methodology, Resources, Software, Writing – original draft, Writing – review & editing. GE: Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing. DH: Conceptualization, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Publisher's note

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EDITED BY
Bei Gao,
Nanjing University of Information Science and Technology, China

REVIEWED BY
Yi Shao,
Shanghai Jiao Tong University, China
Cheng Cao,
Second Affiliated Hospital of Soochow University, China
Zhouzhou Xie,
Meizhou Clinical Institute of Shantou University Medical College, China
Xingzheng Liu,
Guangzhou University of Chinese Medicine, China
Danni Chen,
The Scripps Research Institute, United States

*CORRESPONDENCE
Jianjun Xie
✉ uro_xiejianjun@163.com
Junpeng Deng
✉ djunpeng@outlook.com

†These authors have contributed equally to this work

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National analysis of the dietary index for gut microbiota and kidney stones: evidence from NHANES (2007–2018)

Xinzhou Yan[1,2†], Xianhua Shao[1,2†], Tengyue Zeng[1,2], Qijie Zhang[1,2], Junpeng Deng[1,2*] and Jianjun Xie[1,2*]

[1]Department of Urology, Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou, Jiangsu, China, [2]Gusu School Nanjing Medical University, Suzhou, Jiangsu, China

Background: Previous studies have highlighted the effects of diet and gut microbiota on the incidence of kidney stones, and the dietary index for gut microbiota (DI-GM) is a new dietary index that accurately represents the variety of gut microbiota. The current study intends to examine the potential correlation between DI-GM and kidney stones.

Methods: Data from the 2007–2018 National Health and Nutrition Examination Survey (NHANES) were employed in this cross-sectional study. The history of kidney stones was assessed using a kidney conditions questionnaire. In order to examine the correlation between DI-GM and kidney stones, multivariate logistic regression was implemented. Additionally, smoothed curve fitting, subgroup analyses, and sensitivity analyses were conducted.

Results: The investigation encompassed a total of 21,587 participants. After adjusting for all potential covariates, we found that DI-GM was negatively related to the incidence of kidney stones (OR = 0.96, 95% CI = 0.93–0.98, p = 0.0021). Compared to those in the lowest quartile, participants in the highest quartile had a lower prevalence of kidney stones (OR = 0.86, 95% CI = 0.75–0.98, p = 0.0252). Additionally, smoothed curve fitting revealed that DI-GM was linearly associated with the incidence of kidney stones. The results of the sensitivity analyses proved the robustness of the main analyses.

Conclusion: A negative correlation between the incidence of kidney stones and DI-GM is supported by the evidence presented in this study. This finding emphasizes the potential benefits of adjusting dietary structure according to DI-GM in reducing the incidence of kidney stones. Further research should validate this discovery by employing longitudinal studies.

KEYWORDS

DI-GM, NHANES, kidney stones, gut microbiota, diet

1 Introduction

As a common disease of urology, kidney stones originate from the precipitation of crystals caused by mineral oversaturation in the urine (1). Kidney stones have shown a global rise in prevalence over the past few decades, and this trend is significant across all ages, genders, and races (2). Obesity, diabetes, global warming, depression, and the overintake of salt, animal protein, sucrose, and sugar-sweetened beverages are risk factors for increased incidence of

kidney stones (3, 4). Currently, surgery is the most effective treatment for kidney stones. However, the high cost of surgery, the high recurrence rate after surgery, and the severe physical and psychological burden of the patients remain challenging to resolve (5–7). Consequently, it is crucial to concentrate on the risk factors for kidney stones to establish effective strategies to mitigate the occurrence and recurrence of kidney stones.

Changes in the gut microbiota of patients with kidney stones have been identified in previous studies (8, 9). Gut microbiota dysbiosis is closely related to the environment, diet, drug use, and disease phenotypes (10, 11). A case–control study concluded that the massive use of antibiotics may lead to an increased incidence of kidney stones by causing changes in the microbiome (12). Additionally, the nutritional imbalances due to poor diet can affect the formation of kidney stones by affecting the balance of gut microbiota (13). Most recently, a novel dietary index for gut microbiota (DI-GM) was created to evaluate the correlation between gut microbiota and adult diet. By reviewing 106 articles that investigate the correlation between adult diet and gut microbiota, 14 dietary components, including 10 beneficial components and 4 unfavorable components, were selected as DI-GM components (14). Given that DI-GM was discovered to be positively correlated with indirect biomarkers of gut microbiota diversity, it is likely to become a useful instrument to reflect the impact of diet on gut microbiota. Nevertheless, the association between kidney stones and DI-GM remains unclear.

Consequently, this research employed data from the National Health and Nutrition Examination Survey (NHANES 2007–2018) to explore the correlation between DI-GM and kidney stones. After a comprehensive and rigorous analysis, our study aims to assist patients with kidney stones in maintaining a proper diet, thereby forestalling the development and recurrence of kidney stones.

2 Materials and methods

2.1 Study population

The NHANES dataset is a well-established program that is updated every 2 years to assess the nutritional and health status of participants in the United States. Each participant has offered their informed consent. Our investigation encompassed 59,842 participants from 2007 to 2018. This study's exclusion criteria included the following: (1) age less than 20 years old (n = 25,072); (2) missing data of kidney stones (n = 91); (3) missing data about the components of DI-GM (n = 3,966); (4) missing data of covariates (n = 10,131), leaving a total of 20,582 participants for further analysis. The details of the inclusion and exclusion processes for this study were illustrated in Figure 1.

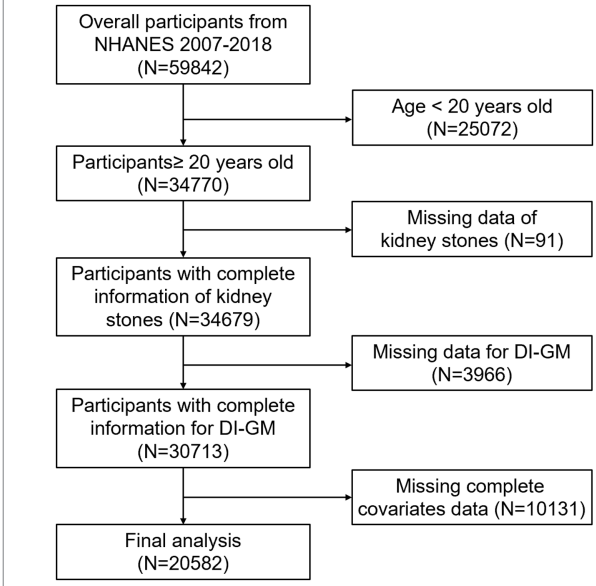

FIGURE 1
Flowchart of participant selection.

2.2 Exposure and outcome definitions

The outcome indicator of this study was whether the participant had kidney stones. Participants who answered affirmatively to the inquiry "Have you/has the sample person (SP) ever had kidney stones?" were detected as having a history of diagnosed kidney stones.

Following the scoring criteria created by Kase et al. (14), DI-GM was determined to consist of 14 food constituents or nutrients. Among them, 10 components, including avocados, broccoli, chickpeas, coffee, cranberries, fermented dairy, fiber, green tea, soybeans, and whole grains, were considered beneficial to gut microbiota. Score 1 for each component if consumption is equal to or above the gender-specific median; otherwise, score 0. On the contrary, 4 components, including processed meat, red meat, refined grains, and a high-fat diet (≥ 40% energy from fat), were considered unfavorable to gut microbiota. Score 0 for each component if consumption is equal to or above the gender-specific median or 40% (for a high-fat diet); otherwise, score 1. Each component's fraction was added to determine the score of DI-GM, which ranged from 0 to 14. In general, a higher DI-GM represents enhanced gut microbiota health.

2.3 Covariates

In order to guarantee the robustness of the correlation between DI-GM and kidney stones, the subsequent covariates were adjusted: demographic data (age, gender, race, educational level, marital status, and poverty income ratio [PIR]), lifestyle factors (body mass index [BMI], drinking status, smoking status, and moderate recreational activity), and chronic disease conditions (diabetes and cardiovascular disease [CVD]). Age was documented as continuous values. Gender was dichotomized into male and female. Races included Mexican American, other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other races. Education level was divided into below high school, high school, and above high school. Marital status was divided into never married, married/living with a partner, and widowed/divorced/separated. PIR was divided into 3 groups (<1.3, 1.3–3.5, and ≥ 3.5). BMI was divided into 3 groups (< 25, 25–30,

and ≥ 30). Smoking status was defined as never, now, and former. Drinking status was determined as never, now, and former.

2.4 Statistical analysis

We integrated and statistically analyzed using R (version 4.2), SPSS (version 26.0), and Empowerstats (version 4.2). The absence of values for covariate variables was represented by dummy variables. The continuous variables were represented as weighted means (standard errors), while the categorical variables were expressed as unweighted counts (weighted percentages). To compare the differences between groups for continuous variables, the *F*-test was implemented, while the chi-squared test was implemented for categorical variables.

