



OPEN ACCESS

EDITED BY

Miroslava Rossenova Atanassova,
Møreforsking AS, Norway

REVIEWED BY

Aurelio Lo Buglio,
University of Foggia, Italy
Damiano Zemp,
Ente Ospedaliero Cantonale (EOC),
Switzerland

*CORRESPONDENCE

Xiubin Tao
✉ 1325609568@qq.com
Ming Zhang
✉ wnyxyzhangming@foxmail.com

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

RECEIVED 18 September 2023

ACCEPTED 16 September 2024

PUBLISHED 08 October 2024

CITATION

Liu H, Tao M, Zhang M, Zhou Z, Ni Y, Wang Q, Zhang X, Chi C, Yang D, Chen M, Tao X and Zhang M (2024) Construction of frailty and risk prediction models in maintenance hemodialysis patients: a cross-sectional study.
Front. Med. 11:1296494.
doi: 10.3389/fmed.2024.1296494

COPYRIGHT

© 2024 Liu, Tao, Zhang, Zhou, Ni, Wang, Zhang, Chi, Yang, Chen, Tao and Zhang. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Construction of frailty and risk prediction models in maintenance hemodialysis patients: a cross-sectional study

Huan Liu^{1†}, Mingfen Tao^{1†}, Man Zhang², Zhiqing Zhou³, Yang Ni³, Qin Wang⁴, Xiang Zhang⁴, Chenru Chi⁴, Dan Yang⁴, Mengqi Chen⁴, Xiubin Tao^{3*} and Ming Zhang^{5,6*}

¹Department of Hemodialysis, The First Affiliated Yijishan Hospital of Wannan Medical College, Wuhu, China, ²Department of Nursing, Shaanxi Provincial People's Hospital, Xi'an, China, ³Department of Nursing, The First Affiliated Yijishan Hospital of Wannan Medical College, Wuhu, China, ⁴Department of Graduate School, Wannan Medical College, Wuhu, China, ⁵School of Educational Science, Anhui Normal University, Wuhu, China, ⁶School of Innovation and Entrepreneurship, Wannan Medical College, Wuhu, China

Objective: As the prevalence of diabetic nephropathy and hypertensive nephropathy increases with age in mainland China, the number of patients with end-stage renal disease is increasing, leading to an increase in the number of patients receiving maintenance hemodialysis. Considering the harmful effects of frailty on the health of maintenance hemodialysis patients, this study aims to identify hemodialysis patients at risk for frailty at an early stage, in order to prevent or delay the progression of frailty in the early stage, so as to prevent the adverse consequences of frailty.

Methods: A total of 479 patients admitted to the blood purification centers of two grade tertiary hospitals in Anhui Province, China, using convenient sampling. The Frailty Scale, the SARC-F questionnaire, the Simplified Food Appetite Questionnaire (SNAQ) and the mini nutritional assessment short-form (MNA-SF) were used in the study. Pearson correlation analysis was used to explore the correlation among the frailty influencing factors.

Results: The incidence of frailty was 24.0% among 479 Chinese hemodialysis patients. Gender ($p < 0.05$), Malnutrition ($p < 0.001$), sarcopenia ($p < 0.001$), and feel tired after dialysis ($p < 0.001$) were highly correlated with frailty in Chinese hemodialysis patients. Serum albumin concentration ($p < 0.05$) was a protective factor of frailty.

Conclusion: This survey shows that frailty was highly prevalent among Chinese hemodialysis patients. Medical staff and their families should make early judgments and carry out interventions on the risk of frailty.

KEYWORDS

frailty, prevalence, hemodialysis patients, multicentre, study

Introduction

Frailty is a clinical syndrome that is marked by a depletion of physical reserves and multiple system disorders. This depletion reduces the body's ability to cope with stress and maintain homeostasis. However, it also increases the body's resilience to stressful events and diseases (1). It is crucial for us to recognize that frailty is a dynamic disease which evolves with time and organ dysfunction (2). Several factors like inflammatory markers, hospitalization, and malnutrition were identified as predictors of frailty transitions (3, 4). As China's population ages rapidly, frailty has become an important and prominent public health problem. With the increasing incidence of end-stage chronic renal failure caused by chronic kidney disease and other chronic diseases, the number of hemodialysis patients in China is also significantly increasing year by year (5).

The number of people underwent renal replacement therapy worldwide was estimated at 262 million in 2010, which is expected to increase to 543.9 million by 2030 (6). Frailty poses a very serious threat to the quality of life and health of the maintenance hemodialysis patients. The incidence rate of frailty in dialysis patients ranges from 14 to 73% (7, 8). Many previous studies reported that frailty was a predictor of adverse outcomes. Clinical outcomes include mortality (9), hospitalization (10), and falls (11). Considering the adverse health outcomes caused by the high incidence and prevalence of frailty and related factors in maintenance hemodialysis patients, should be explored the influencing factors of frailty in maintenance hemodialysis patients, so as to provide a scientific basis for early prevention and intervention. Frailty is divided into three subgroups: social frailty, physical frailty, and cognitive frailty, with sarcopenia being the major component of physical frailty (12). Sarcopenia is defined as a muscle disorder (13, 14) characterized by a gradual and generalized loss of muscle strength and loss of muscle mass (15, 16). Sarcopenia is associated with osteoporosis (17), falls (18), functional disability, death, and other adverse outcomes (19). Studies had shown that sarcopenia could reduce the strength of swallowing muscles (20–22), which was risk factors for dysphagia. Sarcopenia has become an important predictor of frailty in hemodialysis patients. However, the relationship between sarcopenia status and frailty status in maintenance hemodialysis patients is still neglected. Therefore, it is crucial to consider the impact of maintenance hemodialysis patients' sarcopenia on frailty.

Appetite is the state of motivation to eat (23), which is affected by many factors (24). Studies have found that appetite loss is associated with poor mental health (25), decreased quality of life (26), hospitalization (27), and increased mortality (28). Appetite change is one of the symptoms associated with uremia (29). Appetite loss occurs frequently in patients undergoing maintenance hemodialysis (HD). Uremia may cause loss of appetite by changing the levels of leptin, ghrelin, and neuropeptide Y, etc. (30). Appetite loss is associated with an increased risk of death, increased hospitalization, and poorer quality of life (31). When maintenance hemodialysis patients develop a poor appetite for some time, they may become frail through malnutrition, which may harm their health. Although the important role appetite plays in the frailty of maintenance hemodialysis patients, it remains an under-studied variable, especially in China.

Malnutrition is a clinical syndrome caused by nutritional imbalance (deficiency or excess) with measurable adverse effects on body tissue/

morphology (body type, size, composition) or function and/or clinical outcome (32). Malnutrition can be divided into iatrogenic and non-iatrogenic (33). The iatrogenic factor is caused by dialysis treatment. Nutrient losses during dialysis range from 3 to 8 g of amino acids and 3–9 g of protein per day. Non-iatrogenic factors are spontaneously produced by loss of appetite and decreased physical function. Inoue et al. (34) and Goisser et al. (35) found that malnutrition assessed by MNA-SF or MNA-FF was a significant predictor of ADL improvement at discharge and 6 months postoperatively. Miu and Lam (36) reported higher in-hospital mortality in malnourished patients as assessed by MNA-SF compared with high-risk and well-nourished patients. Previous evidence suggests that malnutrition leads to a loss of muscle mass and strength, which can contribute to the onset of sarcopenia and subsequent physical damage, both of which are important factors in frailty (37). A meta-analysis of older adults found that the prevalence of malnutrition in older adults might range from 6% (95% CI, 4.6–7.5) to 29.4% (95% CI, 21.7–36.9) (38). And, Wojziszchke et al. (39) reported approximately 47% of elderly rehabilitation patients were at the risk of malnutrition. Due to its clinical impact on acute and chronic disease, malnutrition is widely recognized as being associated with poor health (40, 41). Furthermore, malnutrition is now recognized as one of the most important modifiable prognostic factors, which worsens prognosis and mortality in elderly patients (42, 43). Malnutrition is also the risk factor for osteoporosis, sarcopenia, and frailty (44). Because of the detrimental effects of malnutrition on the musculoskeletal system, malnourished patients should be screened for sarcopenia and frailty syndromes, and synergies between therapeutic interventions should be enhanced (45). Malnutrition impairs normal brain function and promotes cognitive decline (46). Furthermore, the central role of malnutrition in the pathophysiology of frailty and sarcopenia is well established (47).

