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Nutritional status and frailty in patients receiving maintenance hemodialysis: the role of sarcopenia risk and comorbidity burden

Juan Zhang
Hebei University
Liu Yang
Hebei University
Fan Wu
Suining County Hospital of Traditional Chinese Medicine
Ruili Jia
jiaruili@bddhospital.com.cn

Baoding No.1 Central Hospital

Article

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Abstract

Poor nutritional status and frailty frequently coexist in patients receiving maintenance hemodialysis (MHD), but whether their association varies with disease burden remains unclear. This cross-sectional study included 321 MHD patients at a tertiary hospital in Jiangsu Province, China, between January and March 2026. Nutritional status, sarcopenia risk, and frailty were assessed using the MNA-SF, SARC-F, and FRAIL scales, respectively. Disease burden was quantified using the age-adjusted Charlson Comorbidity Index (aCCI). Mediation and first-stage moderated mediation analyses incorporated aCCI main effects and adjusted for sex, hemoglobin, and dialysis duration, with 5000 bootstrap resamples. Overall, 111 patients (34.6%) were frail. The adjusted indirect association between MNA-SF and FRAIL through SARC-F was − 0.163 (95% confidence interval [CI], − 0.231 to − 0.110). The MNA-SF × aCCI interaction coefficient was − 0.093 (95% CI, − 0.135 to − 0.051), and the index of moderated mediation was − 0.023 (95% CI, − 0.036 to − 0.013). Conditional indirect effects were − 0.124 and − 0.171 at aCCI scores of 4 and 6, respectively. Sensitivity analyses broadly supported these findings. Poorer nutritional status was associated with greater frailty partly through sarcopenia risk, with a stronger indirect association at higher age-adjusted comorbidity burden. Longitudinal studies are needed to establish temporal relationships.

1. Introduction

Frailty is a clinical syndrome characterized by reduced physiological reserve resulting from functional decline across multiple organ systems [1, 2]. It is common among patients receiving maintenance hemodialysis (MHD), with systematic reviews and meta-analyses reporting a prevalence of approximately 34–40% [3–5]. Frailty may compromise patients' tolerance of long-term treatment and is associated with higher risks of all-cause mortality and hospitalization [6–8].

Malnutrition and impaired muscle function often coexist in patients receiving hemodialysis. Inadequate dietary intake and nutrient losses associated with long-term dialysis may deplete protein stores and muscle reserves [9]. Previous studies have linked higher nutritional risk in patients receiving MHD to lower muscle strength, poorer physical performance, and a greater prevalence of sarcopenia [10, 11].

Studies in patients receiving MHD have reported associations among nutritional status, sarcopenia risk, and frailty [12], but less attention has been paid to the pathways linking these measures or whether their associations vary with disease burden. In community-dwelling older adults, Celik et al. [13] found that sarcopenia risk statistically mediated the association between nutritional status and frailty, while physical activity moderated the association between nutritional status and sarcopenia risk. These findings provide a basis for examining similar patterns in patients receiving MHD. In this population, the combined burden of age and comorbidities may influence the strength of the association between nutritional status and sarcopenia risk. Previous studies have reported associations of the Charlson Comorbidity Index with nutritional status, physical function, and frailty in patients receiving dialysis [14–

[16]. However, whether sarcopenia risk statistically mediates the association between nutritional status and frailty in patients receiving MHD, and whether the association between nutritional status and sarcopenia risk varies with age-adjusted comorbidity burden, remain unclear.

This study examined the associations among nutritional status, sarcopenia risk, and frailty in patients receiving MHD, assessed using the MNA-SF, SARC-F, and FRAIL scale, respectively, and evaluated the statistical mediating role of sarcopenia risk. Using the age-adjusted Charlson Comorbidity Index (aCCI) to quantify overall disease burden, we further examined whether this burden moderated the association between nutritional status and sarcopenia risk and estimated conditional indirect effects at different levels of aCCI.

2. Methods

2.1. Study Design and Participants

This cross-sectional study recruited a convenience sample of patients receiving regular maintenance hemodialysis at the blood purification center of a tertiary hospital in Jiangsu Province, China, between January and March 2026. Patients were eligible if they were aged ≥ 18 years, had received maintenance hemodialysis for end-stage kidney disease for > 3 months, were alert and able to understand and complete the questionnaires, and provided informed consent to participate. Exclusion criteria were concurrent peritoneal dialysis or a history of kidney transplantation, irregular hemodialysis attendance, severe cognitive impairment, psychiatric disorders or substantial communication difficulties, and missing data on key study variables in the questionnaires or clinical records.

Of the 332 patients who met the initial screening criteria, 11 declined participation, leaving 321 participants for analysis (participation rate, 96.7%). No duplicate participant identifiers or missing values for the main analytical variables were identified; therefore, no missing-data imputation was performed. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies [17].

The study protocol was approved by the Ethics Committee of Suining County Hospital of Traditional Chinese Medicine (approval no. 2025123101). All participants provided written informed consent after receiving information about the study objectives, procedures, potential risks, and benefits. The study was conducted in accordance with the Declaration of Helsinki and applicable regulations in China.