Additionally, multivariate logistic regression models were implemented to assess the correlation between DI-GM and kidney stones. Participants were grouped into Q1 (0–3), Q2 (4), Q3 (5), and Q4 (6–14) based on DI-GM scores. Specifically, model 1 was an unmodified, rudimentary model. Model 2 was adjusted by age, gender, and race. Model 3 was adjusted by age, gender, race, educational level, marital status, PIR, BMI, smoking status, drinking status, moderate recreational activity, diabetes, and CVD. Smoothed curve fitting was performed to explore the linear associations between kidney stones and DI-GM (15). Additionally, we conducted subgroup analyses to investigate the impact of a variety of covariates on the association. When a two-sided *p*-value was less than 0.05, it was deemed statistically significant.

2.5 Sensitivity analyses

Considering that water intake was regarded as a substantial factor in the prevalence of kidney stones (16), we further adjusted for the water intake based on model 3. In addition, we performed subgroup analyses according to gender, PIR, drinking status, BMI, and moderate recreational activity.

3 Results

3.1 Baseline characteristics

Table 1 describes the characteristics of participants in the 2007–2018 NHANES. Ultimately, 20,582 participants were enrolled in this research, consisting of 1966 participants with kidney stones and 18,616 controls, based on the inclusion and exclusion criteria. Differential characteristics were observed between participants with and without kidney stones in terms of age, gender, race, marital status, PIR, BMI, smoking status, moderate recreational activity, DI-GM, and the history of diabetes and CVD.

3.2 Association of DI-GM with kidney stones

Table 2 showed that in model 1, the incidence of kidney stones decreased by 3% for each point increase in DI-GM (OR = 0.97, 95% CI = 0.94–0.99). The fully adjusted model maintained the significance of the aforementioned associations (OR = 0.96, 95% CI = 0.93–0.98). After grouping DI-GM, in the fully adjusted model, the incidence of kidney stones in Q4 (OR = 0.86, 95% CI = 0.75–0.98) was significantly reduced by 14% compared with Q1. Furthermore, the trend analysis indicates a correlation between DI-GM and kidney stones (*p* for trend = 0.0397).

Figure 2 illustrates the association between the incidence of kidney stones and DI-GM. After adjusting for all covariates, the smoothed curve fitting results showed a linear negative association between DI-GM and the incidence of kidney stones (*P* for log-likelihood ratio test = 0.262).

3.3 Subgroup analysis

Subgroup analysis was implemented across a variety of characteristics (Figure 3). We did not identify any substantial effect modification detected in gender, age, race, educational levels, marital status, PIR, BMI, smoking status, drinking status, diabetes, CVD, and moderate recreational activity ($p > 0.05$), despite more significant effects were observed in female participants (OR = 0.93, 95% CI = 0.89–0.97), participants aged 40–59 years (OR = 0.94, 95% CI = 0.90–0.99), participants aged ≥60 years (OR = 0.96, 95% CI = 0.92–1.00), Non-Hispanic White participants (OR = 0.95, 95% CI = 0.92–0.99), participants with a diploma above high school (OR = 0.94, 95% CI = 0.91–0.98), participants married or living with a partner (OR = 0.95, 95% CI = 0.92–0.99), participants widowed, discovered, or separated (OR = 0.94, 95% CI = 0.89–0.99), participants with a PIR ≥ 1.3 and < 3.5 (OR = 0.94, 95% CI = 0.90–0.98), participants with a BMI < 25 (OR = 0.93, 95% CI = 0.87–0.99), participants with a BMI ≥ 30 (OR = 0.95, 95% CI = 0.91–0.99), non-smokers (OR = 0.95, 95% CI = 0.92–0.99), former smokers (OR = 0.95, 95% CI = 0.90–0.99), current drinkers (OR = 0.95, 95% CI = 0.92–0.98), participants without diabetes (OR = 0.96, 95% CI = 0.92–0.99), participants without CVD (OR = 0.96, 95% CI = 0.94–0.99), participants with CVD (OR = 0.91, 95% CI = 0.84–0.98), participants lack of moderate recreational activity (OR = 0.94, 95% CI = 0.91–0.97).

3.4 Sensitivity analyses

The robustness of our findings was evaluated through the implementation of numerous sensitivity analyses. The association between DI-GM and kidney stones remained consistent when considering the water intake, which was highly associated with the prevalence of kidney stones, and was stable among female participants, participants with a PIR ≥ 1.3 and < 3.5, current drinkers, participants with a BMI ≥ 30, and participants without moderate recreational activity. The details of the sensitivity analyses are shown in Supplementary Tables S1–S6.

4 Discussion

Our study verified that the incidence of kidney stones was inversely correlated with increases in DI-GM. The study population

TABLE 1 Baseline characteristics of 20,582 participants from 2007 to 2018 NHANES.

Characteristics	Overall	Without kidney stones	Kidney stones	*p*-value
Number of participants	20,582	18,616	1966	
Age, year	47.12 (0.28)	46.50 (0.28)	52.82 (0.41)	**<0.001**
Gender				**<0.001**
Male	10,190 (49.00)	9,082 (48.29)	1,108 (55.57)	
Female	10,392 (51.00)	9,534 (51.71)	858 (44.43)	
Race				**<0.001**
Mexican American	3,095 (8.05)	2,839 (8.30)	256 (5.79)	
Other Hispanic	2089 (5.21)	1869 (5.26)	220 (4.74)	
Non-Hispanic White	9,331 (69.93)	8,202 (68.90)	1,129 (79.35)	
Non-Hispanic Black	4,077 (10.13)	3,838 (10.67)	239 (5.22)	
Other Race	1990 (6.68)	1868 (6.87)	122 (4.90)	
Education levels				0.756
< High school	4,833 (15.37)	4,345 (15.32)	488 (15.90)	
High school	4,687 (21.98)	4,251 (21.94)	436 (22.30)	
> High school	11,062 (62.65)	10,020 (62.74)	1,042 (61.80)	
Marital status				**<0.001**
Never married	3,781 (18.06)	3,608 (19.07)	173 (8.83)	
Married or living with a partner	12,310 (63.97)	11,043 (63.26)	1,267 (70.50)	
Widowed, divorced, or separated	4,491 (17.97)	3,965 (17.67)	526 (20.66)	
PIR				**0.027**
< 1.3	6,587 (21.33)	5,963 (21.52)	624 (19.60)	
≥ 1.3, <3.5	7,648 (35.28)	6,890 (34.94)	758 (38.38)	
≥ 3.5	6,347 (43.40)	5,763 (43.55)	584 (42.01)	
BMI				**<0.001**
< 25	5,906 (29.75)	5,519 (30.81)	387 (20.08)	
≥ 25, <30	6,837 (33.43)	6,177 (33.58)	660 (32.06)	
≥ 30	7,839 (36.82)	6,920 (35.61)	919 (47.86)	
Smoking status				**<0.001**
Never	11,293 (55.21)	10,352 (55.92)	941 (48.63)	
Now	4,268 (19.88)	3,871 (19.84)	397 (20.25)	
Former	5,021 (24.91)	4,393 (24.23)	628 (31.11)	
Drinking status				0.392
Never	2,859 (10.71)	2,597 (10.76)	262 (10.28)	
Now	14,963 (78.09)	13,545 (78.17)	1,418 (77.36)	
Former	2,760 (11.20)	2,474 (11.07)	286 (12.36)	
Moderate recreational activity				**0.005**
No	12,088 (53.12)	10,837 (52.66)	1,251 (57.41)	
Yes	8,494 (46.88)	7,779 (47.34)	715 (42.59)	
Diabetes				**<0.001**
No	17,463 (88.57)	16,014 (89.70)	1,449 (78.23)	
Yes	3,119 (11.43)	2,602 (10.30)	517 (21.77)	
CVD				**<0.001**
No	18,895 (93.46)	17,256 (94.18)	1,639 (86.82)	
Yes	1,687 (6.54)	1,360 (5.82)	327 (13.18)	

(Continued)

TABLE 1 (Continued)

Characteristics	Overall	Without kidney stones	Kidney stones	*p*-value
DI-GM	5.08 (0.03)	5.09 (0.03)	4.99 (0.05)	**0.036**
DI-GM groups				0.500
0–3	4,009 (17.60)	3,602 (17.64)	407 (17.29)	
4	4,446 (20.35)	4,026 (20.21)	420 (21.63)	
5	4,749 (22.90)	4,288 (22.83)	461 (23.56)	
≥ 6	7,378 (39.14)	6,700 (39.32)	678 (37.52)	

DI-GM, dietary index for gut microbiota; BMI, body mass index; CVD, cardiovascular disease. The DI-GM ranges from 0 to 14 and is grouped according to 0–3, 4, 5, and ≥ 6. A healthier gut microbiota is suggested by a higher DI-GM score. *p*-value less than 0.05 were bolded to indicate statistical significance.

TABLE 2 Association between DI-GM and kidney stones.