Predictive models can make the most accurate predictions possible by learning from data and can be used to help select prevention and treatment strategies (48). Nevertheless, the present research on frailty in hemodialysis patients in China was limited to current status surveys, and no effective frailty risk identification tool was constructed for hemodialysis patients. Therefore, this study aims to explore the incidence of frailty in hemodialysis patients and its influencing factors and construct a risk prediction nomogram model based on easily available predictors to provide a reference for the early identification of patients with frailty.

Materials and methods

Study design

This multicentre cross-sectional study was conducted at the blood purification centers of two grade A tertiary hospitals in Anhui Province, China, using convenient sampling. The questionnaire and study data were strictly confidential and used only for this study.

Clinical data

Participants strictly meet the following selection criteria: (a) Age \geq 18 years; (b) Dialysis for more than 3 months; (c) Maintenance hemodialysis (MHD) treatment 2–3 times a week; (d) Normal comprehension; and (e) obtaining the informed consent and voluntary

participation of the participants. Exclusion criteria included (a) inpatient MHD during the investigation period; (b) cognitive impairment or mental illness; (c) having serious complications from hemodialysis or suffering from other serious physical diseases and unable to take care of themselves; And (d) refused to participate in the study. Of the 500 maintenance hemodialysis patients who met the inclusion criteria who were invited to participate, 21 eligible participants declined to participate due to low level of compliance. The remaining 479 participants returned complete and valid questionnaires with a valid sample size of 479 (participation rate = 95%).

Data collection

The time for participants to complete the survey was approximately 5–10 min. Four trained nursing graduate students supervised and coordinated the completion of the questionnaire. The investigators received unified training from the members of the research group. Prior to the survey, maintenance hemodialysis patients were informed that the study was conducted under the principle of complete anonymity and strict confidentiality, and that patients could only participate in the study by voluntarily signed informed consent. In addition, the investigators introduced the purpose and significance of the study to the maintenance hemodialysis patients. A total of 500 maintenance hemodialysis patients completed the investigation, of which 21 were excluded, and the remaining 479 respondents met the requirements, with an effective response proportion of 95.8% (details are shown in Figure 1).

Instruments

Sociodemographic variables

The demographic questionnaire was designed by the first author after literature search and according to the purpose of the study, and

collected information such as age, residence, gender, marital status, education level, the times of hemodialysis per week, the duration of hemodialysis, and type of medical insurance, were collected by investigators through face-to-face interviews.

Frailty scale

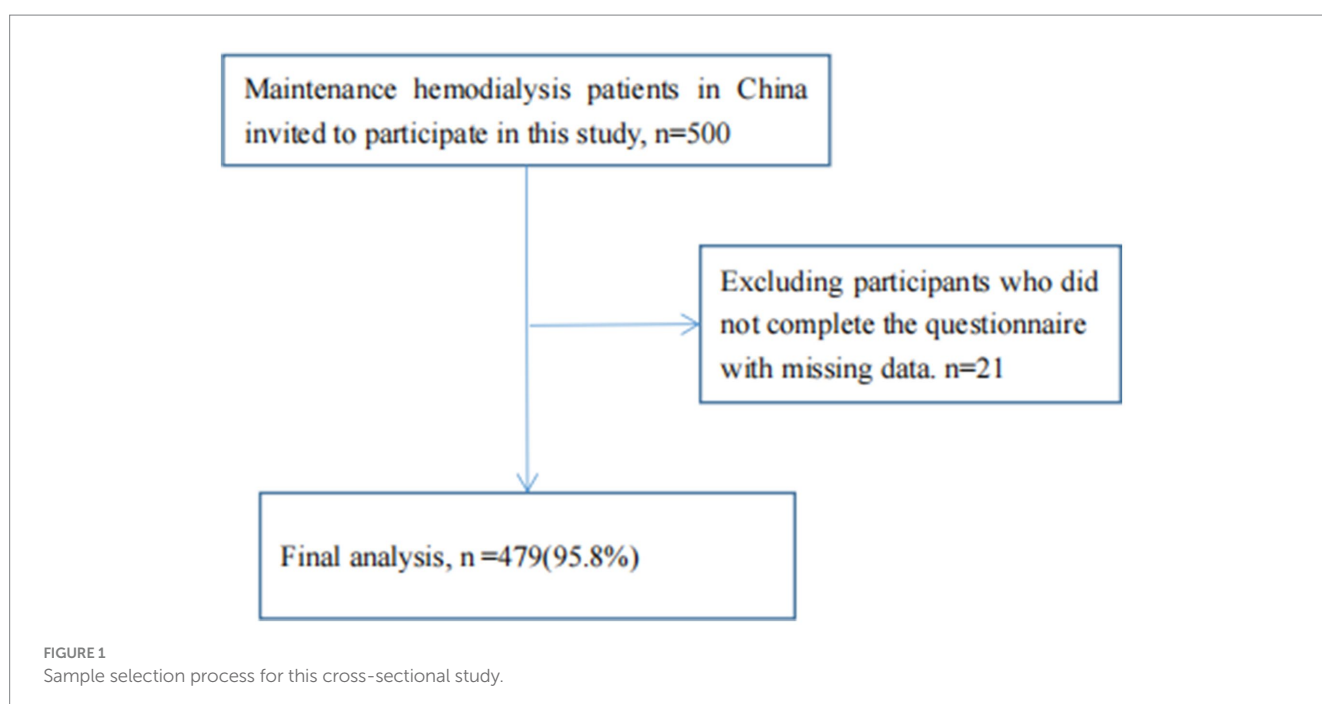
Frailty was measured using the Frailty Scale proposed by the International Society of Gerontology Expert Group (1). The scale consists of 5 items, 1 point for answering “yes” and 0 point for answering “no,” the total score ranges from 0 to 5 points, and ≥ 3 points indicate the presence of frailty. The FRAIL scale has also been verified in Chinese maintenance hemodialysis patients (49). In this study, Cronbach’s alpha coefficient for the FRAIL scale was 0.843.

The SARC-F questionnaire

The SARC-F is a simply, rapidly and conveniently screening questionnaire for rapidly identifying of individuals at risk of sarcopenia, and both the updated EWGSOP consensus and the AWGS consensus recommend the SARC-F questionnaire as a tool for screening patients for sarcopenia (50, 51). The standard SARC-F scale examines five domains: (1) strength, (2) assistance with walking, (3) rising from a chair, (4) climbing stairs, and (5) falls. Each of the first four questions on the sarcopenia scale provides three possible answers: “no problem,” “some problems,” and “a lot of problems or impossible.” For the last question, falls, the possible answers were “never,” “one to three times,” and “four or more times.” Each item was scored with 0, 1, and 2 points, respectively. The Cronbach’s alpha coefficient of this Sarcopenia scale is 0.87, which has relatively high reliability and validity.

