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Phase Angle as an Indicator of Depression in Maintenance Hemodialysis Patients

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Keywords
Phase angle · Depression · Hemodialysis · Bioelectrical impedance analysis

Abstract
Introduction: Depression is a common psychiatric problem in maintenance hemodialysis (MHD) patients. Recent studies have begun to explore the relationship between body composition and depression. Phase angle (PhA), a core parameter for assessing body composition, has been observed to be associated with frailty and cognitive dysfunction. The aim of this study was to investigate the association between PhA and depression in MHD patients. ***Methods:*** This multicenter, cross-sectional study included 843 MHD patients from seven dialysis centers in Shanghai, China. Depressive symptoms were evaluated using the Patient Health Questionnaire (PHQ-9), with a score of ≥10 indicating depression. PhA was measured by bioelectrical impedance analysis. Nutritional status was assessed by malnutrition inflammation score (MIS). Multivariable logistic regression models were used to investigate the association between PhA and depression. Restricted cubic spline (RCS) analysis was utilized to examine the association. Receiver operating characteristic curve was used to identify the cut-off value of PhA for depression. ***Results:*** A total of 15.2% of patients (62.8% male, median age 66 years) had depression. Median PhA level (interquartile range) of depressed patients was 4.4° (3.9–4.9°) for males and 3.9° (3.2–4.7°) for females. There was a significant decrease in the prevalence of depression with increasing quartiles of PhA levels. In multivariable logistic regression analyses, after adjusting for age, sex, education level, spKt/V, dialysis vintage, Charlson comorbidity index, hemoglobin, and serum albumin, lower PhA levels (lowest quartile group) were significantly associated with depressive symptoms (adjusted odds ratio, 2.19; 95% confidence interval, 1.07 to 4.48), compared to higher PhA

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levels (highest quartile group). RCS analysis showed a relatively inverse linear association between PhA and depression. The optimal cut-off value of PhA for depression was 4.9° for males and 3.5° for females. Subgroup analyses validated the findings across patient characteristics, including age, sex, diabetes, education, and malnutrition. ***Conclusion:*** Our findings indicated an inverse association between PhA and depressive symptoms in Chinese MHD patients, suggesting that PhA could serve as a valuable indicator for assessing the risk of depression in this population. Further studies are needed to explore the potential of PhA as a prognostic tool and its implications for intervention strategies.

Introduction

Patients undergoing maintenance hemodialysis (MHD) experience a variety of psychological complications. Depression is usually the most common and debilitating problem, with reported prevalence ranging from 13.1 to 76.3% [1–3], significantly affecting quality of life, complications, treatment outcomes, and prognosis [3]. However, depression may still go undiagnosed, underdiagnosed, or untreated [4] and there is a lack of objective quantitative indicators in clinical settings. The interplay between symptoms, comorbidities, and psychosocial factors highlights the complexity and importance of managing psychosomatic disorders in the context of hemodialysis (HD) management [5]. Therefore, careful identification of depressive symptoms, early assessment of risk factors, and timely intervention are essential.

Recent researches have demonstrated that patients with depression have poorer nutritional status [6], lower physical activity, and a higher risk of sarcopenia [7], and that relationships are bidirectional. Several recent studies [8–10] have initiated investigations into the potential associations between body composition indicators and depressive symptoms, as reliable correlations have been found between body composition and nutritional status, physical function, and muscle mass, shedding light on new avenues for understanding and monitoring depression in HD patients.

Phase angle (PhA), derived from bioelectrical impedance analysis (BIA), has emerged as a marker reflecting cellular health and integrity [11]. As a tool for assessing body composition, a number of studies have shown the strong association between PhA and nutritional status [12, 13], fluid overload [14], sarcopenia [15], and quality of life [16] in individuals on renal replacement therapy. Thus, PhA may serve as a valuable indicator not only of nutritional status, but also of broader health outcomes. Recent studies have suggested that PhA may also be related to mental health, and lower PhA has been demonstrated to be associated with an increased risk of frailty [13] and cognitive dysfunction [17]. Nevertheless, the relationship between PhA and depression remains unexplored.

In this cross-sectional study, our objective was to investigate the association between PhA and depression. Furthermore, we aim to enhance our comprehension of the complex factors influencing depression in HD patients and, hopefully, quantifying the diagnosis of depression. Investigating this association may provide insights into the interactions between depression and other complications in HD patients and inform assessment tools to improve mental health outcomes in this vulnerable population.

Methods

Study Participants

This multicenter, cross-sectional study enrolled MHD patients from seven HD centers in Shanghai between July 2020 and April 2021. Patients had to be over 18 years old and receive HD 4 h each time, 2 or 3 times per week, for at least 3 months (ChiCTR1900027039). Patients who were unable to complete the questionnaire or had contraindications to BIA were excluded.

This work was approved by the Ethics Committee of Tongji Hospital (K-2020-024), and the methods were carried out in accordance with the principles of the Declaration of Helsinki. All the participants were informed and signed informed consent prior to enrollment in the study.

Assessment of Depression

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9), a validated and widely used tool for screening depression in dialysis patients [3]. The PHQ-9 consists of nine self-report questions, as follows: (1) anhedonia, (2) depressed mood, (3) sleep disturbance, (4) fatigue, (5) appetite changes, (6) low self-esteem, (7) concentration problems, (8) psychomotor disturbances, and (9) suicidal ideation, corresponding to the nine criteria for defining depression according to the Diagnostic and Statistical Manual Fourth Edition (DSM-IV) [18]. Using a 4-point severity scale (0 = not at all, 1 = a few

days, 2 = more than half the days, 3 = nearly every day), the PHQ-9 measured the frequency of depressive thoughts or feelings over the past 2 weeks and summed to give a total score of 0–27 for each patient. A cut-off score of ≥10 has been shown in previous studies to be reliable and valid for defining depressive disorder in dialysis patients [19, 20]. In addition to the PHQ-9 total score, we also calculated PHQ-9 cognitive-affective subscale scores by summing items 1, 2, 6, and somatic subscale scores by summing the items 3, 4, 5, and 8 [21] to further examine the association between specific depressive symptom clusters and PhA.