2.2. Data Collection

Sociodemographic information was collected using a questionnaire developed by the investigators, including sex, age, marital status, educational attainment, employment status, place of residence, living arrangements, smoking, and alcohol consumption. Dialysis-related information included dialysis duration and the number of sessions per week. Dialysis duration was categorized as < 5 or ≥ 5 years according to the original records. Height, weight, hemoglobin levels, and comorbidity diagnoses were

obtained from the hospital's electronic medical records and laboratory information system. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Questionnaire and clinical data were collected during the same survey period.

2.3. Main Study Variables

Nutritional status was assessed using the Mini Nutritional Assessment–Short Form (MNA-SF) [18]. This six-item instrument yields a total score ranging from 0 to 14, with higher scores indicating better nutritional status. Scores of 12–14 indicate normal nutritional status, 8–11 indicate a risk of malnutrition, and 0–7 indicate malnutrition [19]. The MNA-SF has been used to assess nutritional risk in patients receiving hemodialysis [20]. Its total score was treated as a continuous predictor in this study.

Sarcopenia risk was assessed using the SARC-F questionnaire [21], which comprises five items: strength, assistance with walking, rising from a chair, climbing stairs, and falls. Total scores range from 0 to 10, with higher scores indicating greater sarcopenia risk; a score ≥ 4 indicates a high risk of sarcopenia. SARC-F has been used to screen for sarcopenia risk in patients with chronic kidney disease and those receiving hemodialysis [22, 23]. Its total score was treated as a continuous mediator.

Frailty was assessed using the FRAIL scale [24], which comprises five items: fatigue, reduced endurance, difficulty walking, number of illnesses, and unintentional weight loss. Total scores range from 0 to 5, with scores of 0, 1–2, and 3–5 indicating robust, prefrail, and frail status, respectively [25]. The total FRAIL score was treated as a continuous outcome in the primary analysis. Sensitivity analyses treated the score as a six-category ordinal outcome (0–5) and as a binary outcome, with frailty defined as a score ≥ 3.

2.4. Comorbidity Burden

The age-adjusted Charlson Comorbidity Index (aCCI) was calculated using patients' ages and comorbidity diagnoses documented in the electronic medical records [26]. Because all participants had end-stage kidney disease requiring maintenance hemodialysis, two points were assigned for renal disease. The aCCI adds age-related points to the weighted Charlson comorbidity score: one point for ages 50–59 years, two for 60–69 years, three for 70–79 years, and four for ages ≥ 80 years. Higher scores indicate a greater overall burden of age and comorbidities. The aCCI was treated as a continuous moderator to assess whether this burden modified the association between nutritional status and sarcopenia risk.

2.5. Quality Control

Before data collection, all study personnel received standardized training on study procedures, questionnaire completion, interpretation of scale items, participant instructions, and clinical data extraction. After obtaining informed consent, study personnel distributed standardized questionnaires to participants. Participants generally completed the questionnaires independently. For those unable to do so because of impaired vision, difficulty writing, or discomfort during dialysis, interviewers recorded their

verbal responses item by item. Questions about individual items were addressed using standardized explanations, without leading participants toward particular responses. Completed questionnaires were checked on site for completeness and logical consistency.

Trained study personnel extracted clinical data from the electronic medical records and laboratory information system using a predefined data extraction form. After data entry, participant identifiers, missing values, variable ranges, and logical consistency were checked.

2.6. Covariate Selection

Covariates were prespecified based on previous evidence, clinical relevance, and their role in the hypothesized pathways, rather than selected according to statistical significance in univariable analyses. The primary models included sex, hemoglobin, and dialysis duration (< 5 or ≥ 5 years). Sex is associated with differences in muscle reserves, nutritional status, and frailty; hemoglobin reflects anemia, which may contribute to fatigue and impaired physical performance; and dialysis duration represents cumulative exposure to dialysis and associated disease burden.

In the simple mediation model, aCCI was included as a covariate alongside sex, hemoglobin, and dialysis duration. In the moderated mediation model, aCCI was included as the moderator, with its main effect retained, while adjusting for sex, hemoglobin, and dialysis duration. Because aCCI incorporates age, age was not entered separately in the primary clinical model or its expanded versions. A model adjusted only for age and sex was examined in a sensitivity analysis. BMI was excluded from the primary models because it is a component of the MNA-SF; additional adjustment for BMI was examined in a sensitivity analysis. The expanded model further included BMI, smoking, educational attainment, employment status, marital status, place of residence, and living arrangements. Alcohol consumption and weekly dialysis frequency were used to describe the sample but were not included in the primary regression models.

Employment status, marital status, and educational attainment were entered as categorical variables using dummy coding, with employed, married, and illiterate participants as the respective reference groups. Because only two participants had a bachelor's degree or higher, this category was combined with high school or vocational secondary education in the expanded model; the original five categories were retained in the descriptive table. The reference categories for the remaining variables were male sex, nonsmoking, rural residence, living alone, and dialysis duration < 5 years.

