

CLINICAL STUDY

Sarcopenia in patients undergoing maintenance hemodialysis: incidence rate, risk factors and its effect on survival risk

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ABSTRACT

Background Sarcopenia is a degenerative syndrome mainly characterized by the atrophy of skeletal muscle, along with the decrease of muscle strength and function. However, there are currently few studies concerning sarcopenia in patients undergoing maintenance hemodialysis (MHD). This study was aimed to investigate the incidence of sarcopenia in MHD patients and its influencing factors, as well as its impact on survival risk. **Method** All 131 MHD patients enrolled in our study were tested with bioelectrical impedance analysis (BIA) and grip strength. Demographic data was collected and anthropometric measurement and laboratory examination were conducted. **Results** The total incidence of sarcopenia within the 131 MHD patients was 13.7% and the incidence of sarcopenia in patients over 60 years was 33.3%. The dialysis duration, with or without diabetes, serum phosphorus and pre-albumin levels of sarcopenic patients were significantly different from those of non-sarcopenic ones; the modified quantitative subjective global assessment (MQSGA) scores of sarcopenic patients were higher than those without sarcopenia. Multivariate analysis showed that dialysis duration, diabetes and serum phosphorus level were independent risk factors for sarcopenia in MHD patients. Kaplan–Meier survival analysis showed a one-year survival of 88.9% in sarcopenic patients, which was significantly lower than non-sarcopenic patients. **Conclusion** The incidence of sarcopenia in MHD patients was high and increased gradually with age. Dialysis duration, diabetes, serum phosphorus level and malnutrition predisposed the patients to sarcopenia. One-year follow-up found that the mortality risk of sarcopenic patients was higher than that of non-sarcopenic patients.

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Introduction

Sarcopenia is a degenerative syndrome mainly characterized by the atrophy of skeletal muscle, along with the decreases of muscle strength and function.¹ With the deterioration of renal function, uremic patients may present with a reduction of muscle strength, a selective change of muscle structure and a significant muscle atrophy, making them more prone to sarcopenia.^{2,3} Uremia with concomitant sarcopenia will not only change the lifestyle of the patients and reduce their life quality, but will also increase cardiovascular complications and mortality rate, and therefore renders more awareness of the clinicians.⁴

Currently, unified testing methods and diagnostic criteria for uremic sarcopenia are lacking, the diagnosis of this condition mainly refers to the diagnostic criteria established by the European Working Group on

Sarcopenia in Older People (EWGSOP).¹ Muscle mass can be measured through many ways including methods of dual energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA). The operation of DXA method is complicated and the results measured by BIA are closed to those measured by DXA. Therefore, it is convenient to choose the combination of BIA and hand grip strength (HGS) for the diagnosis of sarcopenia.

There are few reports providing the incidence of sarcopenia in patients undergoing maintenance hemodialysis (MHD). Kim et al.⁵ studied the incidence of sarcopenia in 95 MHD patients over 50 years old (mean age 63.9 ± 10.0 years) using the EWGSOP diagnostic criteria and discovered a 37% incidence in male and a 29.3% incidence in female. Lamarca et al.⁶ enrolled 102 MHD patients of over 60 years old in a different way and found that the incidence of sarcopenia in those

patients was 3.9–63.3%. The pathogenesis of sarcopenia in MHD patients is still not clear, multiple factors are possibly involved, such as the increase of pro-inflammatory cytokines, insufficient protein intake and insulin resistance.⁴

In the present cross-sectional study, we chose the combination of BIA and HGS for the diagnosis of sarcopenia, and we aimed to investigate the incidence of sarcopenia, possible risk factors and its impact on survival risk in MHD patients.

Subjects and methods

Subjects

Participants were selected from patients undergoing MHD in the blood purification center of our hospital during May–July 2014. Inclusion criteria were: (1) age ≥ 18 years; (2) receiving maintenance hemodialysis for at least 6 months. Exclusion criteria: (1) patients with expected survival time less than 6 months; (2) those who underwent parathyroidectomy or had confirmed diagnosis of malignancies; (3) bioelectrical impedance test could not be performed, such as patients who underwent cardiovascular stent implantation, pacemaker installation, artificial joint replacement or amputation surgery, as well as patients of severe peripheral angiopathy; (4) patients with history of surgery, trauma or serious infection within 3 months; (5) pregnant or lactating women; (6) patients refused to participate and transferred to other centers.