Assessment of BIA

Body composition was evaluated by BIA (InBody S10; BioSpace, Seoul, Korea). BIA was performed before a dialysis session. The patients removed all metal accessories, laid in a supine position, left the trunk with both arms, slightly separated the thighs, and relaxed the whole body for the measurement.

BIA measures body reactance (Xc) and resistance (R) to low-intensity electrical unit ranging from 1 to 1,000 kHz in five body segments – right arm, left arm, trunk, right leg, and left leg. BIA-derived body components, including extracellular water, total body water, fat-free mass, body fat mass, skeletal muscle index, and PhA values, were recorded. PhA of the whole body at the frequency of 50 kHz was considered [22].

Clinical, Anthropometric, and Nutritional Status Assessment

Blood samples for laboratory measurements, anthropometric data, and body composition were taken on the same day before a dialysis session. Data on duration of dialysis and comorbidities were collected by self-report and review of medical records. Comorbidities were assessed using the Charlson comorbidity index (CCI) [23] and nutritional status using the malnutrition inflammation score (MIS), with a score of ≥6 indicating malnutrition [24].

Statistical Analyses

Data were expressed as median with interquartile range (IQR) or numbers or percentages as appropriate. Comparisons between two groups were assessed with the nonparametric Wilcoxon test for continuous variables and the χ^2 test for nominal variables. Comparisons between three or more groups were assessed with the nonparametric Kruskal-Wallis test for continuous variables and χ^2 test for nominal variables. For the main analysis, parameters were compared according to quartiles of PhA.

Multivariable logistic regression models were mainly used to examine the association between PhA and depression. Collinearity between covariates was checked before constructing the models. Model 1 was the unadjusted model. Model 2 was adjusted for age, sex, education, single-pool Kt/V, and dialysis vintage. Model 3 added comorbidities (CCI) and nutritional status (MIS) into model 2 as adjustments. Model 4 added laboratory parameters, such as hemoglobin and serum albumin level. p value for trend was calculated by treating quartiles of PhA as a continuous variable in each model to explore the possibility of a nonlinear relationship.

We also performed restricted cubic spline to examine the association of PhA as a continuous variable with depression. The spline curve was expressed as odds ratio, adjusted for age, sex, education, single-pool Kt/V, dialysis vintage, CCI, MIS, albumin, and hemoglobin. The grouping variables for subgroup analyses included sex, the presence of diabetes mellitus (DM), education level, and nutritional status.

Receiver operating characteristic (ROC) curve and area under the curve (AUC) were used to evaluate the performance of logistic regression model and identify an optimal PhA cut-off point for the detection of depressive symptoms. The point was determined by the maximal value of Youden's index, calculated as follows: sensitivity + specificity − 1.

All tests were two-sided, and statistical significance was set at the level of $p < 0.05$. All statistical analyses were performed using Stata 16.1 (Stata Corporation, College Station, TX, USA).

Results

Characteristics between Nondepressed and Depressed Groups

A total of 843 patients (median age 63 years, 61.4% male) were included in the final analysis (online suppl. Fig. S1; for all online suppl. material, see https://doi.org/10.1159/000540683). Characteristics of all patients stratified by depressive symptoms are presented in Table 1. One hundred twenty-eight patients (15.2%) had depressive symptoms, with a median age of 66 years old, 62.8% were male, 89 patients (70.1%) had cardiovascular disease (CVD), and 58 patients (46%) had DM. Compared to nondepressed patients, depressed patients were older, had more comorbidities