2.7. Statistical Analysis

Statistical analyses were performed using Python version 3.12.14. Continuous variables are presented as means ± standard deviations, and categorical variables as counts and percentages. Participant characteristics were compared across frailty categories using the Kruskal–Wallis test for continuous variables and Pearson's χ^2 test for categorical variables. When any expected cell count was < 5, a Monte Carlo contingency-table test with fixed marginal totals was used, based on 20,000 simulations. Associations among the main study variables were assessed using Pearson correlations, with Spearman

correlations calculated to examine consistency. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Following Hayes' conditional process analysis framework [27], MNA-SF, SARC-F, and FRAIL scores were specified as the predictor, mediator, and outcome, respectively. We first fitted a mediation model and then examined whether aCCI moderated the association between MNA-SF and SARC-F in a first-stage moderated mediation model. The mediation model was adjusted for sex, aCCI, hemoglobin, and dialysis duration. The moderated mediation model included the aCCI main effect and the MNA-SF × aCCI interaction, with adjustment for sex, hemoglobin, and dialysis duration. In the primary analysis, SARC-F and FRAIL total scores were treated as continuous variables, and path coefficients were estimated using ordinary least squares linear regression. MNA-SF and aCCI were mean-centered before the interaction term was constructed.

We used 5000 bootstrap resamples to obtain percentile-based 95% CIs for the indirect effect, the index of moderated mediation, and conditional indirect effects at the 25th, 50th, and 75th percentiles of aCCI. Each resample consisted of patient records sampled with replacement, and all paths were re-estimated within the same resample. The random seed was set to 20261005. The increase in explained variance after adding the interaction term was quantified as ΔR^2. Residual distributions, heteroscedasticity, influential observations, and multicollinearity were assessed using the Shapiro–Wilk test, Breusch–Pagan test, Cook's distance, and variance inflation factors, respectively. Models were refitted after excluding observations with Cook's distance > 4/n as a diagnostic check; all 321 participants were retained in the primary analyses.

Sensitivity analyses included using HC3 heteroscedasticity-robust standard errors, adding quadratic terms for MNA-SF and aCCI, additionally adjusting for BMI and the expanded set of categorical covariates, and treating FRAIL as an ordinal or binary outcome to assess the consistency of association directions. In the ordinal model, MNA-SF and SARC-F were standardized using their sample standard deviations; in the binary model, odds ratios were reported per one-point increase. The proportional odds assumption was assessed using a Wald diagnostic based on the bootstrap-estimated covariance of slope coefficients from five cumulative logit models. This procedure used 500 resamples, retaining resamples in which all slope estimates were finite and had absolute values < 30. We also examined second-stage moderation and fitted an alternative mediation model with the roles of MNA-SF and SARC-F reversed.

3. Results

3.1. Participant Characteristics

The study included 321 patients receiving maintenance hemodialysis, with a mean age of 55.93 ± 13.41 years; 202 (62.9%) were men. Mean MNA-SF, SARC-F, FRAIL, and aCCI scores were 11.77 ± 2.17, 2.26 ±

2.54, 1.90 ± 1.50, and 5.15 ± 1.89, respectively. Based on FRAIL scores, 66 participants (20.6%) were robust, 144 (44.9%) were prefrail, and 111 (34.6%) were frail.

Age, employment status, educational attainment, marital status, place of residence, dialysis duration, hemoglobin, and MNA-SF, SARC-F, and aCCI scores differed significantly across frailty categories (Table 1).

Table 1
Participant characteristics overall and by frailty status.

Variable	Overall (N = 321)	Robust (n = 66)	Prefrail (n = 144)	Frail (n = 111)	P value
Age (years)	55.93 ± 13.41	48.21 ± 10.97	53.30 ± 12.18	63.92 ± 12.25	< 0.001
Sex					0.603
Male	202 (62.9)	45 (68.2)	88 (61.1)	69 (62.2)	
Female	119 (37.1)	21 (31.8)	56 (38.9)	42 (37.8)	
BMI (kg/m²)	24.05 ± 4.00	23.91 ± 3.91	24.12 ± 3.89	24.05 ± 4.22	0.825
Smoking					0.885
No	276 (86.0)	57 (86.4)	125 (86.8)	94 (84.7)	
Yes	45 (14.0)	9 (13.6)	19 (13.2)	17 (15.3)	
Alcohol consumption					0.938
No	308 (96.0)	63 (95.5)	139 (96.5)	106 (95.5)	
Yes	13 (4.0)	3 (4.5)	5 (3.5)	5 (4.5)	
Employment status					< 0.001
Employed	37 (11.5)	16 (24.2)	18 (12.5)	3 (2.7)	
Retired	34 (10.6)	3 (4.5)	14 (9.7)	17 (15.3)	
Unemployed	250 (77.9)	47 (71.2)	112 (77.8)	91 (82.0)	
Educational attainment					< 0.001
Illiterate	61 (19.0)	3 (4.5)	21 (14.6)	37 (33.3)	
Primary school	120 (37.4)	26 (39.4)	59 (41.0)	35 (31.5)	
Junior high school	107 (33.3)	24 (36.4)	47 (32.6)	36 (32.4)	
High school/vocational secondary school	31 (9.7)	12 (18.2)	16 (11.1)	3 (2.7)	

Values are mean ± standard deviation or n (%). Continuous variables were compared using the Kruskal–Wallis test; categorical variables were compared using Pearson's χ^2 test or a Monte Carlo test with fixed marginal totals when expected cell counts were insufficient (20,000 simulations). FRAIL scores of 0, 1–2, and 3–5 indicate robust, prefrail, and frail status, respectively. aCCI, age-adjusted Charlson Comorbidity Index; BMI, body mass index; Hb, hemoglobin; MNA-SF, Mini Nutritional Assessment–Short Form; SARC-F, sarcopenia screening questionnaire; FRAIL, frailty scale.