Selected patients were given hemodialysis and hemodiafiltration treatments using machines of the German Braun Dialog, Fresenius 4008B and 4008s. The REXEED-15UC high-flux polysulfone membrane dialyzer was used with membrane area of 1.5 m², blood flow of 220–300 mL/min and the dialysis time of 4 h. Ultra-pure water dialysate was used and the dialysate concentration was: Na⁺ 138.6 mmol/L, K⁺ 2.0 mmol/L, Ca²⁺ 1.5 mmol/L, Mg²⁺ 0.5 mmol/L, Cl⁻ 102.6 mmol/L, AC⁻ 9.0 mmol/L, and HCO₃⁻ 33 mmol/L. Dialysate flow was 500 mL/min. The body weight, blood pressure and ultrafiltration volume of patients were recorded before and after dialysis. All the selected patients had given informed consent to participate. This study had been reviewed by the Ethics Committee of the Jinling Hospital.

Methods

Enrollment of the patients

Gender, age, dialysis duration and mode, primary diseases, dialysis records and concomitant diseases of all selected patients were documented.

Laboratory examination

Venous blood samples were taken one day after dialysis in fasting state for the testing of the following indicators: routine blood test, plasma albumin and pre-albumin levels, renal function tests, fasting blood glucose, blood fat, high-sensitivity C-reactive protein (hsCRP), homocysteine, serum intact parathyroid hormone (iPTH) and 25-hydroxy Vitamin D [25 (OH) Vitamin D]. Blood urea nitrogen was tested before and after dialysis, Kt/V and normalized protein catabolic rate (nPCR)⁷ were calculated separately.

$$Kt/V = -\ln(R-0.03) + (4 - 3.5 \times R) \times UF/W$$

$$(R = \text{BUN after dialysis} / \text{BUN before dialysis};$$

UF = ultrafiltration volume; W = body weight after dialysis)

$$nPCR = C_0 / (36.3 + 5.48 \times Kt/V + 53.5 / Kt/V) + 0.168$$

(C₀ = BUN before dialysis)

The Modified Quantitative Subjective Global Assessment (MQSGA)

Kalantar-Zadeh K and other modified subjective global nutritional assessment methods were used along with patient's condition and results of physical and laboratory examinations, adding up to seven parts with total score ranging from 7 to 35 points (each part ranges from 1 to 5 points). The nutritional assessments were conducted by two experienced doctors. Higher SGA score indicates worse nutritional situation.⁸

Anthropometric measurements

All patients were measured for body height, HGS, triceps skin fold (TSF), mid-upper arm circumference (MAC) and mid upper arm muscle circumference (MAMC). Among which, TSF was measured using HGKJ sebum clamp (provided by Fresenius Kabi Company, Germany), MAC was measured at the midpoint between acromion and olecranon using standard tape (provided by Fresenius Kabi Company, Germany). MAMC (cm) = MAC – $\pi \times$ TSF (cm). HGS was measured using the Camry Electronic Dynamometer (provided by Guangdong Xiangshan Weighing Apparatus Group, China). TSF, MAC and HGS measurements were all conducted on the non-fistula side by two experienced doctors the next day after dialysis, the measurements were conducted twice continuously for the mean values.

Bioelectrical impedance analysis

A multi-frequency BIA device (Bodystat QuadScan 4000, UK) was used one hour before dialysis. Patients were in

supine position and electrodes were placed in the forearm and ankle on the non-fistula side. Resistances and reactances were measured under discrete frequencies of 5, 50, 100 and 200 kHz. Blood cell mass (BCM), lean body mass (LBM), the percentage of lean body mass (LM%) and fat mass (FM), as well as the percentage of fat mass (FM%), phase angle (PA), fat-free weight (FFM) and fat-free body mass index (FFMI) were calculated according to the formulae. All calculations were completed based on the customized software built in the device. In addition, the nutritional status of patients was further analyzed using the vector method.