Appetite loss

Appetite loss was tested using the Brazilian version of the Simplified Food Appetite Questionnaire (SNAQ) (52). The SNAQ is a simple Likert-type questionnaire with the following questions: (i)



My appetite is very poor; poor; average; good; very good. (ii) When I eat, I feel full after a few bites; I feel full after about a third of a meal; I feel full after half a meal; I feel full after eating; I almost never felt full. (iii) I am rarely hungry; occasionally; sometimes; mostly; all the time. (iv) Food tastes very bad; bad; average; good; very good. The total score is ranging from 4 to 20 points. The lower the score, the worse the appetite. A score of 14 or lower indicates the risk for anorexia (53). The Cronbach's alpha coefficient of this SNAQ is 0.835.

Malnutrition

The nutritional status of patients was assessed using the mini nutritional assessment short-form (MNA-SF) (54). Including 6 items: food intake and food intake reduction in the past 3 months, weight change, activity ability, acute disease or psychological trauma, mental and psychological problems, and body mass index. The total score is 14 points, ≤ 7 points means malnutrition. It has been verified that MNA-SF is suitable for the nutritional assessment of elderly hospitalized patients with chronic diseases (55). The Cronbach's alpha coefficient of this MNA-SF is 0.91.

Statistical analysis

The results of the survey were entered into the questionnaire Star software by two surveyors. The statistical analyses were conducted with STATA 15.0 (StataCorp. College Station, TX, USA). All tests were two-sided and a $p < 0.05$ was used to determine statistical significance. The results of the Kolmogorov–Smirnov test indicated that the data were normally distributed. In the study, categorical variables were represented using numerical values and percentages, while continuous variables were presented using the mean value and standard deviation. SPSS version 21.0 (IBM Corporation, Armonk, NY, USA) was used for all statistical analyses, and $p < 0.05$ were considered statistically significant. Binary logistic regression analysis was performed to analyze the factors associated with frailty, and the odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

Results

Participant characteristics

As shown in Table 1, a total of 479 patients with maintenance hemodialysis were included in this study. Among 479 participants included in the data analysis, the age of the respondents ranged from 20 to 91 years old, which the mean age being (59.36 ± 18.24) years old. A total of 246 (51.4%) were male, and 233 (48.6%) were female. A total of 215 (44.9%) live in the rural, 108 (22.5%) live in the town, and 156 (32.6%) live in the city. A total of 383 (80.0%) of the participants had been hospitalized in the past 6 months, and 96 (20.0%) had not. A total of 302 (63.0%) of the participants had no symptoms of fatigue after dialysis, and 177 (37.0%) of the participants had. A total of 273 (57.0%) of the participants felt lonely, and 206 (43.0%) did not feel lonely. A total of 274 (57.2%) of the participants had comorbidities, and 205 (42.8%) of the participants had no comorbidities. Further socio-demographic information about this study is displayed in Table 1.

TABLE 1 The socio-demographic characteristics of the participants (N = 479).

Variables	N(%)
Gender	
Male	246(51.4)
Female	233(48.6)
Place of residence	
Rural	215(44.9)
Town	108(22.5)
City	156(32.6)
Age	
20–30 years	40(8.4)
31–40 years	78(16.3)
41–50 years	160(33.4)
51–60 years	101(21.1)
61–70 years	83(17.3)
>70 years	17(3.5)
Hospitalized in the past 6 months	
No	383(80.0)
Yes	96(20.0)
Dialysis frequency	
2 times/week	48(10.0)
3 times/week	431(90.0)
Employment status	
No	432(90.2)
Yes	47(9.8)
Frequency of physical exercise per week	
0 times/week	202(42.2)
1–2 times/week	146(30.5)
≥ 3 times/week	131(27.3)
Marital status	
Single	46(9.6)
Married	399(83.3)
Divorced	16(3.3)
Others	18(3.8)
Education	
Elementary school and below	241(50.3)
Junior high school	135(28.2)
High school	62(12.9)
Junior college	31(6.5)
College degree and above	10(2.1)
Feel tired after dialysis	
No	302(63.0)
Yes	177(37.0)
Feel lonely	
No	206(43.0)
Yes	273(57.0)

(Continued)

TABLE 1 (Continued)

Variables	N(%)
Comorbidity	
No	205(42.8)
Yes	274(57.2)
Sleep time per day	
≤5 h/day	79(16.5)
6 h/day	135(28.2)
7 h/day	164(34.2)
8 h/day	83(17.3)
9 h/day	7(1.5)
≥10 h/day	11(2.3)

Factors associated with frailty in the univariate analysis

In this study, the prevalence of frailty among the Chinese hemodialysis patients was 24.0% (115/479). There were significant differences between malnutrition, appetite, sarcopenia, comorbidity, feel tired after dialysis, sleep time per day, frequency of physical exercise per week, employment status, dialysis frequency, hospitalized in the past 6 months, age, place of residence, gender, ($p < 0.05$, Table 2).

Factors associated with frailty

Factors affecting frailty of the Chinese hemodialysis patients are shown in Table 3. When Chinese hemodialysis patients with malnutrition (OR=4.557, 95% CI 2.474–8.393), sarcopenia (OR=18.171, 95% CI 9.811–33.655), male (OR=2.458, 95% CI 1.354–4.462), feel tired after dialysis (OR=3.034, 95% CI 1.657–5.556), the risk of frailty was greater. Serum albumin concentration was a protective factor for frailty (OR=0.866, 95% CI 0.797–0.941).

Construction of a frailty prediction model for Chinese hemodialysis patients

A nomogram model for the risk of frailty in patients with chronic diseases was established based on the independent influencing factors screened out by binary logistic regression. The nomogram model included scores, five independent influencing factors (gender, fatigue, ALB, sarcopenia, and malnutrition), total score, and probability of frailty occurrence, see Figure 1. Figure 2 shows the corresponding Points when the independent variables of gender, fatigue, ALB, sarcopenia, and malnutrition take different values.

Predictive model validation

Discrimination

AUC values were calculated to assess the discriminative power of the predictive model by examining the prevalence of frailty among Chinese hemodialysis patients in the training and validation sets. As

TABLE 2 Characteristics of the participants based on the presence of frailty (n = 479).

Physical symptoms and health status	Non-frailty (N = 364) N (%)	Frailty (N = 115) N (%)	Chi-square statistics (X ²)	p-value
Malnutrition				
Yes	42 (39.6)	64 (60.4)	98.689	<0.001***
Appetite				
Yes	301(73.1)	111 (26.9)	13.892	<0.001***
Sarcopenia				
Yes	31 (28.2)	79 (71.8)	178.899	<0.001***
Comorbidity				
Yes	198 (72.3)	76(27.7)	4.879	0.027*
Feel lonely				
Yes	199 (72.9)	74 (27.1)	3.339	0.068
Feel tired after dialysis				
Yes	122 (68.9)	55 (31.1)	7.681	0.006**
Sleep time per day				
≤5 h/day	40 (50.6)	39 (49.4)	37.138	<0.001***
6 h/day	103 (76.3)	32 (23.7)		
7 h/day	135(82.3)	29(17.7)		
8 h/day	72(86.7)	11(13.3)		
9 h/day	6(85.7)	1(14.3)		
≥10 h/day	8(72.7)	3(27.3)		
Education				
Elementary school and below	171 (71.0)	70 (29.0)	7.827	0.098
Junior high school	112 (83.0)	23 (17.0)		
High school	49(79.0)	13(21.0)		
Junior college	25(80.6)	6(19.4)		
College degree and above	7(70.0)	3(30.0)		
Marital status				
Single	39 (84.8)	7 (15.2)	3.190	0.363
Married	300 (75.2)	99 (24.8)		
Divorced	13(81.3)	3(18.8)		
Others	12(66.7)	6(33.3)		
Frequency of physical exercise per week				
0 times/week	128(63.4)	74 (36.6)	33.760	<0.001***
1–2 times/week	118(80.8)	28 (19.2)		
≥3 times/week	118(90.1)	13(9.9)		
Employment status				
Yes	42 (89.4)	5 (10.6)	5.106	0.024*
Dialysis frequency				
2 times/week	42 (87.5)	6 (12.5)	3.873	0.049*