Variable	Overall (N = 321)	Robust (n = 66)	Prefrail (n = 144)	Frail (n = 111)	P value
Bachelor's degree or higher	2 (0.6)	1 (1.5)	1 (0.7)	0 (0.0)	
Marital status					0.011
Married	291 (90.7)	56 (84.8)	128 (88.9)	107 (96.4)	
Unmarried	20 (6.2)	9 (13.6)	10 (6.9)	1 (0.9)	
Divorced	10 (3.1)	1 (1.5)	6 (4.2)	3 (2.7)	
Place of residence					0.009
Rural	206 (64.2)	33 (50.0)	92 (63.9)	81 (73.0)	
Urban	115 (35.8)	33 (50.0)	52 (36.1)	30 (27.0)	
Living arrangements					0.498
Living alone	9 (2.8)	1 (1.5)	6 (4.2)	2 (1.8)	
Living with others	312 (97.2)	65 (98.5)	138 (95.8)	109 (98.2)	
Dialysis duration					0.026
< 5 years	182 (56.7)	30 (45.5)	79 (54.9)	73 (65.8)	
≥ 5 years	139 (43.3)	36 (54.5)	65 (45.1)	38 (34.2)	
Dialysis sessions per week					0.698
1 session/week	3 (0.9)	0 (0.0)	1 (0.7)	2 (1.8)	
2 sessions/week	7 (2.2)	2 (3.0)	2 (1.4)	3 (2.7)	
3 sessions/week	311 (96.9)	64 (97.0)	141 (97.9)	106 (95.5)	
Hemoglobin (g/L)	91.27 ± 20.96	98.59 ± 21.93	91.79 ± 21.42	86.25 ± 18.42	0.001
MNA-SF score	11.77 ± 2.17	12.70 ± 1.32	12.41 ± 1.61	10.39 ± 2.52	< 0.001
SARC-F score	2.26 ± 2.54	0.77 ± 0.80	1.32 ± 1.47	4.36 ± 2.95	< 0.001

Values are mean ± standard deviation or n (%). Continuous variables were compared using the Kruskal–Wallis test; categorical variables were compared using Pearson's χ^2 test or a Monte Carlo test with fixed marginal totals when expected cell counts were insufficient (20,000 simulations). FRAIL scores of 0, 1–2, and 3–5 indicate robust, prefrail, and frail status, respectively. aCCI, age-adjusted Charlson Comorbidity Index; BMI, body mass index; Hb, hemoglobin; MNA-SF, Mini Nutritional Assessment–Short Form; SARC-F, sarcopenia screening questionnaire; FRAIL, frailty scale.

Variable	Overall (N = 321)	Robust (n = 66)	Prefrail (n = 144)	Frail (n = 111)	P value
FRAIL score	1.90 ± 1.50	0.00 ± 0.00	1.39 ± 0.49	3.68 ± 0.73	—
aCCI score	5.15 ± 1.89	4.03 ± 1.31	4.76 ± 1.67	6.32 ± 1.86	< 0.001

Values are mean ± standard deviation or n (%). Continuous variables were compared using the Kruskal–Wallis test; categorical variables were compared using Pearson's χ^2 test or a Monte Carlo test with fixed marginal totals when expected cell counts were insufficient (20,000 simulations). FRAIL scores of 0, 1–2, and 3–5 indicate robust, prefrail, and frail status, respectively. aCCI, age-adjusted Charlson Comorbidity Index; BMI, body mass index; Hb, hemoglobin; MNA-SF, Mini Nutritional Assessment–Short Form; SARC-F, sarcopenia screening questionnaire; FRAIL, frailty scale.

3.2. Correlation Analysis

MNA-SF scores were negatively correlated with SARC-F (r = − 0.673), FRAIL (r = − 0.520), and aCCI (r = − 0.304) scores. SARC-F scores were positively correlated with FRAIL (r = 0.661) and aCCI (r = 0.535) scores, and aCCI was also positively correlated with FRAIL (all P < 0.001; Table 2). Spearman correlations were broadly consistent with the Pearson correlations (Table S1).

Table 2
Pearson correlation matrix of the main continuous variables.

Variable	MNA-SF	SARC-F	FRAIL	aCCI	Age	BMI	Hb
MNA-SF	1.000						
SARC-F	-0.673***	1.000					
FRAIL	-0.520***	0.661***	1.000				
aCCI	-0.304***	0.535***	0.518***	1.000			
Age	-0.306***	0.447***	0.485***	0.840***	1.000		
BMI	0.358***	-0.169**	-0.035	-0.072	-0.161**	1.000	
Hb	0.117*	-0.122*	-0.230***	-0.167**	-0.161**	0.049	1.000

*P < 0.05; **P < 0.01; ***P < 0.001. Higher MNA-SF scores indicate better nutritional status; higher SARC-F and FRAIL scores indicate greater sarcopenia risk and frailty, respectively. aCCI, age-adjusted Charlson Comorbidity Index; BMI, body mass index; Hb, hemoglobin; MNA-SF, Mini Nutritional Assessment–Short Form; SARC-F, sarcopenia screening questionnaire; FRAIL, frailty scale.

3.3. Mediation Analysis

After adjustment for sex, aCCI, hemoglobin, and dialysis duration, MNA-SF was negatively associated with SARC-F (path a: B = − 0.653; 95% CI, − 0.744 to − 0.563; P < 0.001). In the outcome model including

both MNA-SF and SARC-F, SARC-F was positively associated with FRAIL (path b: B = 0.250; 95% CI, 0.179 to 0.321; P < 0.001).