Characteristics	OR (95% CI), *p*-value		
	Model 1	Model 2	Model 3
DI-GM (continuous)	0.97 (0.94, 0.99) 0.0113	0.94 (0.91, 0.97) <0.0001	0.96 (0.93, 0.98) 0.0021
DI-GM (quartile)			
Quartile 1	Reference	Reference	Reference
Quartile 2	0.92 (0.80, 1.07) 0.2756	0.90 (0.78, 1.05) 0.1738	0.91 (0.79, 1.06) 0.2274
Quartile 3	0.95 (0.83, 1.09) 0.4876	0.92 (0.79, 1.06) 0.2282	0.94 (0.81, 1.08) 0.3914
Quartile 4	0.90 (0.79, 1.02) 0.0948	0.81 (0.71, 0.92) 0.0013	0.86 (0.75, 0.98) 0.0252
p for trend	0.1433	0.0019	0.0397

Model 1: no covariates were adjusted. Model 2: age, gender, and race were adjusted. Model 3: age, gender, race, educational level, marital status, PIR, BMI, smoking status, drinking status, moderate recreational activity, diabetes, and CVD were adjusted. OR, odds ratio; 95% CI, 95% confidence interval; DI-GM, dietary index for gut microbiota.

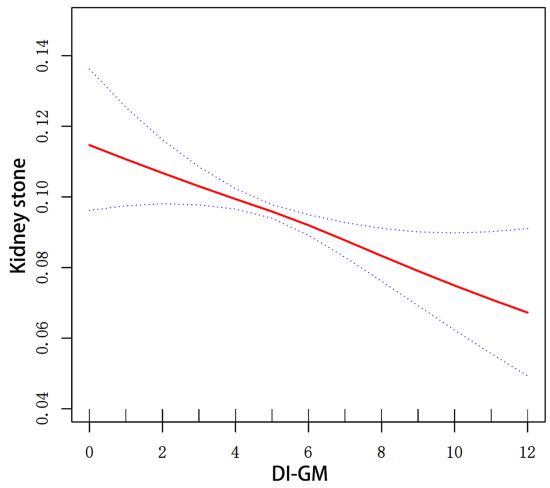

FIGURE 2
Smoothed curve fitting for DI-GM and kidney stones. Smooth curve fitting between variables is illustrated by the red line. Bands of blue color indicate the 95% CI. All covariates in Figure 2 were adjusted.

was divided into four groups based on the quartiles of DI-GM scores. The fully adjusted model demonstrated a substantial decrease in the incidence of kidney stones in Q4, as compared to Q1. The smoothed curve fitting results showed that DI-GM was linearly associated with the incidence of kidney stones. In addition, the robustness of these findings was further confirmed by sensitivity analyses.

Oxalate is the most common component of kidney stones, and the effects of gut microbiota in degrading oxalate have historically been emphasized (17). Initially, an intestinal bacterium named *O. formigenes* was found to be responsible for the degradation of oxalate (18). Subsequently, 18 other gut microbes were identified as capable of degrading oxalate, indicating the possibility of preventing kidney stones by introducing specific bacteria into the human intestine (19). In addition to degrading oxalate, the altered gut microbiota can influence kidney stone formation by promoting lipid metabolism or leading to compromised integrity of the intestinal barrier, thereby enhancing paracellular absorption of oxalate and inducing renal inflammation (20, 21). To verify the effect of gut microbiota on kidney stone formation, a study transplanted feces from patients with kidney stones into rats and found that overgrowth of *Bacteroidota* had a strong influence on the formation of calcium oxalate kidney stones by influencing the intestinal barrier function, hyperoxaluria, and renal inflammation (22). In another study, rats with high dietary oxalate exhibited gut microbiota disturbances, while transplanting microbes from healthy rats effectively reduced CaOx crystal depositions by promoting the expression of intestinal barrier proteins and oxalate transporters (23). Additionally, a two-sample Mendelian randomization study confirmed the causal relationship between kidney stones and gut microbiota (24). In general, these studies emphasized the association between gut microbiota diversity and kidney stone formation, providing the possibility of preventing kidney stone formation by maintaining the stability of gut microbiota.

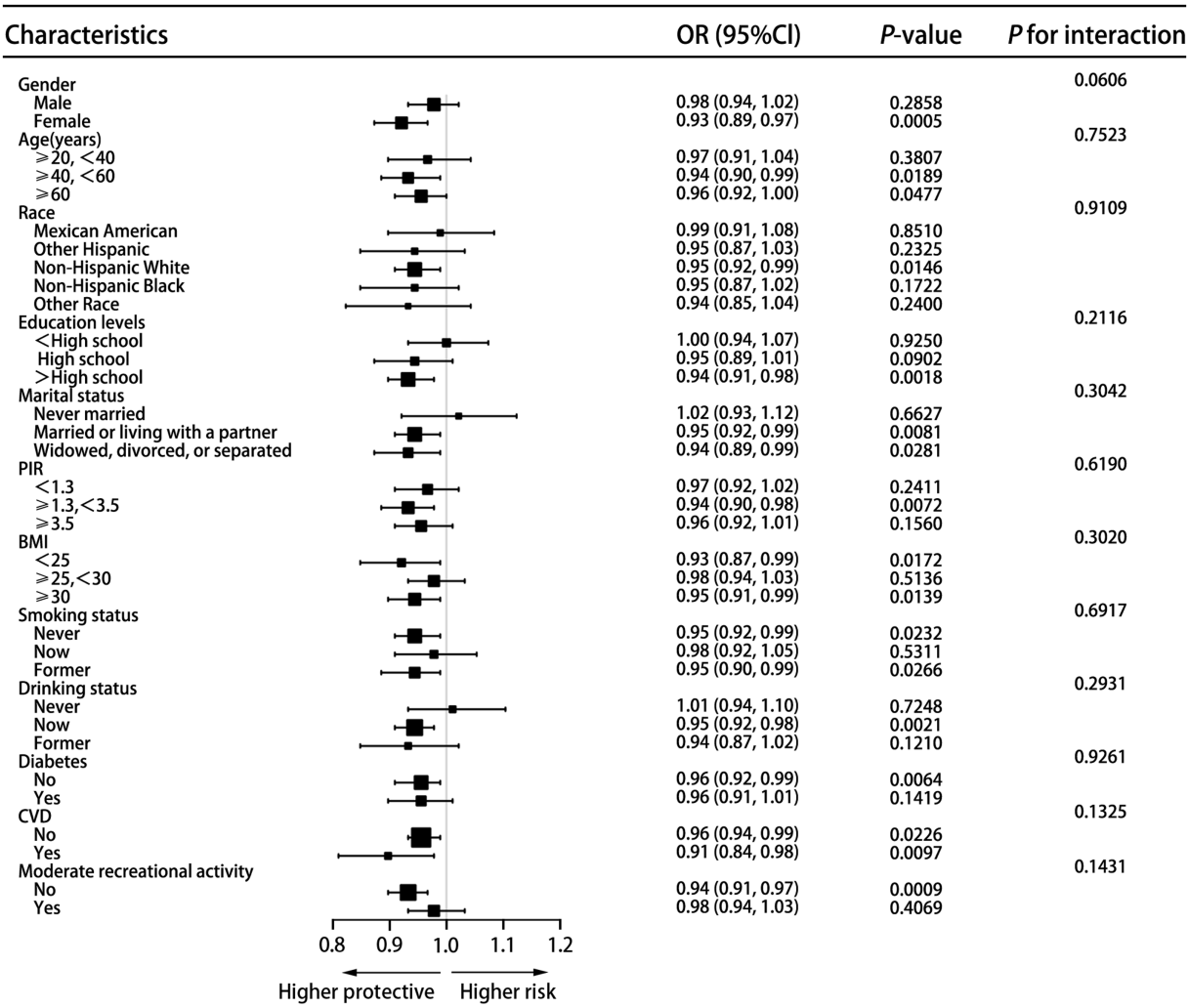

FIGURE 3
Subgroup analysis of the association between DI-GM and kidney stones.

Diet can substantially influence the gut microbiota (25, 26) and then influence the development and recurrence of kidney stones. The intakes of salt, animal proteins, oxalate, calcium, fruit, vegetables, legumes, and water were found to be highly associated with gut microbiota diversity and the incidence of kidney stones (13). However, there is a lack of studies supporting the strong correlation between dietary intake and kidney stone-associated dysbiosis of the gut microbiota. Dietary index is a tool used to evaluate the nutritional health of an individual's diet based on a variety of dietary components. Compared to a single dietary component, a dietary index can provide a multidimensional and comprehensive assessment of dietary quality that helps people better identify potential nutritional problems and guides them to take appropriate steps to improve their diets (27). The newly created dietary index DI-GM can serve as an indicator of the correlation between gut microbiota and diet. The changes of DI-GM suggest changes in dietary structure, which in turn influence the diversity of gut microbiota and are closely related to various pathophysiological processes. In a recent cross-sectional study, the researchers discovered a negative correlation between DI-GM and depression, together with the mediating function of phenotypic age and BMI (28). Another study confirmed the negative correlation between DI-GM and the risk of accelerated aging, with BMI mediating this association (29). Our study identified a negative correlation between DI-GM and kidney stones, but the specific biological mechanisms involved remains unclear.