Table 1. Baseline characteristics of MHD patients by depressive symptoms

Characteristics	Total, *n* = 843	Nondepressed, *n* = 715	Depressed, *n* = 128	*p* value
PhA, °				
Male	4.7 (4.1–5.4)	4.8 (4.2–5.4)	4.4 (3.9–4.9)	<0.001
Female	4.3 (3.8–4.9)	4.3 (3.8–5.0)	3.9 (3.2–4.7)	<0.001
Age, years	63 (54–70)	62 (53–70)	66 (59–72)	<0.001
Male, *n* (%)	518 (61.4)	438 (61.3)	80 (62.5)	0.84
Vintage, months	47.0 (23.9–94)	47.5 (25–96.6)	43.7 (14.2–75.9)	0.020
spKt/V	1.4 (1.2–1.5)	1.4 (1.2–1.5)	1.3 (1.1–1.5)	0.23
Current smoker, *n* (%)	185 (21.9)	161 (22.5)	24 (18.8)	0.42
History of CVD, *n* (%)	445 (53.9)	356 (51.0)	89 (70.1)	<0.001
DM, *n* (%)	274 (33.3)	216 (31.0)	58 (46.0)	0.001
CCI	4 (2–5)	3 (2–5)	4 (3–6)	<0.001
Living alone, *n* (%)	44 (5.3)	39 (5.5)	5 (3.9)	0.67
Education level, *n* (%)				0.020
<High school	486 (57.7)	400 (55.9)	86 (67.2)	
High school or higher education	357 (42.3)	315 (44.1)	42 (32.8)	
MIS	4 (2–6)	4 (2–5)	5 (3–7)	<0.001
Laboratory variables				
Hemoglobin, g/L	112 (101–121)	112 (102–121)	109 (97–121)	0.18
Albumin, g/L	39.8 (37.6–41.9)	39.9 (37.9–41.9)	39 (37–41.3)	0.043
Calcium, mmol/L	2.3 (2.1–2.4)	2.3 (2.1–2.4)	2.2 (2.1–2.4)	0.19
Phosphate, mmol/L	1.9 (1.5–2.3)	1.9 (1.5–2.3)	2.0 (1.5–2.4)	0.43
iPTH, ng/L	276 (143–469)	270 (144–469)	285 (129–457)	0.88
Cholesterol, mmol/L	3.8 (3.2–4.5)	3.8 (3.2–4.5)	3.8 (3.2–4.5)	0.68
Triglyceride, mmol/L	1.7 (1.2–2.7)	1.7 (1.2–2.8)	1.5 (1.1–2.3)	0.007
hsCRP, mg/L	2.3 (1.1–5.7)	2.3 (1.0–5.6)	2.7 (1.3–8.0)	0.055
Anthropometric parameters				
Male				
BMI, kg/m^2	23.1 (21.0–25.2)	23.2 (21.0–25.2)	23.1 (21.1–25.7)	0.87
Mid-arm circumference, cm	26 (25–29)	27 (25–29)	26 (24–28)	0.18
Waist circumference, cm	89 (83–97)	89 (83–97)	88 (83–95)	0.45
Hip circumference, cm	94 (90–98)	94 (90–99)	93 (89–97)	0.084
Calf circumference, cm	33 (31–35)	33 (31–35)	32 (30–34)	0.002
Female				
BMI, kg/m^2	22.7 (20.1–25.8)	22.7 (20.1–25.9)	22.3 (19.6–25.5)	0.50
Mid-arm circumference, cm	25 (23–28)	25 (23–28)	24 (22–28)	0.17
Waist circumference, cm	86 (78–93)	86 (78–93)	86 (77–96)	0.63
Hip circumference, cm	91 (87–97)	91 (87–98)	92 (85–97)	0.43
Calf circumference, cm	32 (29–34)	32 (29–34)	30 (28–33)	0.022
Body composition				
Male				
SMI, kg/m^2	7.5 (6.9–8.1)	7.6 (6.9–8.1)	7.3 (6.7–7.7)	0.015
FFM, kg	49.7 (45.1–54.4)	50.1 (45.5–55.1)	47.4 (43.5–51.9)	0.007
TBW, L	36.9 (33.5–40.3)	37.1 (33.8–40.7)	35.2 (32.2–38.4)	0.008
ECW/TBW	0.39 (0.39–0.41)	0.39 (0.39–0.40)	0.40 (0.39–0.41)	<0.001
BFM, kg	18.6 (13.8–23.6)	18.4 (13.8–23.5)	18.9 (14–25.0)	0.38
Female				
SMI, kg/m^2	6.1 (5.5–6.6)	6.1 (5.6–6.7)	5.9 (5.4–6.6)	0.25
FFM, kg	37.1 (34.1–41.3)	37.2 (34.3–41.4)	36.6 (32.8–40.1)	0.14

Table 1 (continued)

Characteristics	Total, n = 843	Nondepressed, n = 715	Depressed, n = 128	p value
TBW, L	27.4 (25.2–30.5)	27.4 (25.3–30.6)	27.1 (24.4–29.8)	0.15
ECW/TBW	0.40 (0.39–0.41)	0.40 (0.39–0.40)	0.41 (0.40–0.41)	<0.001
BFM, kg	19.8 (14.9–25.7)	19.8 (15.2–25.8)	19.8 (12.6–24.2)	0.27

spKt/V, single-pool Kt/V; CVD, cardiovascular disease; CCI, Charlson comorbidity index; MIS, malnutrition inflammation score; iPTH, intact parathyroid hormone; hsCRP, high-sensitivity C-reactive protein; BMI, body mass index; SMI, skeletal muscle index; FFM, fat-free mass; TBW, total body water; ECW/TBW, extracellular water/total body water; BFM, body fat mass.

Table 2. Characteristics of MHD patients according to quartiles of PhA

Characteristics	Q1 [2, 3.9], n = 210	Q2 [3.9, 4.5], n = 211	Q3 [4.6, 5.2], n = 211	Q4 [5.2, 7.1], n = 211	p value
Age, years	68.5 (62–74)	66 (58–72)	62 (52–70)	54 (44–62)	<0.001
Male, n (%)	100 (47.6)	120 (56.9)	135 (64.0)	163 (77.3)	<0.001
Vintage, months	48.3 (28.0–95.5)	50.6 (24.6–104.7)	46.3 (24.4–92.4)	41.1 (21.5–84.1)	0.27
spKt/V	1.4 (1.2–1.6)	1.4 (1.2–1.6)	1.3 (1.2–1.6)	1.3 (1.2–1.5)	<0.001
History of CVD, n (%)	138 (66.0)	121 (59.9)	104 (50.5)	82 (39.4)	<0.001
DM, n (%)	93 (44.5)	76 (37.6)	69 (33.7)	36 (17.4)	<0.001
CCI	4 (3–6)	4 (3–5)	4 (3–5)	3 (2–4)	<0.001
MIS	6 (3–8)	4 (2–6)	4 (2–5)	3 (1–4)	<0.001
Hemoglobin, g/L	109 (97–117)	111 (102–121)	115 (103–121)	114 (102–124)	<0.001
Albumin, g/L	38.3 (36–40.7)	39.3 (37.3–41)	40.3 (38.2–42)	40.9 (38.4–42)	<0.001
Calcium, mmol/L	2.2 (2.1–2.4)	2.3 (2.1–2.4)	2.3 (2.1–2.5)	2.3 (2.1–2.5)	0.11
Phosphate, mmol/L	1.7 (1.3–2.3)	1.8 (1.5–2.2)	2.0 (1.6–2.4)	2.1 (1.6–2.5)	<0.001
iPTH, ng/L	256 (127–416)	254 (132–466)	268 (140–447)	344 (179–530)	0.003
hsCRP, mg/L	2.6 (1.2–6.9)	2.4 (1.1–5.5)	2.0 (0.9–5.1)	2.2 (1.2–5.8)	0.21
BMI, kg/m^2	22.3 (19.7–24.5)	22.4 (20.4–24.9)	23.3 (20.9–25.8)	24.2 (22.0–26.7)	<0.001
Mid-arm circumference, cm	25 (23–28)	25 (23–28)	26 (24–28)	27 (25–29)	<0.001
Waist circumference, cm	86 (80–95)	88 (81–96)	88 (81–95)	90 (83–98)	0.017
Hip circumference, cm	92 (88–98)	92 (88–98)	92.5 (88–97)	94 (90–99)	0.025
Calf circumference, cm	31 (29–33)	32 (30–34)	33 (30–35)	34 (31–35)	<0.001
Depression, n (%)	50 (23.8)	34 (16.1)	27 (12.8)	17 (8.1)	<0.001

spKt/V, single-pool Kt/V; CVD, cardiovascular disease; CCI, Charlson comorbidity index; MIS, malnutrition inflammation score; iPTH, intact parathyroid hormone; hsCRP, high-sensitivity C-reactive protein; BMI, body mass index.