The total effect linking MNA-SF to FRAIL was − 0.268 (95% CI, − 0.330 to − 0.206; P < 0.001). After inclusion of SARC-F, the direct effect was − 0.105 (95% CI, − 0.178 to − 0.031; P = 0.006). The indirect effect through SARC-F was − 0.163 (bootstrap 95% CI, − 0.231 to − 0.110), accounting for approximately 61.0% of the total effect within the model (Table 3 and Fig. 1). Across alternative covariate adjustment models, indirect effects remained negative, and none of their bootstrap 95% CIs included zero (Table S2).

Table 3
Mediation analysis of the association between MNA-SF and FRAIL through SARC-F.

Path/effect	B	SE	95% CI lower limit	95% CI upper limit	t	P
MNA-SF → SARC-F (a)	-0.653	0.046	-0.744	-0.563	-14.188	< 0.001
SARC-F → FRAIL (b)	0.250	0.036	0.179	0.321	6.968	< 0.001
Direct effect (c')	-0.105	0.038	-0.178	-0.031	-2.787	0.006
Total effect (c)	-0.268	0.031	-0.330	-0.206	-8.518	< 0.001
Indirect effect (a × b)	-0.163		-0.231	-0.110		

Adjusted for sex, aCCI, hemoglobin, and dialysis duration. The indirect-effect confidence interval was estimated using 5000 bootstrap resamples. B, unstandardized regression coefficient; SE, standard error; CI, confidence interval. Paths a and b represent the MNA-SF–SARC-F and SARC-F–FRAIL associations, respectively.

3.4. Moderated Mediation Analysis

In the first-stage moderation model with SARC-F as the outcome, MNA-SF was negatively associated with SARC-F (B = − 0.604; 95% CI, − 0.695 to − 0.513; P < 0.001), whereas aCCI was positively associated with SARC-F (B = 0.427; 95% CI, 0.322 to 0.532; P < 0.001). The MNA-SF × aCCI interaction was statistically significant (B = − 0.093; 95% CI, − 0.135 to − 0.051; P < 0.001). Adding the interaction term increased the variance explained by the model by 2.4 percentage points (Table 4 and Fig. 2).

Table 4
Moderated mediation model with aCCI as the first-stage moderator.

Path/effect	B	SE	95% CI lower limit	95% CI upper limit	t	P
MNA-SF → SARC-F	-0.604	0.046	-0.695	-0.513	-13.083	< 0.001
aCCI → SARC-F	0.427	0.054	0.322	0.532	7.978	< 0.001
MNA-SF × aCCI → SARC-F	-0.093	0.021	-0.135	-0.051	-4.362	< 0.001
SARC-F → FRAIL	0.250	0.036	0.179	0.321	6.968	< 0.001
MNA-SF → FRAIL	-0.105	0.038	-0.178	-0.031	-2.787	0.006
aCCI → FRAIL	0.174	0.038	0.099	0.249	4.574	< 0.001

The first-stage model was adjusted for sex, hemoglobin, and dialysis duration; the outcome model also included the aCCI main effect. MNA-SF and aCCI were mean-centered. B, unstandardized regression coefficient; SE, standard error; CI, confidence interval.

At aCCI scores of 4, 5, and 6, corresponding to the 25th percentile, median, and 75th percentile, respectively, the simple slopes for the association between MNA-SF and SARC-F were − 0.497, − 0.590, and − 0.683 (all P < 0.001; Fig. 3A). Thus, the negative association between MNA-SF and SARC-F became stronger at higher aCCI scores.

The index of moderated mediation was − 0.023 (bootstrap 95% CI, − 0.036 to − 0.013). At aCCI scores of 4, 5, and 6, the conditional indirect effects linking MNA-SF to FRAIL through SARC-F were − 0.124 (bootstrap 95% CI, − 0.194 to − 0.073), − 0.148 (bootstrap 95% CI, − 0.215 to − 0.097), and − 0.171 (bootstrap 95% CI, − 0.238 to − 0.119), respectively. None of these CIs included zero, and the magnitude of the conditional indirect effect increased with aCCI (Table 5 and Fig. 3B).

Table 5
Conditional indirect effects linking MNA-SF to FRAIL through SARC-F at different aCCI scores.

aCCI	Conditional indirect effect	Bootstrap 95% CI lower limit	Bootstrap 95% CI upper limit
4.0	-0.124	-0.194	-0.073
5.0	-0.148	-0.215	-0.097
6.0	-0.171	-0.238	-0.119
Index of moderated mediation	-0.023	-0.036	-0.013

aCCI scores of 4, 5, and 6 correspond to the 25th percentile, median, and 75th percentile, respectively. Confidence intervals were estimated using 5000 bootstrap resamples. aCCI, age-adjusted Charlson Comorbidity Index; CI, confidence interval.

3.5. Sensitivity Analyses

The MNA-SF × aCCI interaction remained statistically significant when HC3 robust standard errors were used (B = − 0.093; 95% CI, − 0.134 to − 0.053; P < 0.001). After adding quadratic terms for MNA-SF and aCCI and using HC3 standard errors, the interaction remained negative (B = − 0.109; P < 0.001). The index of moderated mediation was − 0.022 (bootstrap 95% CI, − 0.035 to − 0.013) after additional adjustment for BMI and − 0.020 (bootstrap 95% CI, − 0.032 to − 0.010) in the expanded model with categorical covariates entered using dummy coding (Table S3).