The potential influence of certain components of DI-GM on the gut microbiota and their regulatory effect on kidney stone formation have been noticed for a long time. Moderate coffee intake was found to be associated with higher gut microbiota diversity and richer beneficial flora (30). Several population-based studies have found the beneficial effect of coffee intake on preventing kidney stones (31, 32). Mechanistically, coffee intake can reduce the release of antidiuretic hormone and thus exert a diuretic effect. Furthermore, caffeine was found to inhibit kidney stone formation by promoting the translocation of annexin A1 to reduce the adhesion of calcium oxalate crystals to renal tubular epithelial cells (33). Cranberry is another component that is beneficial to the gut microbiota. It has been found to modulate the composition of the gut microbiota and increase the content of Bifidobacterium, which can inhibit kidney stones by

degrading oxalate (34, 35). Additionally, the green tea polyphenol was found to exert protective effects on chronic diseases associated with oxidative stress by promoting the growth of beneficial flora (36). An *in vivo* experiment revealed that tea polyphenol intake suppressed the formation of kidney stones by improving oxidative stress (37). However, the specific mechanism of how these components inhibit kidney stone formation by maintaining gut microbiota stability remains unclear.

As far as we are aware, this study is the first to confirm a negative relationship between gut microbiota-related DI-GM and kidney stones. Changes in the DI-GM suggest changes in dietary patterns, which in turn influence the diversity of the gut microbiota and are linked to the prevalence of kidney stones. The gut-kidney axis is typically believed to be influenced by reduced gut microbiota diversity, which may result in kidney stones (38). This understanding may offer potential implications for preventing kidney stones. However, this correlation requires additional investigation through the implementation of more rigorously designed clinical and fundamental research studies that employ substantial samples.

Nevertheless, the current investigation contains numerous constraints. Firstly, considering that this study was conducted using cross-sectional data, the establishment of a causal relationship between kidney stones and DI-GM is impossible, and the results may be susceptible to selection bias. Further prospective cohort studies and Mendelian randomization studies are needed to establish causality. Secondly, it is possible that the correlation between DI-GM and kidney stones in other countries may differ from the American population used in this study due to the influence of cultural and regional differences on dietary composition. Furthermore, it is uncertain whether the negative correlation between DI-GM and kidney stones remains consistent across different types of kidney stones, since diet affects different types of kidney stones to varying degrees. Thirdly, the DI-GM assessment was conducted using self-reported 24-h dietary records, which may have increased recall bias. Additionally, the non-specific indicator of gut microbiota diversity, urinary enterolignans, failed to fully capture the complexity of the gut microbiota. Lastly, the prevalence of kidney stones and the gut microbiota diversity can also be influenced by certain underlying diseases and drug use, especially antibiotics. Nevertheless, the consequences of these factors have not been entirely eradicated in this study.

5 Conclusion

In conclusion, a substantial negative correlation between the prevalence of kidney stones and the newly proposed DI-GM is suggested by the current study. Dietary interventions designed in accordance with the DI-GM score may help reduce the incidence of kidney stones, given the robust correlation between diet, gut microbiota, and kidney stones.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the National Center for Health Statistics (NCHS) Ethical Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

XY: Data curation, Software, Writing – original draft. XS: Formal analysis, Investigation, Writing – original draft. TZ: Conceptualization, Writing – review & editing. QZ: Project administration, Writing – review & editing. JD: Supervision, Writing – review & editing. JX: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Philemon Gukop,
King's College London, United Kingdom

REVIEWED BY
Sho Takagi,
Toyohashi Heart Center, Japan
Vipin Zamvar,
Edinburgh Royal Infirmary, United Kingdom

*CORRESPONDENCE
Young-Lan Kwak
✉ YLKWAK@yuhs.ac

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Predictive value of postoperative prognostic nutritional index trajectory for mortality outcomes after off-pump coronary artery bypass surgery: a retrospective cohort study

Myung Il Bae[1,2], Jae-Kwang Shim[1,2], Hye Sun Lee[3], Soyoung Jeon[3] and Young-Lan Kwak[1,2]*

[1]Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, [2]Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea, [3]Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Republic of Korea

Background: The prognostic nutritional index (PNI) has been widely used as a nutritional metric in patients undergoing cardiac surgery because of its ability to incorporate both nutritional and inflammatory statuses. However, while preoperative PNI is well-known for its predictability of outcomes after coronary artery bypass grafting (CABG), the prognostic value of postoperative PNI has rarely been evaluated. This study investigated the changes in postoperative PNI values following off-pump coronary artery bypass (OPCAB) surgery using a trajectory analysis method and analyzed its influence on mortality outcomes.

Methods: We retrospectively analyzed the data of 983 patients who underwent OPCAB surgery. PNI values from postoperative days 1, 2, 3, and 1 month was analyzed using the trajectory method, and patients were grouped based on the patterns of change in PNI values. The 1-year and overall mortality rates were compared between PNI trajectory groups. Additionally, multivariable logistic regression analysis was performed to identify independent risk factors for 1-year all-cause mortality, and multivariable Cox regression analysis was conducted for overall mortality.

Results: The trajectory analysis categorized patients into two groups: the "PNI-improved group," characterized by a sharp increase in PNI values after surgery, and the "PNI-fixed group," which exhibited minimal changes in PNI values. The PNI-improved group had significantly lower 1-year mortality (1.1% vs. 9.5%, $p < 0.001$) and overall mortality (16.9% vs. 42.4%, $p < 0.001$) compared to the PNI-fixed group. Furthermore, the multivariable regression analysis indicated that the PNI trajectory pattern was an independent predictor of 1-year mortality (odds ratio: 7.931, 95% confidence interval [CI]: 3.117–20.180, $p < 0.001$) and overall mortality (hazard ratio: 2.120, 95% CI: 1.579–2.845, $p < 0.001$).

Conclusions: Patients who exhibited a significant increase in PNI values during the month following OPCAB surgery experienced significantly lower 1-year and overall mortality rates than those with minimal changes in postoperative PNI values. The PNI recovery pattern was identified as an independent predictor of both 1-year and overall mortality after adjusting confounding factors.

Recognizing the recovery patterns of postoperative PNI values after OPCAB surgery may be valuable for screening patients at high risk for mortality.

KEYWORDS

prognostic nutritional index (PNI), objective nutritional index, off-pump coronary artery bypass (OPCAB), coronary artery bypass graft (CABG), trajectory analysis, malnutrition, nutrition monitoring, mortality

1 Introduction

Malnutrition, a common problem in patients undergoing coronary artery bypass grafting (CABG) (1), negatively affects patient outcomes, particularly through the detrimental and reciprocal influence of the inflammatory response (2, 3). The role of nutrition in CABG surgery has been widely studied; however, its impact in the context of off-pump coronary artery bypass (OPCAB) remains relatively underexplored, with conflicting results. One study reported that preoperative nutritional status is associated with unfavorable outcomes and 1-year mortality in OPCAB patients (4). In another study, preoperative nutritional status did not influence immediate postoperative outcomes but had a significant impact on long-term mortality after OPCAB (5).

To estimate the nutritional status, objective nutritional indices, comprising readily available biomarkers, have become popular owing to their convenience and simplicity, compared with subjective nutritional evaluations (6). Furthermore, their prognostic roles have been validated in various subsets of patients (7–9). Among existing objective nutritional indices, the prognostic nutritional index (PNI) became popular because it incorporates both nutritional and inflammatory statuses by adding the lymphocyte count to the serum albumin level in its calculation, representing immune capacity and protein storage (10). Notably, preoperative PNI values are associated with mortality and major adverse events in patients with coronary disease (11), including those undergoing CABG (12–14). However, most previous studies evaluating the prognostic value of PNI in surgical patients have primarily focused on preoperative status, despite the high prevalence of postoperative malnutrition in these individuals (13, 15). Surgical trauma and inflammatory reaction induce impaired protein synthesis, increased nutrient consumption, and immunosuppression (16–18), resulting in serious fluctuations and declines in PNI values (13, 19). Furthermore, as the PNI theoretically reflects recovery from surgical insult, its clinical significance may be enhanced when the impact of postoperative PNI on prognosis is examined at multiple time points rather than through a single assessment; however, comprehensive evidence supporting this notion is currently lacking.

Trajectory projection analysis is an unbiased statistical modeling technique used to identify and cluster subphenotypes with common characteristics within heterogeneous data (20, 21). Accordingly, trajectory analyses of changing patterns of biomarkers in previous studies have provided critical information that static values measured at a single time point could not reveal (22, 23). Thus, we aimed to investigate the changing pattern of postoperative PNI values up to 30 days after surgery using trajectory analysis and its impact on mortality outcomes in patients undergoing OPCAB surgery.

2 Methods

This single-center retrospective study was approved by the Institutional Review Board of Yonsei University Health System Gangnam Severance Hospital (Seoul, South Korea) (approval number: 3-2023-0184, approval date: 12 July 2023). Owing to its retrospective nature, the requirement for informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

2.1 Study population

We retrospectively analyzed the data of patients aged ≥18 years who underwent OPCAB surgery at the Severance Hospital (Seoul, South Korea) between January 2010 and February 2021. Patients without PNI data from days 1 to 3 after surgery were excluded. To collect data at 1 month after surgery, patients without PNI data between 20 and 60 days after surgery were also excluded.

2.2 PNI calculation

PNI values were calculated according to the following formula based on a previous study (10): PNI = 10 × serum albumin level (g/dL) + 0.005 × total lymphocyte count (cells/mm^3).