(DM, CVD, and higher CCI score), lower educational level, and lower serum albumin level. Gender comparisons of anthropometric parameters and body composition between two groups showed that the depressed group had lower calf circumference, PhA level, higher extracellular water/total body water ratio in both sexes, lower skeletal muscle index, and fat-free mass in males.

The median PhA level (IQR) of depressed patients was 4.4° (3.9–4.9°) for males and 3.9° (3.2–4.7°) for females.

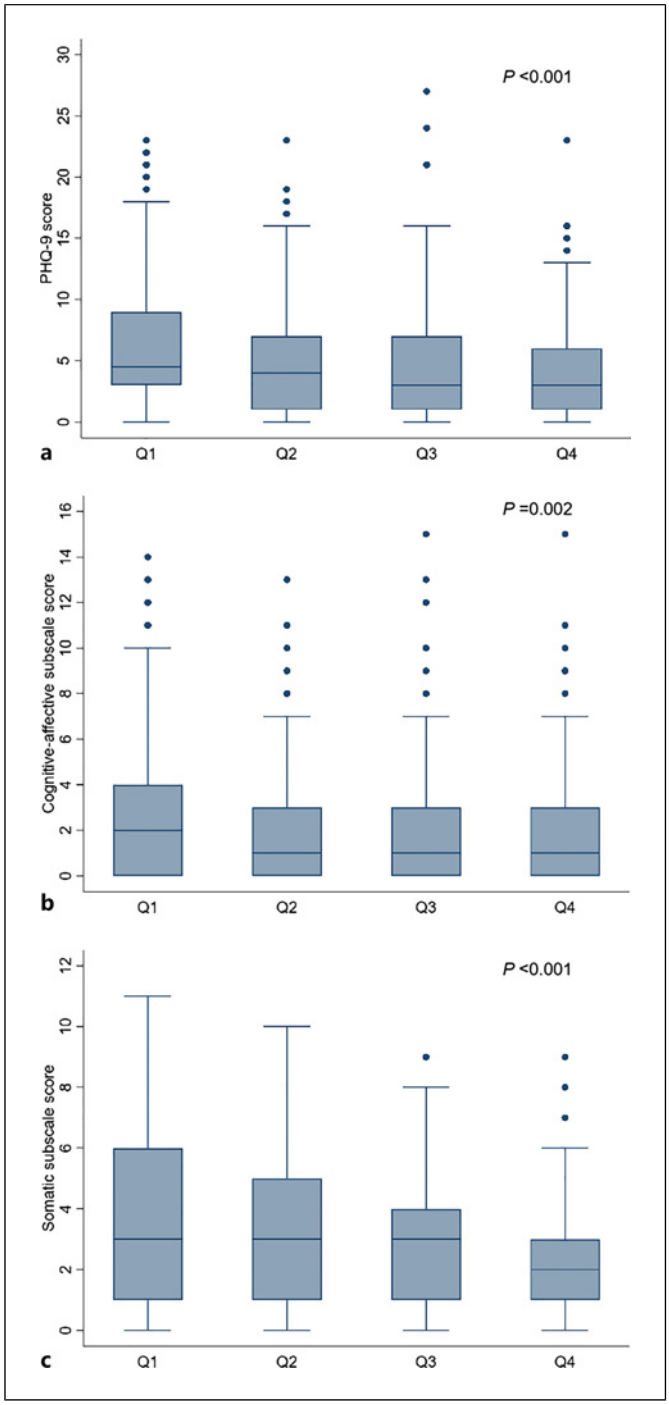

Fig. 1. Box plot of PHQ-9 total score (**a**), cognitive-affective score (**b**), and somatic subscale score (**c**) by quartiles of PhA in MHD patients.

The median PhA level (IQR) of nondepressed patients was 4.8° (4.2–5.4°) for males and 4.3° (3.8–5.0°) for females (Table 1).

Characteristic Comparison of Patients Grouped by PhA Quartiles

Characteristics of patients according to PhA quartiles are shown in Table 2. With increasing PhA in each group, age, MIS, and the proportions of CVD and DM gradually decreased, whereas BMI, hemoglobin, serum albumin, mid-arm, and calf circumferences gradually increased.

The PHQ-9 total scores were 4.5 (3–9), 4 (1–7), 3 (1–7), 3 (1–6), and the prevalence of depression was 23.8%, 16.1%, 12.8%, and 8.1% in the first to fourth quartile groups, respectively. The prevalence of depression decreased significantly with quartiles of PhA increased. Correspondingly, patients in the lower PhA group had both higher cognitive-affective and somatic scores ($p < 0.001$, Fig. 1; online suppl. Table S1).

Association between PhA and Depression

The unadjusted odds ratios for the logistic regression model were 3.57 (95% confidence interval [CI]: 1.98 to 6.43), 2.19 (95% CI: 1.18 to 4.06), and 1.67 (95% CI: 0.88 to 3.17) for the first to third quartiles, respectively, compared with the fourth quartile (model 1 in Table 3). The results were similar after adjustment for age, sex, education level, dialysis parameters, comorbidities, and nutritional status. The final model with adjustment of laboratory parameters revealed that the lowest quartile of PhA had a 2.19-fold higher risk of depression than the highest quartile (95% CI: 1.07 to 4.48; model 4 in Table 3). The distinguished performance of the final adjusted model for depressive symptoms was assessed by the ROC curves (Fig. 2). The AUCs for both sexes (Fig. 2a), males, and females (Fig. 2b) were 0.702, 0.686, and 0.724, respectively.