The first-stage and outcome models had R^2 values of 0.598 and 0.505, respectively, with variance inflation factors ranging from 1.04 to 1.24 and from 1.04 to 2.35. Shapiro–Wilk tests of the residuals yielded P values of < 0.001 and 0.002, respectively. The corresponding Breusch–Pagan P values were < 0.001 and 0.742, indicating heteroscedasticity in the first-stage model. Cook's distance exceeded 4/n for 21 observations in the first-stage model and 10 in the outcome model; the maximum values were 0.198 and 0.033, respectively. After these observations were excluded in diagnostic refits, the first-stage interaction coefficient was − 0.110, and the SARC-F coefficient in the outcome model was 0.255 (both P < 0.001).

When the FRAIL score was treated as a six-category ordinal outcome (0–5), the regression coefficients per one-standard-deviation increase in MNA-SF and SARC-F were − 0.405 (95% CI, − 0.681 to − 0.130; P = 0.004) and 1.008 (95% CI, 0.682 to 1.333; P < 0.001), respectively. The approximate bootstrap Wald diagnostic for the proportional odds assumption yielded $\chi^2 = 34.665$ with 24 degrees of freedom (P = 0.074); 489 of the 500 resamples met the diagnostic screening criteria. When frailty was defined as a FRAIL score ≥ 3, the odds ratios per one-point increase in MNA-SF and SARC-F were 0.812 (95% CI, 0.679 to 0.971; P = 0.022) and 1.647 (95% CI, 1.344 to 2.018; P < 0.001), respectively (Table S4).

In the alternative second-stage moderation model, the SARC-F × aCCI interaction was not significantly associated with FRAIL (B = − 0.003; P = 0.775). In the reverse mediation model, with SARC-F as the

predictor, MNA-SF as the mediator, and FRAIL as the outcome, the indirect effect through MNA-SF was 0.081 (bootstrap 95% CI, 0.015 to 0.106; Table S5).

4. Discussion

In this study, 34.6% of patients receiving hemodialysis were frail and 44.9% were prefrail. Lower nutritional scores were associated with higher sarcopenia risk and frailty scores. Mediation analysis indicated that part of the association between MNA-SF and FRAIL was accounted for by SARC-F, and this indirect association was stronger at higher aCCI scores. These findings suggest that nutritional status, physical function, and overall disease burden should be considered together when interpreting frailty in patients receiving dialysis.

Previous studies in patients receiving hemodialysis have examined the coexistence of undernutrition, sarcopenia, and frailty and their clinical consequences [28–30]. In our study, the indirect effect through SARC-F was attenuated from − 0.264 in the unadjusted model to − 0.163 after adjustment for sex, aCCI, hemoglobin, and dialysis duration, but remained statistically significant. This attenuation suggests that the associations among these scores also reflect disease burden and other clinical characteristics. A study of dietary intake found no clear differences in protein or energy intake between groups defined by sarcopenia or frailty status, suggesting that composite nutritional scores should not be interpreted as direct measures of dietary intake.A recent prospective cohort study found that patients receiving hemodialysis who had oral frailty were more likely to experience worsening nutritional status and sarcopenia over one year of follow-up [31]. Although these studies used measures different from ours, they underscore that nutritional risk often coexists with other health problems and that nutritional scores alone may not adequately explain patients' functional status and frailty. In the prespecified adjusted model, the indirect effect through SARC-F accounted for approximately 61.0% of the total association between MNA-SF and FRAIL, while a direct association remained. This proportion represents a decomposition of the association within the fitted linear model, rather than the causal contribution of sarcopenia to frailty. Celik et al. [13] reported similar statistical relationships among nutritional status, sarcopenia risk, and frailty in community-dwelling older adults. We observed a comparable pattern in patients receiving MHD, with SARC-F accounting for only part of the association between MNA-SF and frailty scores. Further research is needed to identify the nutritional, disease-related, and functional factors underlying the remaining association, particularly in patients receiving long-term dialysis who have multiple comorbidities.

Another finding was that overall disease burden moderated the association between nutritional status and sarcopenia risk. At aCCI scores of 4 and 6, the slopes for the association between MNA-SF and SARC-F were − 0.497 and − 0.683, respectively, and the corresponding conditional indirect effects were − 0.124 and − 0.171. Thus, the association between nutritional and sarcopenia risk scores was stronger among patients with a greater disease burden. Previous dialysis studies have examined nutritional risk, muscle quality, and comorbidities in relation to clinical characteristics and outcomes [20, 32–34]. Our analysis extends these observations by showing that the strength of the association varied with aCCI.

However, adding the interaction term increased the variance explained by the model by only 2.4 percentage points.Although this difference was statistically supported, its magnitude and clinical relevance require validation in other populations. In patients receiving dialysis who have lower nutritional scores and higher aCCI scores, clinical assessment could also address mobility difficulties and frailty. Previous dialysis cohort and screening studies have likewise considered nutritional status, physical function, and frailty together [35–38]. Our findings demonstrate associations among these scores, but whether their combined assessment identifies subsequent functional decline more accurately than any individual measure remains untested. Longitudinal studies with repeated assessments of nutritional status, objective muscle strength, physical performance, and frailty could determine the additional information provided by SARC-F and aCCI.