PNI values on postoperative days (POD) 1, 2, and 3 were calculated using the serum albumin level and peripheral blood lymphocyte count at each time point. The "1-month PNI" was defined as the PNI value closest to POD 30 among the PNI values between 20 and 60 days after surgery.

2.3 Data collection

We collected data by reviewing the hospital's electronic medical records. Data regarding age, sex, body mass index (BMI), preoperative medication, and preoperative comorbidities, such as hypertension, diabetes mellitus, cerebrovascular accident, chronic renal failure, chronic obstructive pulmonary disease (COPD), congestive heart failure, acute myocardial infarction (MI) within 1 month, and anemia, were collected. Acute MI was defined according to the fourth universal definition by the Joint Task

Force (24). Additionally, we collected information on the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) scores, left ventricular ejection fraction, and preoperative laboratory results. These laboratory results included peripheral blood lymphocyte count, white blood cell count, platelet count, and serum levels of hemoglobin, albumin, glucose, creatinine, and creatine kinase-MB. We also gathered the following operative data: emergency status, number of grafts, operative time, intraoperative fluid input, intraoperative urine output, estimated bleeding volume, and perioperative transfusion requirements.

Regarding postoperative data, serum albumin concentration and peripheral blood lymphocyte counts from POD 1 to POD 3 and 1 month after surgery were collected. Serum albumin concentration was measured using either an Atellica CH930 (Siemens, Marburg, Germany) or Cobas c702 (Roche, Mannheim, Germany) device, while peripheral blood lymphocyte count was measured using either a Siemens Advia (Siemens, Marburg, Germany) or Sysmex XN (Sysmex, Kobe, Japan) system. Additionally, we collected information on the length of stay in the intensive care unit (ICU) and hospital, as well as on acute kidney injury (AKI), cerebrovascular accidents, cardiac reoperation, prolonged mechanical ventilation (>24 h), deep sternal wound infection, and both 1-year and overall mortality rates. AKI was defined according to the Kidney Disease Improving Global Outcomes guidelines (25), and cerebrovascular accidents were defined according to the American Heart Association and American Stroke Association (26). Information on surgery, death, and last follow-up dates was also collected. Information regarding the date of death was obtained from the Ministry of the Interior and Safety of the Republic of Korea. The data were provided after excluding personal information in accordance with the relevant laws and were used only for statistical analysis.

2.4 Study endpoints

The primary endpoint was 1-year all-cause mortality after OPCAB surgery. The secondary endpoint was overall all-cause mortality after OPCAB surgery.

2.5 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA), R software version 3.6.0 (The R Foundation for Statistical Computing), and MedCalc version 22.014 (MedCalc Software, Bvba, Ostend, Belgium). The Kolmogorov–Smirnov test was used to evaluate the normality of continuous variables. Since no continuous variable in this study demonstrated a normal distribution, they were expressed as medians (interquartile ranges [IQR]). Dichotomous variables were expressed as numbers (percentages). The Mann–Whitney *U* test was used to compare continuous variables, while the chi-square or Fisher's exact test was used to compare dichotomous variables.

Trajectory analysis was conducted using the longitudinal k-means method from the "latrend" package (20) in R version 3.6.0. This specialized statistical method analyzes patterns in longitudinal data and clusters similar patterns (20, 21). In this study, postoperative PNI values on POD1, POD2, POD3, and 1 month after surgery were analyzed using this trajectory method. Since the longitudinal k-means method requires that the last measurement of variables occur at the same time point, the date of the "1-month PNI" was set to 30 days after surgery, reflecting the average postoperative period for 1-month PNI values. The number of clusters was determined to ensure appropriate representativeness and assignment probabilities. The estimated assignment probabilities for the trajectory clusters are summarized in Supplementary Table S1. When classified into two clusters, each cluster had a sample size of over 300 patients, ensuring representativeness, and each cluster demonstrated an average assignment probability of over 90%. Therefore, trajectory analysis was conducted by classifying the data into two clusters.

Logistic regression analysis was performed to investigate the risk factors for 1-year mortality. Multivariable logistic regression analysis included variables with $p < 0.05$ from the univariable analysis. The variance inflation factor was calculated to assess multicollinearity. Since the PNI, chronic renal failure, and anemia were included in the regression model, peripheral blood lymphocyte counts, serum albumin level, creatinine level, hemoglobin level, and transfusion requirements were excluded to prevent multicollinearity. The EuroSCORE II was included in the multivariable model, while variables used in the EuroSCORE II calculation, such as COPD and left ventricular ejection fraction, were excluded from the model to avoid multicollinearity. "Post-PNI," defined as the highest PNI value between postoperative days 1 and 3, was included in the multivariable model to represent immediate postoperative PNI values. Additionally, receiver operating characteristic (ROC) curve analysis of the multivariable regression model was performed. The areas under the ROC curve (AUROC) of the multivariable models were compared using Delong's method to determine whether the PNI trajectory pattern significantly improved the model's predictive power.

Cox regression analysis was performed to investigate the risk factors for overall all-cause mortality. The multivariable Cox regression model incorporated variables with $p < 0.05$ from the univariable analysis. The EuroSCORE II score was included in the multivariable model, while the factors used to calculate the EuroSCORE II score were omitted. Although age is included in the EuroSCORE II score calculation, it was added to the multivariable model due to its significant impact on overall mortality.

Kaplan–Meier curves representing 1-year and overall survival were plotted, and the log-rank test was performed to identify statistical differences between the groups. Statistical significance was set at $p < 0.05$.

3 Results

A total of 1,619 patients who underwent OPCAB surgery between January 2010 and February 2021 were screened for eligibility. Of these patients, 636 were excluded due to insufficient PNI data: 27 lacked immediate postoperative PNI data (POD 1–3), and 609 did not have 1-month PNI data (POD 20–60). Ultimately, 983 patients were included in the study (Figure 1). The median follow-up duration was 2,136 days (IQR 1,387–3,000).

The trajectory analysis results for postoperative PNI values are summarized in Figure 2. One cluster exhibited a steep increase in PNI values during the first month after surgery (number of patients = 646, average probability of assignment = 94.43%) and was named as the "PNI-improved group." The second cluster, referred to as the "PNI-fixed group," showed minimal changes in PNI values during the same period (number of patients = 337, average probability of assignment = 91.83%).

Patients in the PNI-fixed group were older (68 [62–74] vs. 66 [59–72] years, $p < 0.001$) and had lower BMIs compared to those in the PNI-improved group. The prevalence of hypertension, chronic renal failure, cerebrovascular accidents, congestive heart failure, COPD, recent MI, and anemia was higher in the PNI-fixed group. Preoperative PNI was also lower in the PNI-fixed group (44.4 [39.1, 48.6] vs. 50.9 [47.1, 54.8], $p < 0.001$), as were hemoglobin levels, platelet counts, and left ventricular ejection fraction. EuroSCORE II scores were higher in the PNI-fixed group (1.67 [1.12, 2.80] vs. 1.08 [0.78, 1.69], $p < 0.001$), as was the frequency of perioperative transfusions (Table 1).

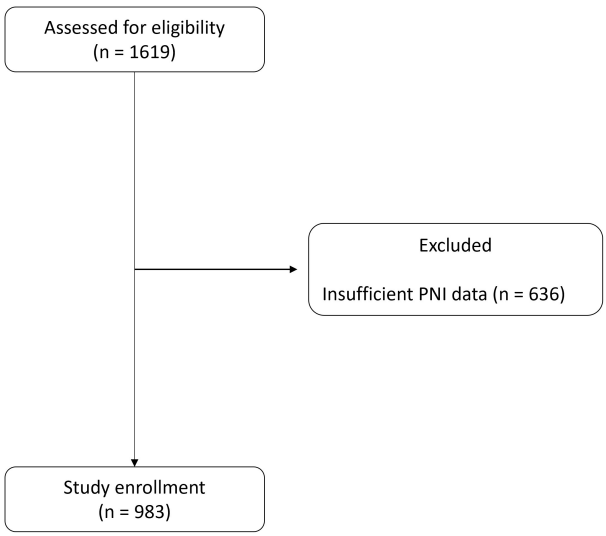

FIGURE 1
Flow diagram.

The incidence of 1-year all-cause mortality (9.5% vs. 1.1%, $p < 0.001$) and overall mortality (42.4% vs. 16.9%, $p < 0.001$) was significantly higher in the PNI-fixed group than in the PNI-improved group. The PNI-fixed group also had significantly lower PNI values on POD1, POD2, POD3, and 1 month after surgery compared to the PNI-improved group. Additionally, the lengths of stay in the ICU and hospital were significantly longer, while the incidence of AKI, prolonged ventilation, and sternal infection was significantly higher in the PNI-fixed group than in the PNI-improved group (Table 2).

Table 3 shows the results of the multivariable logistic regression analysis for predicting 1-year mortality. The PNI trajectory pattern (odds ratio [OR]: 7.931, 95% confidence interval [CI]: 3.117–20.180, $p < 0.001$) and preoperative anemia (OR: 2.964, 95% CI: 1.126–7.797, $p = 0.028$) were identified as independent predictors of 1-year all-cause mortality following OPCAB surgery. The results of the univariable analysis are presented in Supplementary Table S2.