(Continued)

TABLE 2 (Continued)

Physical symptoms and health status	Non-frailty (N = 364)	Frailty (N = 115)	Chi-square statistics (X ²)	p-value
	N (%)	N (%)		
3 times/week	322 (74.7)	109 (25.3)		
Hospitalized in the past 6 months				
Yes	62 (64.6)	34 (35.4)	8.565	0.003**
Age				
18–30	33 (82.5)	7 (17.5)	27.084	<0.001***
31–40	70 (89.7)	8 (10.3)		
41–50	128 (80.0)	32 (20.0)		
51–60	73 (72.3)	28 (27.7)		
61–70	52 (62.7)	31 (37.3)		
>70	8 (47.1)	9 (52.9)		
Place of residence				
Rural	153 (71.2)	62 (28.8)	9.585	0.008**
Town	79 (73.1)	29 (26.9)		
City	132 (84.6)	24 (15.4)		
Gender				
Male	202 (82.1)	44 (17.9)	10.390	0.001***
Female	162 (69.5)	71 (30.5)		

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

shown in Figure 3, the ROC curves of the training set and the test set, respectively. Taking the training set ROC curve (left picture) as an example, the abscissa is 1-specificity, which is the false negative rate; the ordinate is the sensitivity, which is the true positive rate. The 45° black dotted line represents the reference line, and the solid black curve represents the ROC curve. The results show that the sensitivity of the training set is 0.791, the specificity is 0.901, and the area under the AUC curve is 0.905. The sensitivity of the test set is 0.862, the specificity is 0.803, and the area under the AUC curve is 0.901, indicating that the accuracy of both the training set and the test set is good.

Calibration of the predictive model

The Hosmer–Lemeshow test was used to evaluate the goodness of fit of the model. The results showed that the training set $p = 0.625 > 0.05$ and the test set $PP = 0.798 > 0.05$. It indicates that the model is working well. The calibration curves of the modal plots show that the predicted vulnerability probabilities in the training set (Figure 4A) and validation set (Figure 4B) are in good agreement with the actual vulnerability probabilities.

Evaluation of clinical validity

Figure 5 shows the DCA curves of the training set and test set, respectively. The decision curve shows that the net advantage of the predictive model in the internal validation set is significantly greater than the net advantage in the two extreme cases, indicating that the net advantage of the predictive model and the predictive accuracy nomogram model are better.

Discussion

There is a growing body of evidence that actual age does not independently predict disease outcomes or death, and that the emergence of the concept of frailty is a more objective and direct response to chronic diseases and the health status and medical needs of older persons (56). The frailty is a systemic change that reduces the ability of the elderly to build up physiological reserves in neuromuscular, metabolic and immune systems for multisystem functional decline. This reduces their ability to fight stress and significantly increases the risk of adverse events (57).

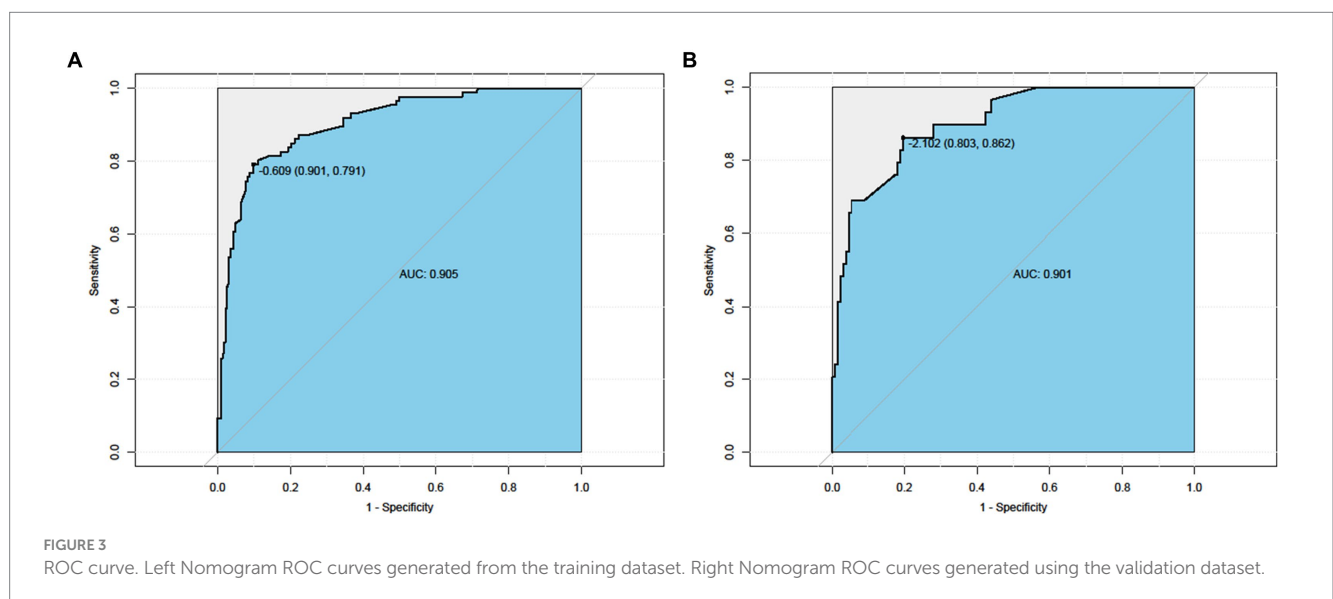
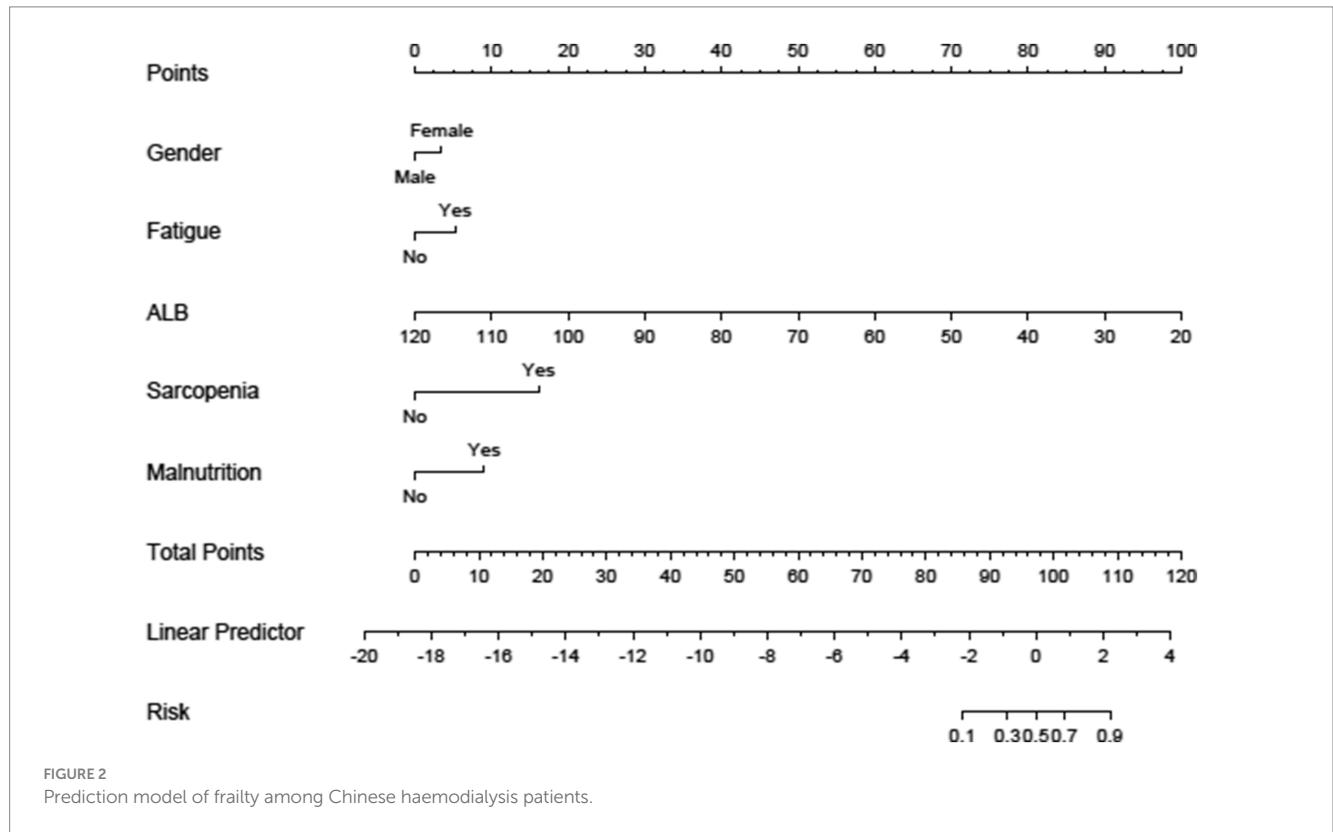
Finally, as expected, sarcopenia was independently associated with frailty in our population. Previous evidence (37) suggests that malnutrition leads to a loss of muscle mass and strength, which can contribute to the onset of sarcopenia and subsequent physical damage, both of which are important factors in frailty. The present study has demonstrated that hemodialysis patients with sarcopenia were two times more likely to develop frailty than those without sarcopenia (58). Furthermore, metabolic acidosis, uremia toxin accumulation, and chronic catabolism have been identified as causes of imbalance in protein production and breakdown in hemodialysis patients (59).