Diagnostic criteria of sarcopenia and grouping of patients

Referring to the diagnostic criteria established by EWGSOP, sarcopenia was diagnosed if the following two criteria were met¹: (1) Muscle mass: The skeletal muscle mass index (SMI) of normal male and female measured by BIA is $SMI \geq 10.76 \text{ kg/m}^2$ and $SMI \geq 6.76 \text{ kg/m}^2$, respectively; moderate sarcopenic is diagnosed when the SMI of male and female is $8.51\text{--}10.75 \text{ kg/m}^2$ and $5.76\text{--}6.75 \text{ kg/m}^2$, respectively; severe sarcopenia is diagnosed when the SMI of male and female is $SMI \leq 8.50 \text{ kg/m}^2$ and $SMI \leq 5.75 \text{ kg/m}^2$, respectively. (2) Muscle strength: commonly evaluated using HGS, the HGS of male and female sarcopenic patients are $HGS < 30 \text{ kg}$ and $HGS < 20 \text{ kg}$, respectively. Based on the diagnostic results, all patients were divided into sarcopenia group and non-sarcopenia group and followed up for one year.

Statistical analyses

Experimental data was statistically analyzed using SPSS 18.0 software (version 18.0, SPSS Inc, Chicago, IL). The normal distributed measurement data was presented as mean $\pm$ standard deviation ($\bar{X} \pm S$), non-normal distributed data was presented as median and interquartile range. The measurement data between the two groups were compared using independent sample *t* test. The categorical data between the two groups were compared using chi-square test (χ^2 test) with Fisher's exact test. Nutritional factors were analyzed using binary Logistic regression analysis, the included criteria for variants of univariate and multivariate were $p \leq 0.20$ and $\alpha = 0.05$, respectively, and the exclusion criteria was $\alpha = 0.10$. Survival analysis was conducted using the Kaplan–Meier method and compared using a log-rank test. Difference was considered existed if $p < 0.05$, the difference was considered significant if $p < 0.01$.

Results

General information

A total of 137 patients participated in the screening, among which 131 eligible patients were enrolled in the study. The patients enrolled included 80 males (61.1%) and 51 females (38.9%) aged 49.4 ± 11.7 years (23–72 years), and their dialysis duration was 5.94 ± 4.76 (0.5–23) years. The primary diseases of the enrolled patients were: 50 patients had primary glomerular disease (38.2%), 16 had hypertensive renal damage (12.2%), 11 had hereditary renal disease (8.39%), 10 had diabetic nephropathy (7.63%), seven had lupus nephritis (5.34%), four had interstitial nephritis (3.05%), and 33 had unknown diagnoses (25.2%). Among the enrolled patients, 115 had hemodialysis and 16 had hemodiafiltration. The Kt/V was 1.57 ± 0.32 and the mean body weight was $61.9 \pm 10.6 \text{ kg}$.

Six patients, who were unable to undergo bioelectrical impedance test, were excluded. One patient developed septic shock, one patient underwent stent placement because of right subclavian phlebostenosis, three patients were transferred to other centers, and one patient underwent artificial joint replacement.

Incidence of sarcopenia

Eighteen of the 131 patients met diagnostic criteria, thus the incidence of sarcopenia of 13.7% was calculated with an average age of 56.4 ± 10.3 years, among which were 12 males and six females, i.e., the incidences of sarcopenia in male and female patients were 15% and 11.8%, respectively.

Further analysis showed that there were 11 patients fitting the diagnostic criteria among the 61 patients aged over 50, i.e., the incidence of sarcopenia was 18% in this subgroup, among which seven were male and four were female, i.e., the incidence of sarcopenia for male and female were 18.4% and 17.4%, respectively; there were eight patients fitting in the diagnostic criteria among the 24 patients aged over 60, the incidence was 33.3% in this subgroup, among which were six males and two females, and the incidences of sarcopenia for male and female were both 33.3% (Figure 1).

Two of all the patients met the diagnostic criteria of severe sarcopenia, they were both male patients and their SMI were 8.31 kg/m^2 and 7.96 kg/m^2 , respectively, and the incidence was 1.53%.

General information, MQSGA and anthropometric results of the two groups

Table 1 shows the significant differences between the two groups in the aspects of age, dialysis duration and

the presence of diabetes, while there was no difference in the aspects of gender, dialysis mode, body weight and blood pressure. In addition, the comparison of the medication compliances among the two groups taking phosphate binders, calcitriol and calcimimetics showed no significant statistical difference.