Figure 3 shows the ROC curves of the multivariable logistic regression models for predicting 1-year mortality. Model-1 comprises a multivariable model consisting of pre-PNI, post-PNI, EuroSCORE II, BMI, emergency surgery, and anemia, which excluded the PNI trajectory pattern from the model. Model-2 combined the variables from Model-1 with the PNI trajectory pattern. By adding the PNI trajectory pattern, the AUROC of Model-2 was significantly greater than that of Model-1 (0.817 [0.760–0.874] vs. 0.745 [0.677–0.813], $p = 0.003$).

Table 4 shows the results of the multivariable Cox regression analysis for predicting overall mortality. The PNI trajectory pattern (hazard ratio [HR]: 2.120, 95% CI: 1.579–2.845, $p <$

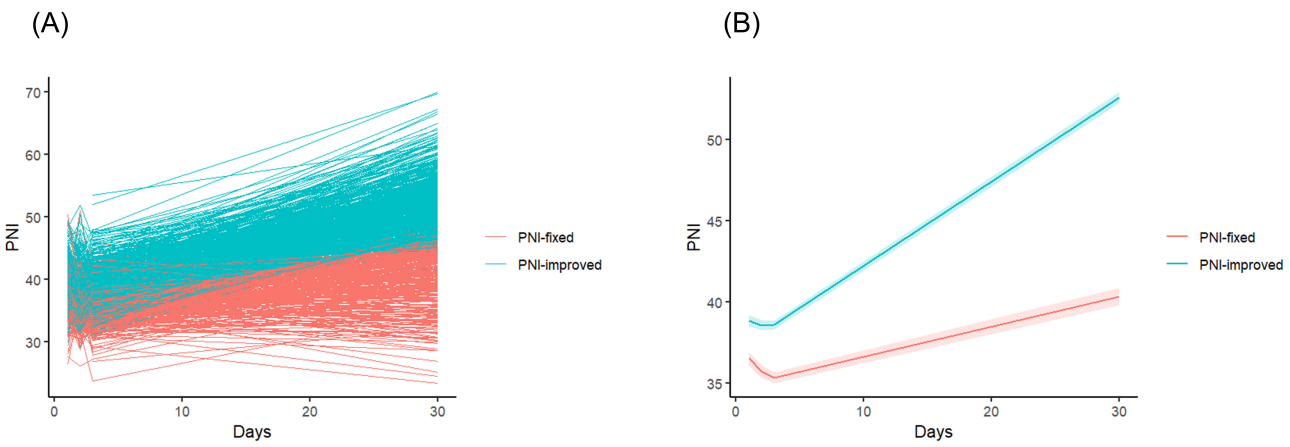

FIGURE 2
Trajectory analysis of PNI values after off-pump coronary artery bypass surgery. (A) Spaghetti plot showing the pattern of individual PNI value changes. The red line represents the cluster with minimal changes in PNI values after surgery (PNI-fixed group). The blue line represents the cluster with a steep increase in PNI values after surgery (PNI-improved group). (B) Mean profile plot according to trajectory clusters. The solid line represents the mean PNI values, and the shaded area represents the 95% confidence interval. PNI, prognostic nutritional index.

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TABLE 1 Patient demographics, perioperative clinical data according to the PNI trajectory groups.

Variables	Total ($N = 983$)	PNI-fixed ($n = 337$)	PNI-improved ($n = 646$)	p-value
Sex (female)	242 (24.6%)	86 (25.5%)	156 (24.1%)	0.636
Age (years)	67 (60, 73)	68 (62, 74)	66 (59, 72)	<0.001
Body mass index (kg/m^2)	24.2 (22.1, 26.3)	23.4 (21.5, 25.6)	24.5 (22.5, 26.8)	<0.001
Emergency	24 (2.4%)	12 (3.6%)	12 (1.9%)	0.101
Comorbidities				
Hypertension	736 (74.9%)	274 (81.3%)	462 (71.5%)	0.001
Chronic renal failure	177 (18.0%)	117 (34.7%)	60 (9.3%)	<0.001
Cerebrovascular accident	155 (15.8%)	68 (20.2%)	87 (13.5%)	0.006
Diabetes mellitus	538 (54.7%)	219 (65.0%)	319 (49.4%)	<0.001
Congestive heart failure	127 (12.9%)	60 (17.8%)	67 (10.4%)	0.001
COPD	45 (4.6%)	22 (6.5%)	23 (3.6%)	0.035
Recent MI	304 (30.9%)	122 (36.2%)	182 (28.2%)	0.010
Anemia	497 (50.6%)	242 (71.8%)	255 (39.5%)	<0.001
Medication				
Beta blocker	566 (57.6%)	198 (58.8%)	368 (57.0%)	0.590
Calcium channel blocker	393 (40.0%)	130 (38.6%)	263 (40.7%)	0.516
RAS inhibitor	534 (54.3%)	204 (60.5%)	330 (51.1%)	0.005
Statin	784 (79.8%)	267 (79.2%)	517 (80.0%)	0.766
Diuretics	248 (25.2%)	108 (32.0%)	140 (21.7%)	<0.001
Preoperative data				
PNI	49.0 (44.0, 53.4)	44.4 (39.1, 48.6)	50.9 (47.1, 54.8)	<0.001
Albumin (g/dL)	4.0 (3.6, 4.3)	3.7 (3.3, 4.1)	4.1 (3.8, 4.4)	<0.001
Lymphocyte (/μl)	1,750 (1,360, 2,220)	1,410 (1,120, 1,770)	1,960 (1,560, 2,383)	<0.001
EuroSCORE II	1.24 (0.85, 2.10)	1.67 (1.12, 2.80)	1.08 (0.78, 1.69)	<0.001
White blood cells (/μl)	6,300 (4,920, 7,750)	6,100 (4,780, 7,315)	6,455 (4,990, 7,990)	0.042
Hemoglobin (g/dL)	12.5 (11.1, 14.0)	11.6 (10.1, 12.9)	13.1 (11.9, 14.3)	<0.001
Platelet (x10^3/μl)	214 (178, 256)	203 (160, 254)	217 (184, 258)	0.001
Glucose (mg/dL)	123 (101, 166)	126 (102, 176)	121 (100, 162)	0.187
Creatinine (mg/dL)	0.92 (0.76, 1.16)	1.04 (0.84, 1.91)	0.88 (0.74, 1.05)	<0.001
CK-MB (μg/L)	1.8 (1.3, 2.6)	2.0 (1.4, 3.2)	1.7 (1.2, 2.4)	<0.001
Ejection fraction (%)	56 (44, 66)	49 (39, 63)	59 (47, 67)	<0.001
Operation data				
Graft number	3 (3, 4)	3 (3, 4)	3 (3, 4)	0.421
Operation time (min)	230 (207, 254)	230 (209, 253)	230 (206, 255)	0.569
Fluid Input/Output (ml)*	1,760 (1,340, 2,250)	1,750 (1,300, 2,210)	1,790 (1,350, 2,270)	0.294
Bleeding (ml)	600 (440, 780)	620 (460, 800)	600 (428, 773)	0.157
Perioperative Transfusion	520 (52.9%)	225 (66.8%)	295 (45.7%)	<0.001

Values are median (interquartile range) or number (%). *Fluid Input/Output was defined as intraoperative fluid input minus urine output. PNI, prognostic nutritional index; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; RAS inhibitor, renin-angiotensin system inhibitor; CK-MB, Creatine Kinase-MB.

0.001), preoperative PNI (HR: 0.972, 95% CI: 0.950–0.996, $p = 0.020$), age (HR: 1.040, 95% CI: 1.024–1.057, $p < 0.001$), and preoperative anemia (HR: 1.558, 95% CI: 1.153–2.106, $p = 0.004$) were independent predictors of overall all-cause mortality. The results of the univariable analysis are presented in Supplementary Table S3.

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TABLE 2 Postoperative data according to the PNI trajectory groups.