This study evaluated a prespecified mediation model linking nutritional status, sarcopenia risk, and frailty and found that aCCI moderated the association between nutritional status and sarcopenia risk scores. These findings offer insight into the relationships among nutrition, physical function, and frailty in patients receiving dialysis, although several limitations should be considered. First, the cross-sectional design precludes establishing the temporal ordering of the variables. The reverse mediation analysis also yielded a significant indirect effect; thus, the findings describe patterns of association rather than causal mechanisms. Second, MNA-SF, SARC-F, and FRAIL are scale-based measures with some overlap in functional content, whereas aCCI was calculated from age and comorbidity diagnoses recorded in medical records. The absence of objective measurements of muscle mass and strength limits the interpretation of indirect effects involving SARC-F. Third, the single-center convenience sample may be subject to selection bias, limiting generalizability to patients receiving dialysis in other regions or with different characteristics. Finally, potential confounders, including inflammation and dietary intake, were not included and may have influenced the observed associations. Overall, nutritional status, sarcopenia risk, and frailty were associated, and the indirect association through SARC-F varied with aCCI. These findings support further longitudinal investigation of the temporal relationships among these variables and the value of their combined assessment.

5. Conclusions

Poorer nutritional status was associated with greater sarcopenia risk and frailty in patients receiving maintenance hemodialysis, with sarcopenia risk statistically mediating part of the association between nutritional status and frailty. At higher levels of age-adjusted comorbidity burden, as measured by aCCI, the negative association between nutritional status and sarcopenia risk was stronger, as was the corresponding conditional indirect effect. Alternative covariate adjustments and sensitivity analyses broadly supported this pattern. These findings suggest that nutritional status, physical function, and overall disease burden should be considered together when assessing frailty in patients receiving dialysis, with particular attention to functional difficulties among those with poorer nutritional status and a greater disease burden. Longitudinal studies are needed to establish the temporal relationships among

nutritional status, sarcopenia risk, and frailty and to evaluate the clinical value of their combined assessment.

Declarations

Ethical Statement

The study protocol was approved by the Ethics Committee of Suining County Hospital of Traditional Chinese Medicine on 31 December 2025 (approval no. 2025123101). All studies were conducted after fully explaining the study objectives, procedures, potential risks, and benefits; participants voluntarily participated and signed written informed consent forms. The research process strictly adhered to the requirements of the Declaration of Helsinki and relevant Chinese regulations.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Author Contribution

JZ and LY performed data management and statistical analysis and drafted the manuscript. FW was responsible for patient recruitment, clinical data collection, and questionnaire administration. RJ contributed to the conception and design of the study, supervised the project, and critically revised the manuscript. All authors contributed to the interpretation of the findings and reviewed and approved the final manuscript.

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Data Availability

Data are not publicly available because of privacy and ethical restrictions but may be obtained from the corresponding author on reasonable request.

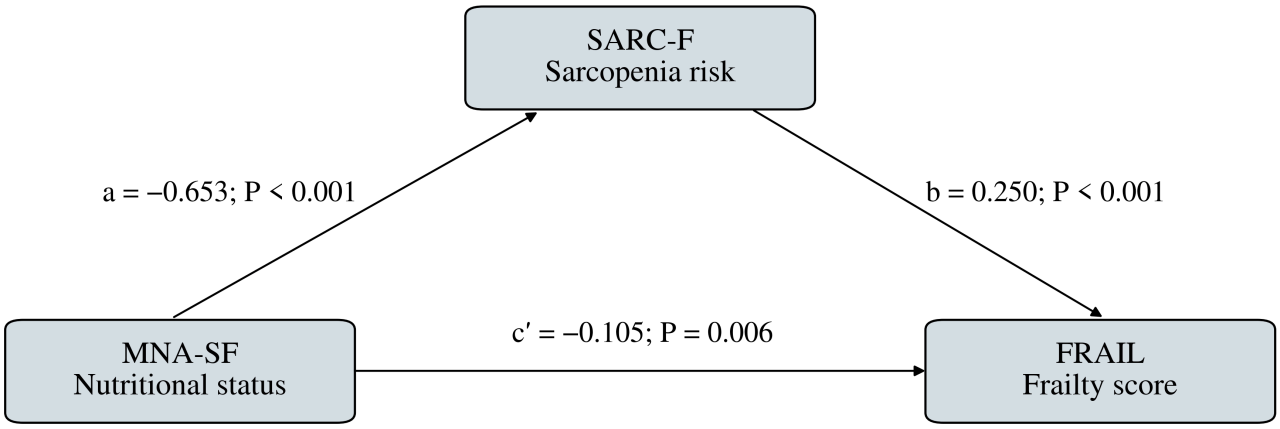
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Figures