The ROC curves were plotted to identify the optimal PhA cut-off for detecting depressive symptoms. The optimal PhA cut-off was 4.9° with an AUC of 0.631 (sensitivity = 80%, specificity = 43.2%) for males and 3.5° with an AUC of 0.654 (sensitivity = 43.8%, specificity = 84.8%) for females, as shown in Table 4. Restricted cubic spline regression analysis clearly showed a relatively inverse linear relationship between PhA and depression (Fig. 3).

Subgroup Analyses for the Associations between PhA and Depression

To evaluate the modification effects of subgroups on the association between PhA and depression, subgroup analyses of multivariable logistic regression (PhA as a continuous independent variable) were performed stratified by age (<65 or ≥65 years old), sex (male or female), diabetes (with or without), education level

Table 3. Associations of PhA with depressive symptoms in multivariable logistic regression analysis

	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	*p* value for trend	OR (95% CI)	*p* value for trend	OR (95% CI)	*p* value for trend	OR (95% CI)	*p* value for trend
PhA, °								
Q1: 2–3.9	3.57 (1.98, 6.43)	<0.001	3.62 (1.87, 7.03)	<0.001	2.17 (1.06, 4.42)	0.021	2.19 (1.07, 4.48)	0.015
Q2: 3.9–4.5	2.19 (1.18, 4.06)		2.32 (1.19, 4.51)		1.92 (0.98, 3.77)		1.93 (0.98, 3.80)	
Q3: 4.6–5.2	1.67 (0.88, 3.17)		1.66 (0.85, 3.23)		1.39 (0.71, 2.73)		1.29 (0.65, 2.55)	
Q4: 5.2–7.1	1.00		1.00		1.00		1.00	

Model 1: unadjusted crude OR. Model 2: adjusted for age, sex, education, spKt/V, and dialysis vintage. Model 3: model 2 plus comorbid disease (CCI) and MIS. Model 4: model 3 plus HB and albumin. PhA, phase angle; OR, odds ratio; CI, confidence interval; spKt/V, single-pool Kt/V.

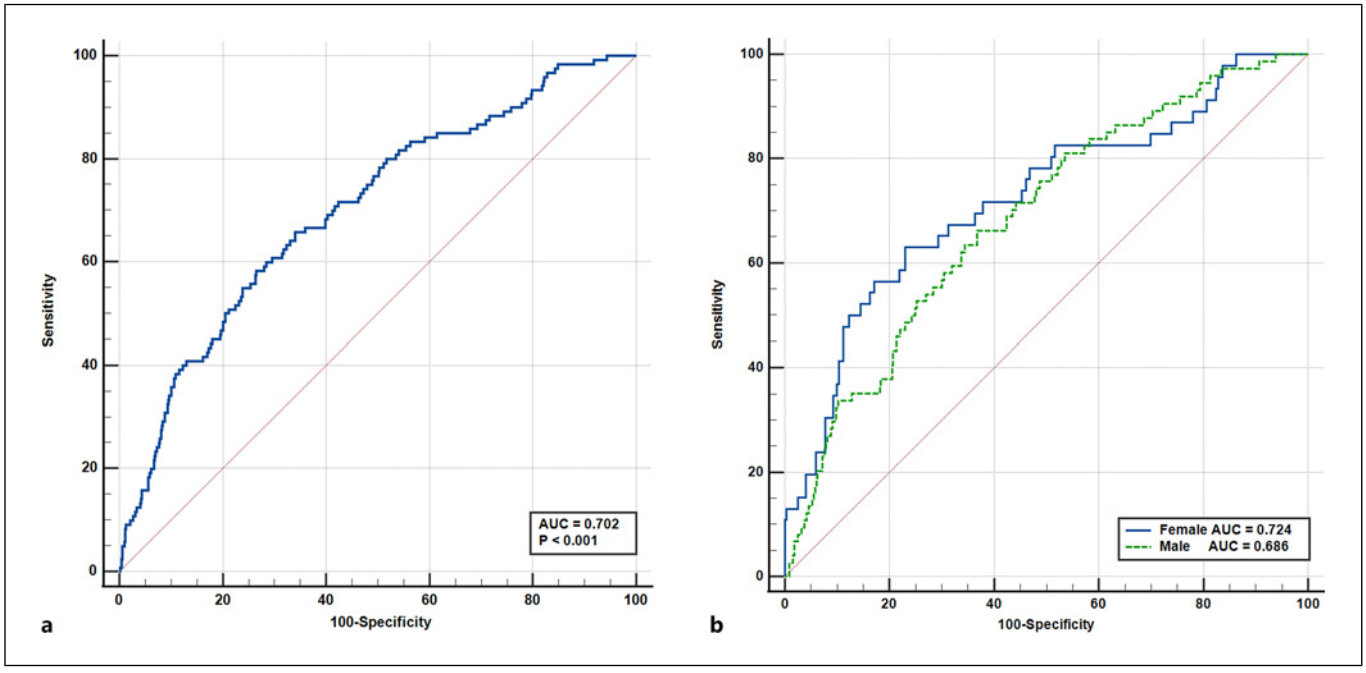

Fig. 2. ROC curves of logistic regression model for depressive symptoms in both sexes (**a**), males and females (**b**). AUC, area under the curve.

(<high school or ≥high school), and nutritional status (MIS <6 or MIS ≥6). *p* values for interactions were greater than 0.05 for all the subgroups, indicating that the increased risk of depression associated with low PhA was evident regardless of these factors (Fig. 4).

Discussion

In this study, we observed that PhA levels were inversely associated with depressive symptoms in MHD patients, and this finding was not modified by age, sex,

Table 4. ROC curve for identifying the optimal PhA cut-off for depression in terms of gender

Depression	AUC (95% CI)	Cut-off	Sensitivity, %	Specificity, %	*p* value
Male	0.631 (0.588, 0.672)	4.9°	80.0	43.2	<0.001
Female	0.654 (0.599, 0.705)	3.5°	43.7	84.8	0.001

AUC, area under the curve; CI, confidence interval.