Using correlation, our study showed that appetite factors were closely related to frailty in maintenance hemodialysis patients. When maintenance hemodialysis patients develop poor appetite for a period of time, they may become frailty through malnutrition. And, nutritional status is a risk factor for frailty in patients with MHD (60). This study showed that the more malnutrition the maintenance hemodialysis patients were, the more their frailty was affected. This confirms our observation from another perspective of nutrition (61). Studies (62) have found that debilitation can be remedied to varying degrees through comprehensive post-assessment interventions, including nutritional and exercise regimens and appropriate vitamin D3 supplementation. Simple exercise, cognitive stimulation, debilitating education and nutritional counseling all improved daily activities and debilitating conditions in a one-arm, prospective, non-randomized intervention study. After 4 months of intervention, the length of stay, medical costs and admission rates for frailty patients were successfully reduced (63).

Serum albumin, a negative acute phase agent and marker of systemic inflammation, has been previously associated with an increased risk of cardiovascular death in several patient subgroups (64–66). Studies have found that albuminemia is an indicator of malnutrition, which is considered an important parameter of frailty, and is associated with poor prognosis in patients with heart disease (67). Serum albumin reflects nutritional status and is closely related to frailty (68, 69). Frail older adults often experience unintentional weight loss, indicating that they are malnourished or at risk for malnutrition (70). This study found that maintenance hemodialysis patients have a higher proportion of frailty, so in clinical practice, biochemical indicators must be measured regularly for hemodialysis patients. At the same time, The SARC-F and the SNAQ used in this study are concise and easy to use. They can also be used regularly as regular scales to grasp the patient's health status on time. This study draws a frailty risk prediction nomogram for hemodialysis patients based on independent influencing factors selected by binary logistic regression analysis. It verifies the model's validity and practicality by drawing ROC, calibration, and DCA curves. The results show that the

TABLE 3 Binary logistic regression analysis of factors associated with frailty.

Variable	B	SE	Wald	P	OR	95% CI
Malnutrition	1.517	0.312	23.689	0.000	4.557	2.474–8.393
Sarcopenia	2.900	0.314	85.041	0.000	18.171	9.811–33.655
Gender	0.899	0.304	8.732	0.003	2.458	1.354–4.462
Feel tired after dialysis	1.110	0.309	12.925	0.000	3.034	1.657–5.556
Serum albumin concentration	−0.144	0.042	11.518	0.001	0.866	0.797–0.941
Constant	2.293	1.672	1.881	0.170	9.904	



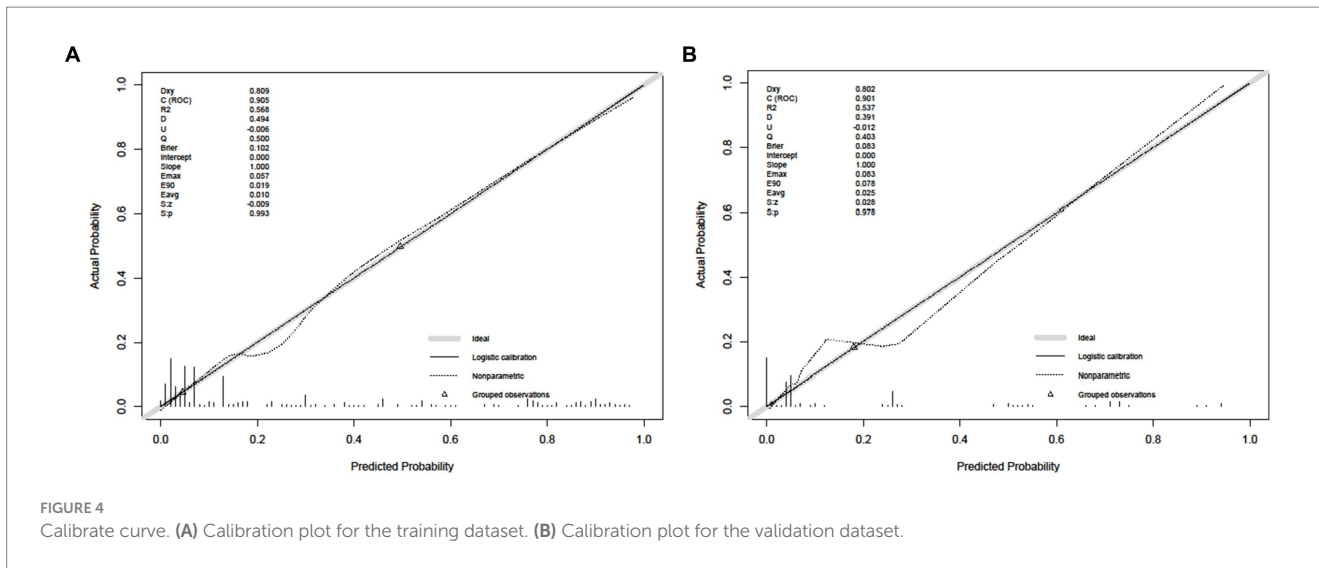


FIGURE 4 Calibrate curve. (A) Calibration plot for the training dataset. (B) Calibration plot for the validation dataset.