Variables	Total ($N = 983$)	PNI-fixed ($n = 337$)	PNI-improved ($n = 646$)	p-value
POD1-PNI	37.7 (35.5, 40.1)	36.5 (34.5, 38.5)	38.5 (36.3, 41.1)	<0.001
POD1-Albumin (g/dL)	3.3 (3.1, 3.5)	3.2 (3.0, 3.4)	3.3 (3.1, 3.5)	<0.001
POD1-Lymphocyte (/μl)	970 (750, 1,260)	815 (640, 1,123)	1,070 (840, 1,340)	<0.001
POD2-PNI	37.4 (35.0, 39.5)	35.7 (33.7, 37.7)	38.3 (36.4, 40.5)	<0.001
POD2-Albumin (g/dL)	3.1 (3.0, 3.3)	3.1 (2.9, 3.2)	3.2 (3.0, 3.3)	<0.001
POD2-Lymphocyte (/μl)	1,170 (885, 1,515)	960 (733, 1,200)	1,280 (1,035, 1,650)	<0.001
POD3-PNI	37.2 (35.0, 39.8)	35.4 (33.3, 37.1)	38.3 (36.1, 40.9)	<0.001
POD3-Albumin (g/dL)	3.1 (2.9, 3.3)	3.0 (2.9, 3.2)	3.1 (3.0, 3.3)	<0.001
POD3-Lymphocyte (/μl)	1,230 (940, 1,550)	950 (758, 1,263)	1,380 (1,100, 1,710)	<0.001
1month-PNI	49.6 (44.0, 53.5)	41.4 (37.1, 44.3)	52.2 (49.6, 55.2)	<0.001
1month-Albumin (g/dL)	4.0 (3.6, 4.3)	3.4 (3.0, 3.7)	4.2 (4.0, 4.4)	<0.001
1month-Lymphocyte (/μl)	1,780 (1,380, 2,270)	1,330 (1,060, 1,645)	2,040 (1,678, 2,410)	<0.001
ICU length of stay (days)	3 (3, 4)	3 (3, 5)	3 (2, 3)	<0.001
Hospital length of stay (days)	10 (8, 13)	12 (9, 20)	9 (8, 11)	<0.001
Acute kidney injury	267 (27.2%)	141 (41.8%)	126 (19.5%)	<0.001
Cerebrovascular accident	16 (1.6%)	9 (2.7%)	7 (1.1%)	0.062
Cardiac reoperation	19 (1.9%)	10 (3.0%)	9 (1.4%)	0.089
Prolonged ventilation	104 (10.6%)	59 (17.5%)	45 (7.0%)	<0.001
Sternum infection	73 (7.4%)	47 (13.9%)	26 (4.0%)	<0.001
One-year mortality	39 (4.0%)	32 (9.5%)	7 (1.1%)	<0.001
Overall mortality	252 (25.6%)	143 (42.4%)	109 (16.9%)	<0.001

Values are median (interquartile range) or number (%). POD, postoperative day; PNI, prognostic nutritional index, ICU, intensive care unit.

TABLE 3 Multivariable logistic regression analysis of chosen variables for predicting one-year mortality.

Variable	Adjusted odds ratio (95% CI)	p-value
PNI trajectory pattern (PNI-Fixed)*	7.931 (3.117, 20.180)	<0.001
Pre-PNI	0.993 (0.935, 1.056)	0.832
Post-PNI	1.075 (0.966, 1.196)	0.186
EuroSCORE II	0.963 (0.819, 1.132)	0.645
Body mass index (kg/m^2)	0.899 (0.804, 1.005)	0.061
Emergency	3.093 (0.785, 12.189)	0.107
Anemia	2.964 (1.126, 7.797)	0.028

*Odds ratio of the PNI-Fixed pattern compared to the PNI-Improved pattern. PNI, prognostic nutritional index.

Figure 4 displays the Kaplan–Meier curves for 1-year and overall all-cause survival according to the PNI trajectory groups. The log-rank test showed that 1-year and overall survival probabilities were significantly lower in the PNI-fixed group compared to the PNI-improved group ($p < 0.001$).

4 Discussion

In the current study, we analyzed the changing patterns of postoperative PNI values after OPCAB surgery using a trajectory analysis method. Our findings indicated that patients who demonstrated significant improvements in PNI values early after surgery showed markedly lower 1-year and overall all-cause mortality rates than did those with minimal changes in PNI values. The PNI recovery pattern was identified as an independent predictor of 1-year and overall all-cause mortality, even after adjusting for confounding factors. Furthermore, incorporating the PNI trajectory patterns further enhanced the predictability of the regression model for 1-year mortality when compared to the model that included only individual preoperative and postoperative PNI values.

In patients undergoing cardiac surgery, postoperative malnutrition is a common complication (1–3). Underlying comorbidities, such as reduced cardiac function, can exacerbate intestinal dysfunction after surgery (1, 27), and inadequate nutritional support also contributes to the high prevalence of postoperative malnutrition after cardiac surgery (15). Therefore, screening for malnourished patients and providing nutritional support during the postoperative period is critical in this population. However, previous studies on nutritional monitoring have primarily focused on preoperative nutritional status, and there

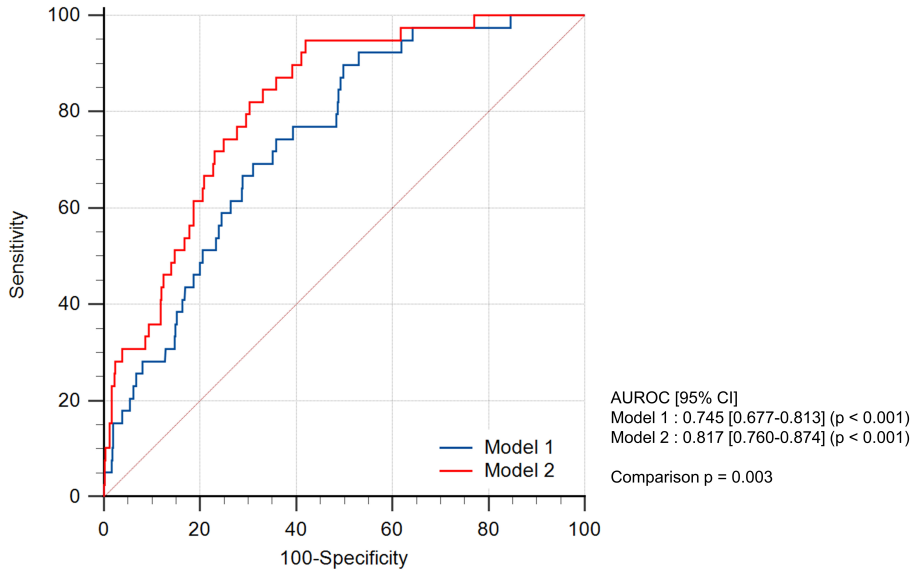

FIGURE 3
ROC curves for predicting 1-year mortality, derived from multivariable logistic regression models. This illustration shows the ROC curves derived from the multivariable logistic regression models predicting 1-year mortality. The blue line represents the curves of Model-1, which includes the pre-PNI, post-PNI, EuroSCORE II, BMI, emergency surgery, and anemia data. The red line represents the curves of Model-2, which includes the PNI trajectory pattern and the variables from Model 1. The AUROC of Model-2 was significantly higher than that of Model-1 ($p = 0.003$). PNI, prognostic nutritional index; ROC, receiver operating characteristic; AUROC, area under the receiver operating characteristic curve.

is no global consensus on postoperative nutritional monitoring and support, apart from the recommendation to initiate oral feeding early after surgery (18). Therefore, we examined the prognostic value of the postoperative recovery patterns of nutritional status. The Geriatric Nutritional Risk Index (GNRI), Controlling Nutritional Status (CONUT), and PNI are objective nutritional indices that have been widely studied in cardiac surgery. The GNRI incorporates albumin levels, ideal body weight, and actual body weight in its calculation. However, as postoperative body weight is greatly influenced by intraoperative fluid management (28, 29), the GNRI may not be an ideal tool for monitoring immediate postoperative nutritional status. The CONUT offers the advantage of incorporating cholesterol into its calculation alongside albumin and lymphocytes. Nevertheless, the widespread use of cholesterol-lowering medications in patients with coronary artery disease may significantly influence the trajectory pattern of CONUT scores after surgery. PNI was originally developed to assess the nutritional status of cancer patients, and its applicability in individuals with coronary artery disease has been subject to debate (30). However, a recent meta-analysis supports its utility as a prognostic marker in coronary artery disease patients (11). Moreover, PNI has the practical advantage of being easily calculated from routine blood test results, making it a convenient and suitable indicator for monitoring postoperative changes.

This study investigated the changing pattern of postoperative PNI values using trajectory analysis, a specialized statistical method for analyzing repeatedly measured data over time (20, 21). This approach uncovers meaningful patterns that static measures cannot capture and is being actively studied in various clinical fields as a useful tool to analyze the repeatedly measured biomarkers (22, 23), including in cardiovascular diseases (31, 32). In this study,

TABLE 4 Multivariable Cox regression analysis of chosen variables for predicting overall mortality.