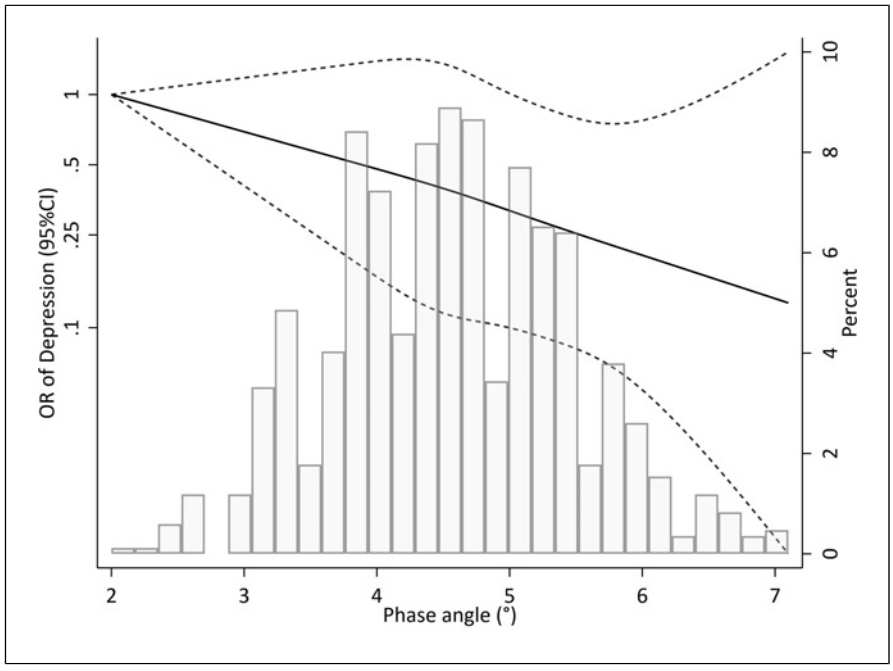

Fig. 3. Spline curve illustrating the association of PhA as continuous variable with depressive symptoms. We adjusted for age, sex, education, spKt/V, dialysis vintage, CCI, MIS, albumin, and hemoglobin. The black line represented the odds ratio. The gray dash line showed 95% CI. The histogram represented the frequency distribution of PhA. spKt/V, single-pool Kt/V.

education level, nutritional status, and the presence of diabetes. Depression is the most common psychological problem in patients receiving MHD due to its relative prevalence and association with a variety of adverse clinical outcomes. In our study, the prevalence of depressive symptoms using the PHQ-9 was 15.2%. This is similar to another multicenter cross-sectional study of Chinese patients with MHD using the Beck Depression Inventory II (BDI-II), which showed a prevalence of 16.5% [9]. It is worth noting that there is variation in the prevalence of depression in the literature, partly due to differences in countries and regions, HD mode, and the assessment scales used to screen for depression [3, 20]. In addition, basic diseases, complications, medications, family support, economic status, health insurance, etc., may also contribute to the differences.

To our knowledge, this is the first large-sample, multicenter study to specifically explore the relationship between depression and PhA in MHD patients in a Chinese patient population. Our study confirmed that the lower PhA group had significantly higher PHQ-9 total scores, as well as cognitive-affective and somatic subscale scores. A previous study by Vuckovic et al. [10] showed that body composition including PhA was correlated with depression assessed by the BDI-II self-administered questionnaire in both peritoneal dialysis and HD patients. Another study by Markaki et al. [6] also found that nutritional status including PhA was associated with depression assessed by the Center for Epidemiologic Studies Depression Scale (CES-D) in HD patients. Although the sample size of these two studies was small and different depression assessment scales were used in different races, the results supported our findings and further validated the inverse association between PhA and depression.

After adjustment for confounders, PhA remained independently associated with depressive symptoms, suggesting PhA may have other properties that are also

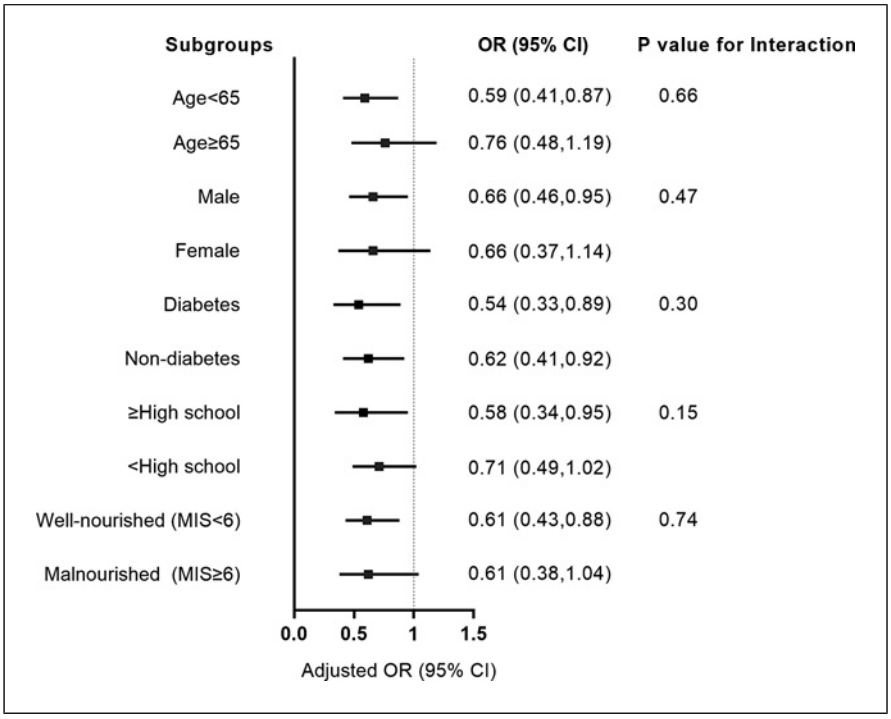

Fig. 4. Subgroup associations between PhA and depressive symptoms stratified by age, sex, diabetes, education, and nutritional status. ORs were adjusted for age, sex, education, spKt/V, dialysis vintage, CCI, MIS, albumin, and hemoglobin if not stratified. Malnutrition was defined as MIS ≥6. spKt/V, single-pool Kt/V; OR, odds ratio.