Compared with non-sarcopenia group, the MQSGA score of sarcopenia group was higher and the difference was statistically significant. However, other anthropometric indexes, namely TSF, BMI, MAC and MAMC, between the two groups showed no statistically significant difference.

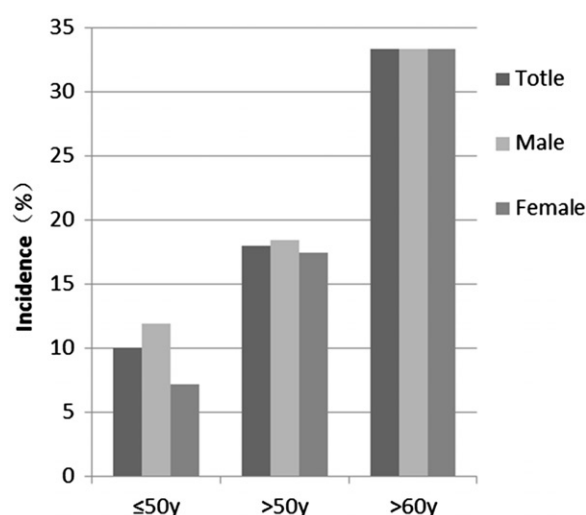


Figure 1. Incidence of sarcopenia in patients of different ages.

Comparison of the nutrition indicators measured by BIA between the two groups

Besides BCM, all the other BIA indicators such as LBM, LM%, FM and FM%, as well as PA, FFM, and FFMI showed statistically significant differences between the two groups, among which the LBM, LM%, PA, FFM and FFMI of the sarcopenia group were lower than those of non-sarcopenia group, while the FM and FM% were higher (Table 2).

Vector analysis found that the 18 patients in the sarcopenia group were all distributed in the malnourished and emaciated sections, while 58 of 113 patients in the non-sarcopenia group were distributed in the same section, the difference between the two groups was statistically significant ($\chi^2 = 15.1$, $p < 0.001$). In the malnourished and emaciated section, 10 (55.6%) patients distributed outside the 75% range in the sarcopenia group, while the number in the non-sarcopenia group was two (1.77%). The difference between the two groups was statistically significant ($\chi^2 = 53.9$, $p < 0.001$) (Figure 2).

Laboratory examination results of the two groups

The serum phosphorus, pre-albumin and calcium-phosphorus product of patients in the sarcopenia group were lower than the non-sarcopenia group, while the fasting plasma glucose level was higher, the differences between the two groups were statistically significant. Other indicators between the two groups showed no statistically significant difference (Table 3).

Table 1. General information, MQSGA and anthropometric results of MHD patients.

	All patients (N = 131)	Sarcopenic patients (N = 18)	Non-sarcopenic patients (N = 113)	p-Values
Gender (M/F)	80/51	12/6	68/45	0.599
Age (y)	49.4 ± 11.7	56.4 ± 10.3	48.3 ± 11.5	0.006
Dialysis duration (year)	5.94 ± 4.76	8.66 ± 7.52	5.51 ± 4.04	0.008
Dialysis mode (HD/HDF)	115/16	14/4	101/12	0.162
Diabetes (n, %)	10 (7.63%)	4 (22.2%)	6 (5.31%)	0.012
Concomitant medication				
Calcium carbonate (n, %)	75 (57.3)	11 (61.1)	64 (56.6)	0.723
Lanthanum carbonate (n, %)	8 (6.11)	1 (5.56)	7 (6.19)	0.916
Calcitriol (n, %)	82 (62.6)	11 (61.1)	71 (62.8)	0.888
Cinacalcet (n, %)	4 (3.05)	0 (0.00)	4 (3.54)	0.417
Body weight (kg)	61.9 ± 10.6	61.7 ± 11.8	62.0 ± 10.4	0.921
SBP (mmHg)	144.9 ± 19.8	145.6 ± 20.3	144.8 ± 19.8	0.873
DBP (mmHg)	86.9 ± 13.5	85.6 ± 13.1	87.1 ± 13.6	0.659
MQSGA	10.6 ± 1.77	11.4 ± 1.97	10.5 ± 1.72	0.047
TSF (mm)	14.4 ± 6.79	14.2 ± 6.69	13.9 ± 6.35	0.852
MAC (cm)	26.5 ± 2.75	25.8 ± 3.09	26.7 ± 2.67	0.235
MAMC (cm)	21.8 ± 3.10	21.4 ± 2.38	22.1 ± 2.44	0.243
BMI (kg/m ²)	22.8 ± 3.16	22.8 ± 3.29	22.8 ± 3.15	0.986

Notes: MQSGA, modified quantitative subjective global assessment; TSF, triceps skin fold; MAC, mid-upper arm circumference; MAMC, mid upper arm muscle circumference; BMI, body mass index.