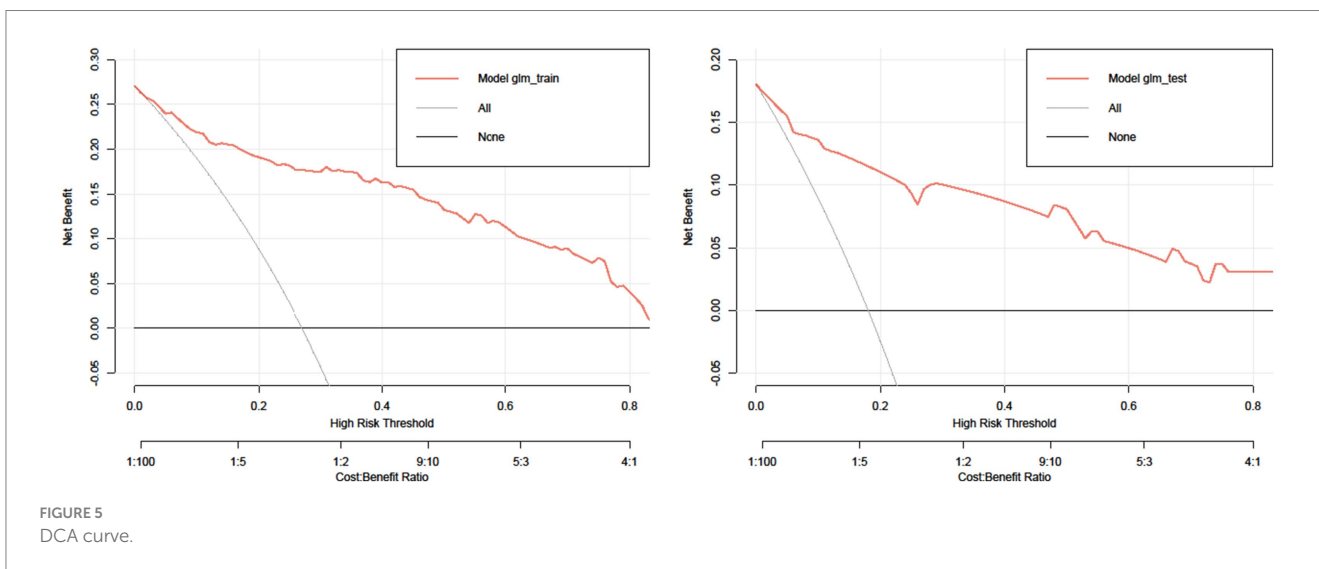


FIGURE 5 DCA curve.

model’s diagnostic performance, calibration, discrimination, and clinical practicability are good.

Limitations, First, the main limitation of the current study was its design. Because it was a cross-sectional study, it was not possible to explore a causal relationship between variables. Second, the limitation of this cross-sectional study is that only three hospitals in Anhui Province were surveyed, which may adversely affect the representativeness of the sample, and the sample size of hemodialysis patients will be further expanded to investigate the frailty of patients in different regions of Anhui Province. Third, other objective factors that may be associated with frailty in hemodialysis patients, including inflammatory markers or dialysis adequacy, were not included in this cross-sectional study.

Conclusion

In conclusion, the incidence of frailty in hemodialysis patients in this study is high. Malnutrition, sarcopenia, gender, and feeling

tired after dialysis are independent influencing factors for frailty in hemodialysis patients. The risk prediction model was constructed based on the above-influencing factors. It has good predictive value and is helpful for clinical early screening and early intervention of frailty in hemodialysis patients to reduce adverse outcomes.

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 the Department of Nursing, Yijishan Hospital, Wannan Medical College. 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: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. MT: Writing – review & editing, Writing – original draft, Supervision, Data curation. MaZ: Investigation, Funding acquisition, Formal analysis, Conceptualization, Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration. ZZ: Writing – original draft, Resources, Methodology, Formal analysis, Data curation. YN: Writing – original draft, Visualization, Resources, Formal analysis, Data curation, Conceptualization. QW: Writing – original draft, Visualization, Supervision, Software, Data curation. XZ: Writing – original draft, Validation, Supervision, Resources, Data curation. CC: Writing – review & editing, Validation, Resources, Investigation, Data curation. DY: Writing – review & editing, Visualization, Investigation, Data curation. MC: Writing – review & editing, Visualization, Validation, Investigation, Data curation. XT: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. MiZ: Writing – review & editing, Validation, Project administration, Investigation, Conceptualization.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This research

References

- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* (2001) 56:M146–57. doi: 10.1093/gerona/56.3.M146
- Chu NM, Deng A, Ying H, Haugen CE, Garonzik Wang JM, Segev DL, et al. Dynamic frailty before kidney transplantation: time of measurement matters. *Transplantation.* (2019) 103:1700–4. doi: 10.1097/TP.0000000000002563
- Chan GC, Ng JK, Chow KM, Kwong VWK, Pang WF, Cheng PMS, et al. Progression in physical frailty in peritoneal Dialysis patients. *Kidney Blood Press Res.* (2021) 46:342–51. doi: 10.1159/000515635
- Johansen KL, Dalrymple LS, Delgado C, Chertow GM, Segal MR, Chiang J, et al. Factors associated with frailty and its trajectory among patients on hemodialysis. *Clin J Am Soc Nephrol.* (2017) 12:1100–8. doi: 10.2215/CJN.12131116
- Zhang N, Lai F, Guo Y, Wang L. Status of and factors influencing the stigma of Chinese young and middle-aged maintenance hemodialysis patients: a preliminary study. *Front Psychol.* (2022) 13:873444. doi: 10.3389/fpsyg.2022.873444
- Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. *Lancet.* (2015) 385:1975–82. doi: 10.1016/S0140-6736(14)61601-9
- Kutner NG, Zhang R, Allman RM, Bowling CB. Correlates of ADL difficulty in a large hemodialysis cohort. *Hemodial Int.* (2014) 18:70–7. doi: 10.1111/hdi.12098
- Bao Y, Dalrymple L, Chertow GM, Kaysen GA, Johansen KL. Frailty, dialysis initiation, and mortality in end-stage renal disease. *Arch Intern Med.* (2012) 172:1071–7. doi: 10.1001/archinternmed.2012.3020
- Narula S, Lawless A, D'Alessandro P, Jones CW, Yates P, Seymour H. Clinical frailty scale is a good predictor of mortality after proximal femur fracture: a cohort study of 30-day and one-year mortality. *Bone Jt Open.* (2020) 1:443–9. doi: 10.1302/2633-1462.18.BJO-2020-0089.R1
- Schwenk M, Mohler J, Wendel C, D'Huyvetter K, Fain M, Taylor-Piliae R, et al. Wearable sensor-based in-home assessment of gait, balance, and physical activity for discrimination of frailty status: baseline results of the Arizona frailty cohort study. *Gerontology.* (2015) 61:258–67. doi: 10.1159/000369095
- Shirai N, Inoue T, Ogawa M, Okamura M, Morishita S, Suguru Y, et al. Relationship between nutrition-related problems and falls in hemodialysis patients: a narrative review. *Nutrients.* (2022) 14:3225. doi: 10.3390/nu14153225
- Nishikawa H, Fukunishi S, Asai A, Yokohama K, Ohama H, Nishiguchi S, et al. Sarcopenia, frailty and type 2 diabetes mellitus (review). *Mol Med Rep.* (2021) 24:854. doi: 10.3892/mmr.2021.12494
- Cao L, Morley JE. Sarcopenia is recognized as an independent condition by an international classification of disease, tenth revision, clinical modification (ICD-10-CM) code. *J Am Med Dir Assoc.* (2016) 17:675–7. doi: 10.1016/j.jamda.2016.06.001
- Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle.* (2016) 7:512–4. doi: 10.1002/jcsm.12147
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing.* (2010) 39:412–23. doi: 10.1093/ageing/afq034
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* (2019) 48:16–31. doi: 10.1093/ageing/afy169
- Edwards MH, Dennison EM, Aihie Sayer A, Fielding R, Cooper C. Osteoporosis and sarcopenia in older age. *Bone.* (2015) 80:126–30. doi: 10.1016/j.bone.2015.04.016
- Yamada M, Nishiguchi S, Fukutani N, Tanigawa T, Yukutake T, Kayama H, et al. Prevalence of sarcopenia in community-dwelling Japanese older adults. *J Am Med Dir Assoc.* (2013) 14:911–5. doi: 10.1016/j.jamda.2013.08.015

was supported by the Anhui Provincial University Scientific Research Key Project (2023AH051733 and 2023AH040237), the Key Laboratory of Philosophy and Social Science of Anhui Province on Adolescent Mental Health and Crisis Intelligence Intervention (SYS2023B09), the Industry-University Cooperation Collaborative Education Project of the Ministry of Education (220905875062412), the Anhui Provincial College Outstanding Young Talents Support Program (gxyq2022045), the Teaching Quality and teaching reform project of Wannan Medical College (2020jyxm58), the Teaching Reform Project of Wannan Medical College (2021zybz06), Anhui Higher Education Scientific Research Commission Project “Psychological Health Education in Chinese Schools in the Post-epidemic Era: Theory and Policy Research” (2022AH040291), and the Teaching Quality and Teaching Reform Project of Anhui Provincial Department of Education (2020jyxm2076). 2023 Provincial Key Clinical Specialty Construction Project of Anhui Province.