Variable	Adjusted hazard ratio (95% CI)	*p*-value
PNI trajectory pattern (PNI-Fixed)*	2.120 (1.579, 2.845)	<0.001
Pre-PNI	0.972 (0.950, 0.996)	0.020
Post-PNI	1.012 (0.969, 1.057)	0.578
EuroSCORE II	1.055 (0.998, 1.115)	0.061
Age (years)	1.040 (1.024, 1.057)	<0.001
Body mass index (kg/m^2)	0.985 (0.946, 1.027)	0.478
Anemia	1.558 (1.153, 2.106)	0.004
Graft number	0.939 (0.814, 1.084)	0.393

*Hazard ratio of the PNI-Fixed pattern compared to the PNI-Improved pattern. PNI, prognostic nutritional index.

our trajectory analysis of changing postoperative PNI patterns categorized patients into two distinct clusters: one group exhibited a steep increase in PNI values 1 month after surgery, while another showed minimal changes in PNI values compared to their values immediately after surgery. This distinction led to a stark contrast in 1-year and long-term overall all-cause mortality rates, with the "PNI-improved" group demonstrating markedly improved survival rates. The odds ratio of the PNI trajectory pattern for 1-year mortality was 7.931 (95% CI: 3.117–20.180), and the hazard ratio for overall mortality was 2.120 (95% CI: 1.579–2.845), which can be considered clinically meaningful results. Additionally, the PNI trajectory pattern remained an independent predictor of 1-year and

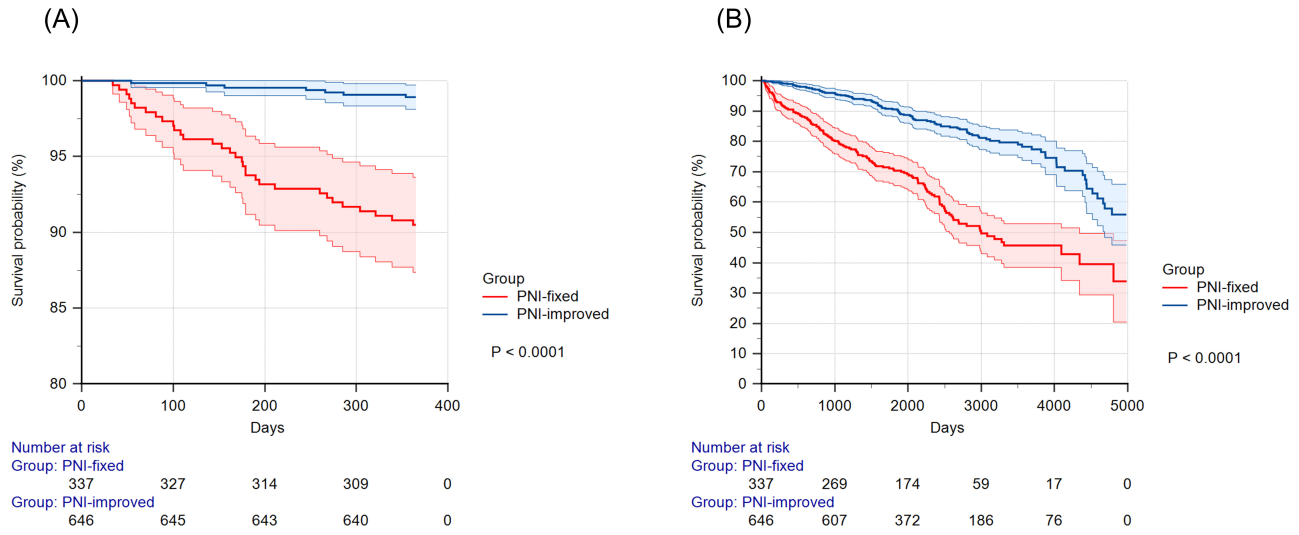

FIGURE 4
Kaplan–Meier survival curves according to PNI trajectory groups. (A) Kaplan–Meier curves for 1-year survival. (B) Kaplan–Meier curves for overall survival. The figures show the patients' Kaplan–Meier survival curves according to PNI trajectory groups. The red line represents the group with minimal changes in PNI values after surgery (PNI-fixed group). The blue line represents the group with a steep increase in PNI values after surgery (PNI-improved group). The shaded area represents the 95% confidence interval. PNI, prognostic nutritional index.

overall mortality in multivariable models adjusted for confounding factors, including pre- and postoperative PNI values. Furthermore, the predictive power for mortality significantly improved when the PNI trajectory pattern was added to the multivariable regression model. These findings highlight the importance of the PNI recovery pattern, which cannot be captured by a single-point static PNI value, and provide novel insights into postoperative nutritional monitoring and support in OPCAB surgery. They also highlight the necessity of enhancing nutritional status in the early postoperative period after OPCAB surgery to improve prognosis.

As the PNI incorporates lymphocyte counts and albumin levels, postoperative PNI values can be significantly affected by the inflammatory reaction and intravascular volume changes. Therefore, we focused on patients undergoing OPCAB surgery to minimize the confounding influences of cardiopulmonary bypass regarding systemic inflammation and hemodilution (33, 34). Nevertheless, PNI values decreased after surgery in 92% (904/983) of patients compared to their preoperative values in this study, indicating the limited discriminative value of PNI values measured at a single point during the immediate postoperative period. Consequently, static postoperative PNI values measured at a single point were not an independent predictor of mortality in this study. Instead, observing PNI recovery patterns proved instrumental in identifying patients with a poor clinical course following OPCAB surgery.

Interestingly, the preoperative PNI value was significantly lower in the PNI-fixed group than in the PNI-improved group in the present study. This finding is consistent with a previous study reporting that patients with low preoperative PNI values had poorer nutritional status perioperatively after CABG surgery (13). In this context, it is assumed that inadequate immune function and nutritional supplementation before surgery may synergistically interact with postoperative suppression of the immune system and metabolic synthesis, potentially negatively affecting the patient's prognosis.

Our study has several strengths. First, the novel attempt to analyze the changing pattern of postoperative PNI using trajectory analysis may provide valuable insights into postoperative nutritional monitoring, which has previously been somewhat subjective, unclear, and often overlooked. Moreover, the significant impact of the PNI recovery pattern on mortality outcomes provides an important rationale for postoperative nutritional support, which may greatly influence survival. Additionally, a considerable number of patients were enrolled in the present study ($n = 983$), enhancing statistical reliability. Despite the above strengths, this study also has some limitations. First, due to the retrospective nature and single-center design of this study, the generalizability of the findings may be limited. Second, while our trajectory analysis offers a new methodological approach for evaluating nutritional changes, it inherently categorizes patients into broad groups, potentially overlooking subtle individual variations. Additionally, the results of the trajectory analysis may vary depending on the analysis tool owing to methodological differences (21). Nonetheless, trajectory analysis is based on rigorous statistical computations (20, 21), and has been widely validated in clinical studies as a reliable approach for characterizing heterogeneous temporal trends (22, 23, 31). While this method has inherent limitations, we believe that it provides a novel perspective on the dynamic patterns of postoperative nutritional recovery. Third, the incidence of 1-year mortality was relatively low, which may have restricted the statistical power for conducting multivariable regression analysis. Fourth, 636 patients with insufficient PNI data were excluded from the analysis, representing a significant proportion of the screened patients. However, the exclusion process was conducted without bias, and the analysis was performed on a robust sample of 983 patients after exclusions. Fifth, the analysis did not encompass other

outcomes such as cardiac mortality or major adverse cardiac and cerebrovascular events (MACCE) due to data limitations. Future research should focus on investigating the impact of postoperative PNI changes on various outcomes, including cardiac mortality and MACCE. Finally, our study did not incorporate a comprehensive evaluation of postoperative nutritional status. Incorporating a wider range of nutritional parameters—such as caloric intake, body composition, and functional capacity—could provide a more in-depth understanding of nutritional recovery in future studies.

5 Conclusions

This study found that patients who demonstrated a meaningful improvement in their postoperative PNI values in the month following OPCAB surgery had significantly lower 1-year and overall all-cause mortality rates than patients with minimal changes in PNI values. Furthermore, the PNI recovery pattern was an independent predictor of 1-year and overall mortality, even after adjusting the confounding factors. Therefore, identifying the PNI recovery pattern following OPCAB surgery could help screen patients at high risk for mortality.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Institutional Review Board of Yonsei University Health System Gangnam Severance Hospital (Seoul, South Korea). The studies were conducted in accordance with the local legislation and institutional requirements. The Ethics Committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because Owing to its retrospective nature, the requirement for informed consent was waived.

Author contributions

MB: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Visualization, Writing – original draft, Writing – review & editing. J-KS: Conceptualization, Investigation, Methodology, Validation, Writing – review & editing. HL: Conceptualization, Formal analysis, Methodology, Software, Visualization, Writing – review & editing. SJ: Conceptualization, Formal analysis, Methodology, Software, Visualization, Writing – review & editing. Y-LK: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2025.1530651/full#supplementary-material

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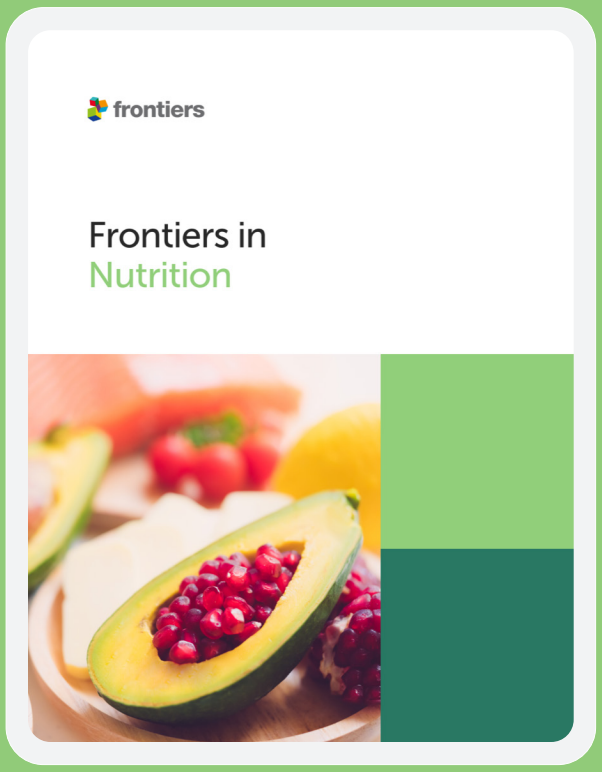

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