Table 2. Comparison of the nutrition indicators measured by bioelectrical impedance analysis between sarcopenia and non-sarcopenic patients.

	All patients (N = 131)	Sarcopenic patients (N = 18)	Non-sarcopenic patients (N = 113)	p-Value
LBM (kg)	31.9 ± 8.57	22.8 ± 5.61	33.4 ± 8.07	0.000
LBM (%)	51.9 ± 12.8	37.6 ± 8.96	54.2 ± 11.9	0.000
BCM (kg)	28.4 ± 5.92	26.9 ± 5.53	28.6 ± 5.97	0.272
FM (kg)	26.5 ± 10.5	34.4 ± 11.2	25.2 ± 9.88	0.000
FM % (%)	42.2 ± 13.4	55.3 ± 10.5	40.1 ± 12.7	0.000
Phase angle (50 K)	5.13 ± 0.94	4.09 ± 0.57	5.29 ± 0.87	0.000
FFM (kg)	35.4 ± 8.74	27.3 ± 6.24	36.7 ± 8.39	0.000
FFMI (kg/m ²)	12.9 ± 2.65	10.1 ± 1.81	13.4 ± 2.48	0.000

Notes: LBM, lean body mass; LBM, the percentage of lean body mass; BCM, blood cell mass; FM, fat mass; FM%, the percentage of fat mass; FFM, fat-free weight; FFMI, fat-free body mass index.

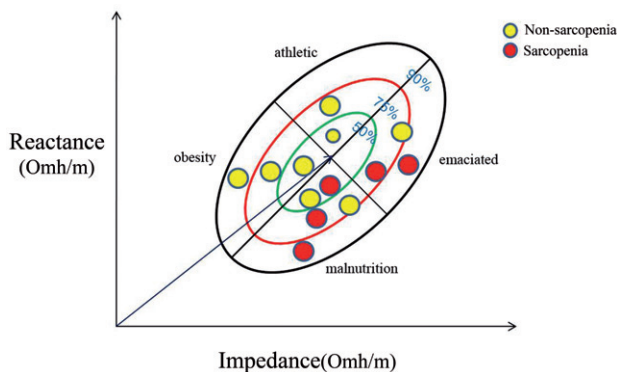


Figure 2. Comparison of the bioelectrical impedance analysis of sarcopenia group and non-sarcopenia group through vector method.

Multivariate analysis

In order to further clarify the risk factors for sarcopenia in patients undergoing hemodialysis to develop, we defined the critical point as whether sarcopenia existed or not and performed binary Logistic regression analysis. Univariate regression analysis was performed first with $p \leq 0.20$ as the significant level and variables such as age, dialysis duration, MQSGA, as well as diabetes, serum phosphorus, albumin and pre-albumin levels were entered into the regression equation. The results showed that dialysis duration, diabetes and serum phosphorus levels were independent risk factors for developing sarcopenia in MHD patients (Table 4).

Survival analysis of the two groups

After one year of follow-up, two patients of the sarcopenia group died with a mortality rate of 11.1%, and only one patient of the non-sarcopenia group died with the mortality rate of 0.88%. Kaplan–Meier survival analysis showed a 88.9% one-year survival rate in the sarcopenia group, which was significantly lower than that in the non-sarcopenia group ($p = 0.007$) (Figure 3).

Discussion

Our study found that the incidence of sarcopenia in MHD patients was 13.7% (15% and 11.8% in males and females, respectively). Age was reported to be closely related to the incidence of sarcopenia.^{2,9} Therefore, we stratified subjects by age and further study found that the incidence of sarcopenia was 18.0% in patients over 50 and 33.3% in patients over 60. The results of our study were consistent with those of Lamarca et al.⁶

The pathogenesis of sarcopenia is still not clear, previous studies have reported that sarcopenia may be associated with multiple factors including the increase of pro-inflammatory cytokines and the decrease of protein intake, exercises, sex and growth hormones, insulin and Vitamin D levels, as well as the reduction of stellate cells.^{4,10–12} There are few reports discussing the pathogenesis of sarcopenia in MHD patients. Kim et al.⁵ reported that sarcopenia of MHD patients was mainly associated with MQSGA, hsCRP and β 2-microglobulin and relatively irrelevant with age, diabetes, hemoglobin, blood lipids, albumin, pre-albumin, spKt/V, nPCR and intact PTH.