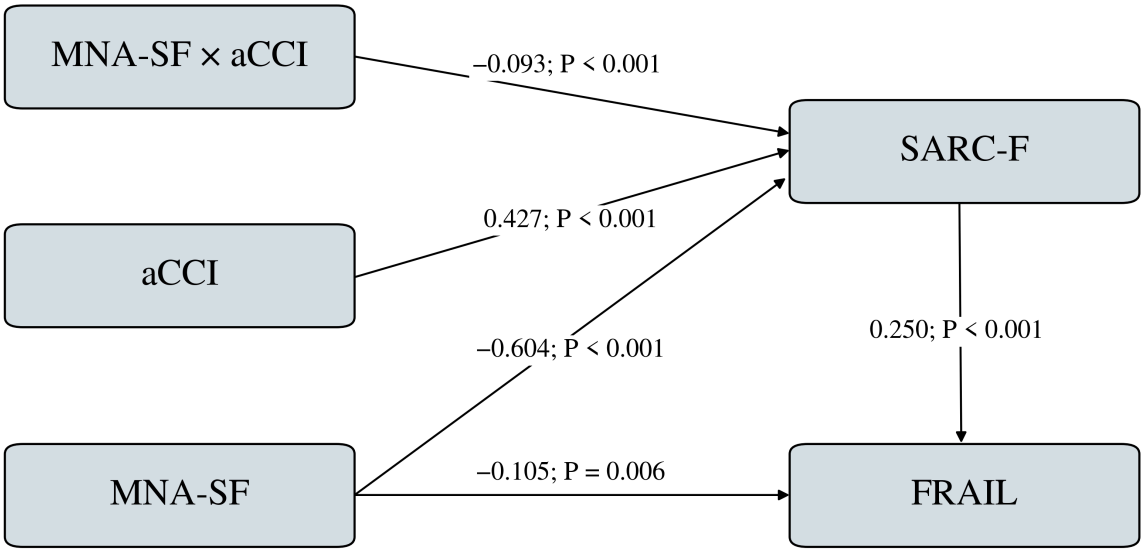
Indirect association: −0.163 (95% bootstrap CI −0.231 to −0.110)

Adjusted for sex, aCCI, hemoglobin and dialysis duration

Figure 1

Mediation model of the association between MNA-SF and FRAIL through SARC-F.

Path coefficients are unstandardized regression coefficients. The model was adjusted for sex, aCCI, hemoglobin, and dialysis duration.



Moderated mediation index: −0.023 (95% bootstrap CI −0.036 to −0.013)

Figure 2

First-stage moderated mediation model with aCCI moderating the association between MNA-SF and SARC-F. MNA-SF and aCCI were mean-centered.

The first-stage equation was adjusted for sex, hemoglobin, and dialysis duration; the outcome equation additionally included the aCCI main effect. Path coefficients are unstandardized regression coefficients.

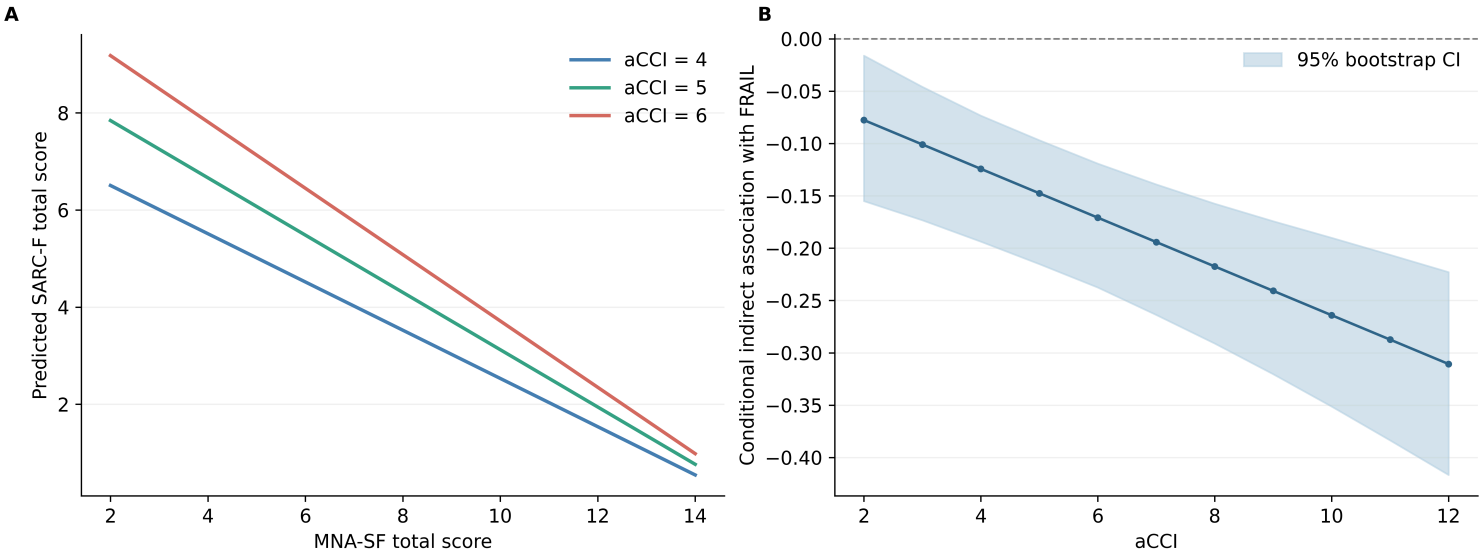


Figure 3

Moderating role of aCCI and conditional indirect effects.

(A) Simple slopes for the association between MNA-SF and SARC-F at the 25th percentile, median, and 75th percentile of aCCI. (B) Conditional indirect effects linking MNA-SF to FRAIL through SARC-F across the range of aCCI scores, with 95% bootstrap confidence intervals.

Supplementary Files

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- SupplementaryMaterials.docx