important for depressive symptoms. PhA has demonstrated the prognostic utility in multiple diseases including MHD [16, 22]. As a raw parameter of BIA, PhA measures the electrical unit of the tissue. Lower values indicate reduced cell integrity or even cell death, while higher values show an adequate health state of the whole cell membrane [25]. Pathophysiological mechanisms such as volume overload, inflammation, and oxidative stress may affect cellular health [26, 27], resulting in changes in PhA levels. These conditions make PhA a reliable and noninvasive warning indicator for HD patients.

Given that PhA is an indicator of body composition, we speculated that it might be more closely related to the somatic symptoms of depression; thus, we further analyzed the association between somatic cluster, cognitive-affective cluster, and PhA, respectively. The results showed that patients in the lower PhA group suffered both more somatic and cognitive-affective depressive symptoms. Differences in symptom improvement after effective interventions may help further clarify the strength of the link between somatic, cognitive-affective symptoms and PhA.

The cut-off values of PhA obtained from the ROC curve were ≤4.9° for males and ≤3.5° for females to detect depression in our study. So far, there is a lack of reported optimal cut-off value of PhA for depression in MHD patients. Previous studies have shown that the cut-off value of PhA for sarcopenia was 4.67° and 4.60° for males and females [28], while it was identified as a predictor of death risk at 4.50° [29]. It is important to note that PhA levels vary based on age, sex, ethnicity, and health status. Despite the lack of a universally accepted threshold for direct diagnosis of disease, the advantage of PhA lies in its real-time monitoring capability which allows for personalized assessment over time. The adjusted logistics regression model in our study showed superior discriminating performance, suggesting that in clinical practice, the combination of PhA and traditional risk factors may offer improved identification of patients at risk for depression, thereby enabling more timely and effective psychological interventions.

The study has some strengths. First, it is the largest multicenter study of PhA and depression in China to date. Moreover, we further validated the robustness of the results using restrictive cubic spline and subgroup analyses, which contribute to extrapolate our findings to similar clinical population. This study also has some limitations. This study followed a cross-sectional design. Therefore, it cannot definitively establish causal links between PhA and depressive symptoms in HD patients. Second, due to the observational nature of the study and the complexity of the disease, we were unable to rule out residual confounding, despite the inclusion of potential confounders from clinical realities and previous relevant studies.

In conclusion, our study delved into the correlation between PhA and depression, revealing an inverse association between PhA and depressive symptoms in Chinese MHD patients. We propose that PhA, as a noninvasive, reliable, and cost-effective indicator, could serve as an efficient tool for individualized assessment of depression risk in clinical practice. Subsequent research endeavors may explore the clinically significant changes in PhA through longitudinal studies and with different health interventions.

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Statement of Ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki. This study protocol was reviewed and approved by the Ethics Committee of Tongji Hospital, Approval No. K-2020-024. All the participants were informed and signed written informed consent prior to enrollment.

Conflict of Interest Statement

All authors have no conflicts of interest to declare.

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Author Contributions

X.L., K.Z., C.Y., and Q.G. designed the present study. C.Y., W.D., J.N., J.Z., L.Z., H.Q., and S.Z. acquired the data and interpreted the results. X.L. prepared the figures and tables and drafted the manuscript. Q.G. and C.Y. revised the manuscript. All authors contributed to the manuscript and approved the final version of the manuscript.

Data Availability Statement

For ethical reasons, the data generated and analyzed in this study are not publicly available. For further information, contact the corresponding author.

References

1 Cukor D, Coplan J, Brown C, Friedman S, Cromwell-Smith A, Peterson RA, et al. Depression and anxiety in urban hemodialysis patients. Clin J Am Soc Nephrol. 2007;2(3):484–90. https://doi.org/10.2215/CJN.00040107

2 Hung KC, Wu CC, Chen HS, Ma WY, Tseng CF, Yang LK, et al. Serum IL-6, albumin and co-morbidities are closely correlated with symptoms of depression in patients on maintenance haemodialysis. Nephrol Dial Transpl. 2011;26(2):658–64. https://doi.org/10.1093/ndt/gfq411

3 Tian N, Chen N, Li PK. Depression in dialysis. Curr Opin Nephrol Hypertens. 2021;30(6):600–12. https://doi.org/10.1097/MNH.0000000000000741

4 Lopes AA, Albert JM, Young EW, Satayathum S, Pisoni RL, Andreucci VE, et al. Screening for depression in hemodialysis patients: associations with diagnosis, treatment, and outcomes in the DOPPS. Kidney Int. 2004;66(5):2047–53. https://doi.org/10.1111/j.1523-1755.2004.00977.x

5 Kimmel PL, Emont SL, Newmann JM, Danko H, Moss AH. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. Am J Kidney Dis. 2003;42(4):713–21. https://doi.org/10.1016/s0272-6386(03)00907-7

6 Markaki AG, Charonitaki A, Psylinakis E, Dimitropoulakis P, Spyridaki A. Nutritional status in hemodialysis patients is inversely related to depression and introversion. Psychol Health Med. 2019;24(10):1213–9. https://doi.org/10.1080/13548506.2019.1612074

7 Yuenyongchaiwat K, Jongritthiporn S, Somsamarn K, Sukkho O, Pairojkittrakul S, Traitanon O. Depression and low physical activity are related to sarcopenia in hemodialysis: a single-center study. PeerJ. 2021;9:e11695. https://doi.org/10.7717/peerj.11695