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

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

19. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. (2019) 393:2636–46. doi: 10.1016/S0140-6736(19)31138-9
20. de Sire A, Giachero A, Santi DE, Inglese K, Solaro C. Screening dysphagia risk in 534 older patients undergoing rehabilitation after total joint replacement: a cross-sectional study. *Eur J Phys Rehabil Med*. (2021) 57:131–6. doi: 10.23736/S1973-9087.20.06321-2
21. Cha S, Kim WS, Kim KW, Han JW, Jang HC, Lim S, et al. Sarcopenia is an independent risk factor for dysphagia in community-dwelling older adults. *Dysphagia*. (2019) 34:692–7. doi: 10.1007/s00455-018-09973-6
22. Maeda K, Takaki M, Akagi J. Decreased skeletal muscle mass and risk factors of Sarcopenic dysphagia: a prospective observational cohort study. *J Gerontol A Biol Sci Med Sci*. (2017) 72:1290–4. doi: 10.1093/gerona/glw190
23. Drapeau V, King N, Hetherington M, Doucet E, Blundell J, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. *Appetite*. (2007) 48:159–66. doi: 10.1016/j.appet.2006.08.002
24. Berthoud HR, Morrison C. The brain, appetite, and obesity. *Annu Rev Psychol*. (2008) 59:55–92. doi: 10.1146/annurev.psych.59.103006.093551
25. Bossola M, Ciciarelli C, di Stasio E, Panocchia N, Conte GL, Rosa F, et al. Relationship between appetite and symptoms of depression and anxiety in patients on chronic hemodialysis. *J Ren Nutr*. (2012) 22:27–33. doi: 10.1053/j.jrn.2011.02.005
26. Zabel R, Ash S, King N, Juffs P, Bauer J. Relationships between appetite and quality of life in hemodialysis patients. *Appetite*. (2012) 59:194–9. doi: 10.1016/j.appet.2012.02.016
27. Burrows JD, Larive B, Chertow GM, Cockram DB, Dwyer JT, Greene T, et al. Self-reported appetite, hospitalization and death in haemodialysis patients: findings from the hemodialysis (HEMO) study. *Nephrol Dial Transplant*. (2005) 20:2765–74. doi: 10.1093/ndt/gfi132
28. Gama-Axelsson T, Lindholm B, Bárány P, Heimbürger O, Stenvinkel P, Qureshi AR. Self-rated appetite as a predictor of mortality in patients with stage 5 chronic kidney disease. *J Ren Nutr*. (2013) 23:106–13. doi: 10.1053/j.jrn.2012.04.009
29. Salazar-Robles E, Lerma A, Calderón-Juárez M, Ibarra A, Pérez-Grovas H, Bermúdez-Aceves LA, et al. Assessment of factors related to diminished appetite in hemodialysis patients with a new adapted and validated questionnaire. *Nutrients*. (2021) 13:1371. doi: 10.3390/nu13041371
30. Bossola M, Tazza L, Luciani G. Mechanisms and treatment of anorexia in end-stage renal disease patients on hemodialysis. *J Ren Nutr*. (2009) 19:2–9. doi: 10.1053/j.jrn.2008.10.003
31. Kalantar-Zadeh K, Block G, McAllister CJ, Humphreys MH, Kopple JD. Appetite and inflammation, nutrition, anemia, and clinical outcome in hemodialysis patients. *Am J Clin Nutr*. (2004) 80:299–307. doi: 10.1093/ajcn/80.2.299
32. Lochs H, Allison SP, Meier R, Pirlich M, Kondrup J, Schneider S, et al. Introductory to the ESPEN guidelines on enteral nutrition: terminology, definitions and general topics. *Clin Nutr*. (2006) 25:180–6. doi: 10.1016/j.clnu.2006.02.007
33. Sahathevan S, Khor BH, Ng HM, Abdul Gafor AH, Mat Daud ZA, Mafra D, et al. Understanding development of malnutrition in hemodialysis patients: a narrative review. *Nutrients*. (2020) 12:3147. doi: 10.3390/nu12103147
34. Inoue T, Misu S, Tanaka T, Sakamoto H, Iwata K, Chuman Y, et al. Pre-fracture nutritional status is predictive of functional status at discharge during the acute phase with hip fracture patients: a multicenter prospective cohort study. *Clin Nutr*. (2017) 36:1320–5. doi: 10.1016/j.clnu.2016.08.021
35. Goisser S, Schrader E, Singler K, Bertsch T, Gefeller O, Biber R, et al. Malnutrition according to Mini nutritional assessment is associated with severe functional impairment in geriatric patients before and up to 6 months after hip fracture. *J Am Med Dir Assoc*. (2015) 16:661–7. doi: 10.1016/j.jamda.2015.03.002
36. Miu KYD, Lam PS. Effects of nutritional status on 6-month outcome of hip fractures in elderly patients. *Ann Rehabil Med*. (2017) 41:1005–12. doi: 10.5535/arm.2017.41.6.1005
37. Bollwein J, Volkert D, Diekmann R, Kaiser MJ, Uter W, Vidal K, et al. Nutritional status according to the mini nutritional assessment (MNA[®]) and frailty in community dwelling older persons: a close relationship. *J Nutr Health Aging*. (2013) 17:351–6. doi: 10.1007/s12603-013-0034-7
38. Cereda E, Pedrolli C, Klersy C, Bonardi C, Quarleri L, Cappello S, et al. Nutritional status in older persons according to healthcare setting: a systematic review and meta-analysis of prevalence data using MNA[®]. *Clin Nutr*. (2016) 35:1282–90. doi: 10.1016/j.clnu.2016.03.008
39. Wojzischke J, van Wijngaarden J, van den Berg C, Cetinyurek-Yavuz A, Diekmann R, Luiking Y, et al. Nutritional status and functionality in geriatric rehabilitation patients: a systematic review and meta-analysis. *Eur Geriatr Med*. (2020) 11:195–207. doi: 10.1007/s41999-020-00294-2
40. Bai AV, Agostini F, Bernetti A, Mangone M, Fidenzi G, D'Urzo R, et al. State of the evidence about rehabilitation interventions in patients with dysphagia. *Eur J Phys Rehabil Med*. (2021) 57:900–11. doi: 10.23736/S1973-9087.21.06716-2
41. Eroğlu AG. Malnutrition and the heart. *Turk Pediatri Ars*. (2019) 54:139–40. doi: 10.14744/TurkPediatriArs.2019.03764
42. Raposeiras Roubin S, Abu Assi E, Cespon Fernandez M, Barreiro Pardal C, Lizancos Castro A, Parada JA, et al. Prevalence and prognostic significance of malnutrition in patients with acute coronary syndrome. *J Am Coll Cardiol*. (2020) 76:828–40. doi: 10.1016/j.jacc.2020.06.058
43. Wells JC, Sawaya AL, Wibaek R, Mwangome M, Poulas MS, Yajnik CS, et al. The double burden of malnutrition: aetiological pathways and consequences for health. *Lancet*. (2020) 395:75–88. doi: 10.1016/S0140-6736(19)32472-9
44. Cruz-Jentoft AJ, Kiesswetter E, Drey M, Sieber CC. Nutrition, frailty, and sarcopenia. *Aging Clin Exp Res*. (2017) 29:43–8. doi: 10.1007/s40520-016-0709-0
45. Damanti S, Azzolino D, Roncaglione C, Arosio B, Rossi P, Cesari M. Efficacy of nutritional interventions as stand-alone or synergistic treatments with exercise for the Management of Sarcopenia. *Nutrients*. (2019) 11:1991. doi: 10.3390/nu11091991
46. Malara A, Sgrò G, Caruso C, Ceravolo F, Curinga G, Renda GF, et al. Relationship between cognitive impairment and nutritional assessment on functional status in Calabrian long-term-care. *Clin Interv Aging*. (2014) 9:105–10. doi: 10.2147/CIA.S54611
47. Verlaan S, Ligthart-Melis GC, Wijers SLJ, Cederholm T, Maier AB, van der Schueren MA. High prevalence of physical frailty among community-dwelling malnourished older adults—a systematic review and meta-analysis. *J Am Med Dir Assoc*. (2017) 18:374–82. doi: 10.1016/j.jamda.2016.12.074
48. Rajula HSR, Verlatto G, Manchia M, Antonucci N, Fanos V. Comparison of conventional statistical methods with machine learning in medicine: diagnosis, drug development, and treatment. *Medicina*. (2020) 56:455. doi: 10.3390/medicina56090455
49. Chang J, Hou W, Li Y, Li S, Zhao K, Wang Y, et al. Prevalence and associated factors of cognitive frailty in older patients with chronic kidney disease: a cross-sectional study. *BMC Geriatr*. (2022) 22:681. doi: 10.1186/s12877-022-03366-z
50. Fang Q, Zhu G, Huang J, Pan S, Fang M, Li Q, et al. Current status of sarcopenia in the disabled elderly of Chinese communities in Shanghai: based on the updated EWGSOP consensus for sarcopenia. *Front Med*. (2020) 7:552415. doi: 10.3389/fmed.2020.552415
51. Krzyżmińska-Siemaszko R, Deskur-Śmielecka E, Kaluźniak-Szymanowska A, Murawiak M, Wieczorowska-Tobis K. Comparison of diagnostic value of the SARC-F and its four modified versions in polish community-dwelling older adults. *Clin Interv Aging*. (2023) 18:783–97. doi: 10.2147/CIA.S408616
52. Zukeran MS, Aprahamian I, Vicente BM, Ribeiro SML. Portuguese version of the SNAQ questionnaire: translation and cultural adaptation. *Arq Gastroenterol*. (2020) 57:178–81. doi: 10.1590/s0004-2803.202000000-33
53. Wilson MM, Thomas DR, Rubenstein LZ, Chibnall JT, Anderson S, Baxi A, et al. Appetite assessment: simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. *Am J Clin Nutr*. (2005) 82:1074–81. doi: 10.1093/ajcn/82.5.1074
54. Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T, et al. Validation of the Mini nutritional assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging*. (2009) 13:782–8. doi: 10.1007/s12603-009-0214-7
55. Yan Z, Lixian W, Xiaohua L. Application of mini nutritional assessment-short form in nutritional screening of in elderly in patients with chronic diseases. *Chin J Multiple Organ Dis Aged*. (2019) 18:107–11.
56. Kim E, Sok SR, Won CW. Factors affecting frailty among community-dwelling older adults: a multi-group path analysis according to nutritional status. *Int J Nurs Stud*. (2021) 115:103850. doi: 10.1016/j.ijnurstu.2020.103850
57. Kojima G. Frailty as a predictor of nursing home placement among community-dwelling older adults: a systematic review and Meta-analysis. *J Geriatr Phys Ther*. (2018) 41:42–8. doi: 10.1519/JPT.0000000000000097
58. Slee A, McKeaveney C, Adamson G, Davenport A, Farrington K, Fouque D, et al. Estimating the prevalence of muscle wasting, weakness, and sarcopenia in hemodialysis patients. *J Ren Nutr*. (2020) 30:313–21. doi: 10.1053/j.jrn.2019.09.004
59. Wong L, Duque G, McMahon LP. Sarcopenia and frailty: challenges in mainstream nephrology practice. *Kidney Int Rep*. (2021) 6:2554–64. doi: 10.1016/j.ekir.2021.05.039
60. Daniel SC, Azuero A, Gutierrez OM, Heaton K. Examining the relationship between nutrition, quality of life, and depression in hemodialysis patients. *Qual Life Res*. (2021) 30:759–68. doi: 10.1007/s11136-020-02684-2
61. Chen Y, Li P, Zhang L, Zhang Y, Xie L, Niu J. Prevalence and predisposing factors of depressive symptoms in continuous ambulatory peritoneal dialysis patients: a cross-sectional single center study. *BMC Nephrol*. (2023) 24:104. doi: 10.1186/s12882-023-03166-6
62. Mohd Suffian NI, Adznam SNA, Abu Saad H, Chan YM, Ibrahim Z, Omar N, et al. Frailty intervention through nutrition education and exercise (FINE). A health promotion intervention to prevent frailty and improve frailty status among pre-frail elderly—a study protocol of a cluster randomized controlled trial. *Nutrients*. (2020) 12:2758. doi: 10.3390/nu12092758
63. Wang YC, Liang CK, Chou MH, Chiu CF, Lin HC, Hsu YH, et al. The effectiveness of frailty intervention for older patients with frailty during hospitalization. *J Nutr Health Aging*. (2023) 27:413–20. doi: 10.1007/s12603-023-1924-y
64. Koifman E, Magalhaes MA, Ben-Dor I, Kiramijyan S, Escarcega RO, Fang C, et al. Impact of pre-procedural serum albumin level on outcome of patients undergoing transcatheter aortic valve replacement. *Am J Cardiol*. (2015) 115:1260–4. doi: 10.1016/j.amjcard.2015.02.009

65. Kalyoncuoglu M, Durmus G. Relationship between C-reactive protein-to-albumin ratio and the extent of coronary artery disease in patients with non-ST-elevated myocardial infarction. *Coron Artery Dis.* (2020) 31:130–6. doi: 10.1097/MCA.0000000000000768
66. Yap FH, Joynt GM, Buckley TA, Wong EL. Association of serum albumin concentration and mortality risk in critically ill patients. *Anaesth Intensive Care.* (2002) 30:202–7. doi: 10.1177/0310057X0203000213
67. Horwich TB, Kalantar-Zadeh K, MacLellan RW, Fonarow GC. Albumin levels predict survival in patients with systolic heart failure. *Am Heart J.* (2008) 155:883–9. doi: 10.1016/j.ahj.2007.11.043
68. Liang YD, Zhang YN, Li YM, Chen YH, Xu JY, Liu M, et al. Identification of frailty and its risk factors in elderly hospitalized patients from different wards: a cross-sectional study in China. *Clin Interv Aging.* (2019) 14:2249–59. doi: 10.2147/CIA.S225149
69. Hong X, Yan J, Xu L, Shen S, Zeng X, Chen L. Relationship between nutritional status and frailty in hospitalized older patients. *Clin Interv Aging.* (2019) 14:105–11. doi: 10.2147/CIA.S189040
70. Chen CY, Chandran T, Barrera VC, Tan-Pantanao RT, Quicho TJZ, Thant ZT, et al. Frailty prevalence and its associations in a subacute geriatric ward in Singapore. *Singapore Med J.* (2023) 64:196–202. doi: 10.11622/smedj.2022020