8 Barros A, Costa BE, Mottin CC, d'Avila DO. Depression, quality of life, and body composition in patients with end-stage renal disease: a cohort study. Braz J Psychiatry. 2016;38(4):301–6. https://doi.org/10.1590/1516-4446-2015-1681

9 Tian M, Qian Z, Long Y, Yu F, Yuan J, Zha Y. Decreased intracellular to total body water ratio and depressive symptoms in patients with maintenance hemodialysis. Psychol Res Behav Manag. 2023;16:4367–76. https://doi.org/10.2147/PRBM.S436574

10 Vuckovic M, Radic J, Kolak E, Nenadic DB, Begovic M, Radic M. Body composition parameters correlate to depression symptom levels in patients treated with hemodialysis and peritoneal dialysis. Int J Environ Res Public Health. 2023;20(3):2285. https://doi.org/10.3390/ijerph20032285

11 Lukaski HC, Kyle UG, Kondrup J. Assessment of adult malnutrition and prognosis with bioelectrical impedance analysis: phase angle and impedance ratio. Curr Opin Clin Nutr Metab Care. 2017;20(5):330–9. https://doi.org/10.1097/MCO.0000000000000387

12 Han BG, Lee JY, Kim JS, Yang JW. Clinical significance of phase angle in non-dialysis CKD stage 5 and peritoneal dialysis patients. Nutrients. 2018;10(9):1331. https://doi.org/10.3390/nu10091331

13 Saitoh M, Ogawa M, Kondo H, Suga K, Takahashi T, Itoh H, et al. Bioelectrical impedance analysis-derived phase angle as a determinant of protein-energy wasting and frailty in maintenance hemodialysis patients: retrospective cohort study. BMC Nephrol. 2020;21(1):438. https://doi.org/10.1186/s12882-020-02102-2

14 Wang K, Zelnick LR, Chertow GM, Himmelfarb J, Bansal N. Body composition changes following dialysis initiation and cardiovascular and mortality outcomes in cric (chronic renal insufficiency cohort): a bioimpedance analysis substudy. Kidney Med. 2021;3(3):327–34.e1. https://doi.org/10.1016/j.xkme.2020.12.008

15 Do JY, Kim AY, Kang SH. Association between phase angle and sarcopenia in patients undergoing peritoneal dialysis. Front Nutr. 2021;8:742081. https://doi.org/10.3389/fnut.2021.742081
16 Kang SH, Do JY, Kim JC. Impedance-derived phase angle is associated with muscle mass, strength, quality of life, and clinical outcomes in maintenance hemodialysis patients. PLoS One. 2022;17(1):e0261070. https://doi.org/10.1371/journal.pone.0261070
17 Yamada Y, Watanabe K, Fujisawa C, Komiya H, Nakashima H, Tajima T, et al. Relationship between cognitive function and phase angle measured with a bioelectrical impedance system. Eur Geriatr Med. 2024;15(1):201–8. https://doi.org/10.1007/s41999-023-00894-8
18 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–13. https://doi.org/10.1046/j.1525-1497.2001.016009606.x
19 Levis B, Benedetti A, Thombs BD; DEPRESsion Screening Data DEPRESSD Collaboration. Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. BMJ. 2019;365:l1476. https://doi.org/10.1136/bmj.l1476
20 Chen X, Han P, Song P, Zhao Y, Zhang H, Niu J, et al. Mediating effects of malnutrition on the relationship between depressive symptoms clusters and muscle function rather than muscle mass in older hemodialysis patients. J Nutr Health Aging. 2022;26(5):461–8. https://doi.org/10.1007/s12603-022-1778-8
21 Vrany EA, Berntson JM, Khambaty T, Stewart JC. Depressive symptoms clusters and insulin resistance: race/ethnicity as a moderator in 2005-2010 NHANES data. Ann Behav Med. 2016;50(1):1–11. https://doi.org/10.1007/s12160-015-9725-0
22 Beberashvili I, Azar A, Sinuani I, Shapiro G, Feldman L, Stav K, et al. Bioimpedance phase angle predicts muscle function, quality of life and clinical outcome in maintenance hemodialysis patients. Eur J Clin Nutr. 2014;68(6):683–9. https://doi.org/10.1038/ejcn.2014.67
23 Fried L, Bernardini J, Piraino B. Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. Am J Kidney Dis. 2001;37(2):337–42. https://doi.org/10.1053/ajkd.2001.21300
24 Marini ACB, Pimentel GD. Is body weight or muscle strength correlated with the Malnutrition Inflammation Score (MIS)? A cross-sectional study in hemodialysis patients. Clin Nutr ESPEN. 2019;33:276–8. https://doi.org/10.1016/j.clnesp.2019.07.009
25 Garlini LM, Alves FD, Ceretta LB, Perry IS, Souza GC, Clausell NO. Phase angle and mortality: a systematic review. Eur J Clin Nutr. 2019;73(4):495–508. https://doi.org/10.1038/s41430-018-0159-1
26 Bellido D, Garcia-Garcia C, Talluri A, Lukaski HC, Garcia-Almeida JM. Future lines of research on phase angle: strengths and limitations. Rev Endocr Metab Disord. 2023;24(3):563–83. https://doi.org/10.1007/s11154-023-09803-7
27 da Silva BR, Orsso CE, Gonzalez MC, Sicchieri JMF, Mialich MS, Jordao AA, et al. Phase angle and cellular health: inflammation and oxidative damage. Rev Endocr Metab Disord. 2023;24(3):543–62. https://doi.org/10.1007/s11154-022-09775-0
28 Ding Y, Chang L, Zhang H, Wang S. Predictive value of phase angle in sarcopenia in patients on maintenance hemodialysis. Nutrition. 2022;94:111527. https://doi.org/10.1016/j.nut.2021.111527
29 Xu Y, Ling S, Liu Z, Luo D, Qi A, Zeng Y. The ability of phase angle and body composition to predict risk of death in maintenance hemodialysis patients. Int Urol Nephrol. 2024;56(2):731–7. https://doi.org/10.1007/s11255-023-03708-9