In order to identify the risk factors of sarcopenia in MHD patients, we separated all subjects into two groups, sarcopenia and non-sarcopenia group. Our study found that there were significant differences between the two groups in terms of age, dialysis duration, diabetes, serum phosphorus, calcium-phosphorus product, pre-albumin, fasting plasma glucose and MQSGA. Further analysis using binary Logistic regression method showed that dialysis duration, diabetes and serum phosphorus level were independent risk factors for developing sarcopenia in MHD patients. The reason for the inconsistent results of our study compared to that of Kim et al.⁵ was mainly because the average age of our subjects was over 18, while the average age of their subjects was over 50. Meanwhile, the numbers of enrolled patients were different, our study had 131 patients while their study only had 95,

Table 3. Laboratory examination results of sarcopenia and non-sarcopenic patients.

	All patients (N = 131)	Sarcopenic patients (N = 18)	Non-sarcopenic patients (N = 113)	p-Value
Hb (g/L)	120.4 ± 20.6	119.2 ± 17.3	120.6 ± 21.2	0.791
Hct (%)	37.0 ± 6.99	36.5 ± 4.99	37.1 ± 7.27	0.723
BUN (mg/dL)	69.8 ± 15.8	65.6 ± 19.1	70.5 ± 15.1	0.224
SCr (mg/dL)	10.1 ± 3.88	8.77 ± 3.43	10.3 ± 3.92	0.114
UA (μmol/L)	346.4 ± 90.6	354.9 ± 82.5	345.1 ± 92.2	0.670
Ca (mmol/L)	2.46 ± 0.21	2.44 ± 0.21	2.46 ± 0.21	0.662
P (mmol/L)	1.66 ± 0.44	1.36 ± 0.43	1.71 ± 0.43	0.002
IgPTH	2.59 ± 0.42	2.56 ± 0.47	2.59 ± 0.42	0.752
25(OH)VitD	26.5 ± 10.7	23.7 ± 9.75	26.9 ± 10.8	0.240
Glu (mmo/L)	5.34 ± 2.32	6.69 ± 5.51	5.13 ± 1.15	0.007
ALB (g/L)	47.2 ± 3.54	45.8 ± 3.09	47.4 ± 3.57	0.096
Pre-ALB (g/L)	341.2 ± 62.5	304.5 ± 62.3	347.1 ± 60.7	0.007
TCH (mmol/L)	4.77 ± 0.99	4.61 ± 0.96	4.79 ± 1.00	0.491
TG (mmol/L)	1.70 ± 0.88	1.60 ± 0.57	1.72 ± 0.92	0.595
HDL (mmol/L)	0.85 ± 0.29	0.85 ± 0.37	0.85 ± 0.28	0.958
LDL (mmol/L)	2.48 ± 0.74	2.43 ± 0.70	2.49 ± 0.74	0.743
hsCRP (μg/mL)	2.3 (0.9,5.0)	1.9 (0.9,4.1)	2.3 (0.9,5.1)	0.674
Homocysteine (μmol/L)	34.1 ± 26.4	42.9 ± 23.9	32.7 ± 26.6	0.131
nPCR (g/kg/d)	1.04 ± 0.21	0.99 ± 0.28	1.05 ± 0.19	0.253
Kt/V	1.57 ± 0.32	1.58 ± 0.46	1.57 ± 0.29	0.941

Notes: Hb, hemoglobin; Hct, hematocrit; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; iPTH, intact parathyroid hormone; Glu, fasting blood glucose; ALB, albumin; Pre-ALB, pre-albumin; TCH, cholesterol; TG, triglycerides; HDL, high density lipoprotein; LDL, low density lipoprotein; hsCRP, high-sensitivity C-reactive protein; nPCR, normalized protein catabolic rate.

Table 4. Univariate and multivariate logistic regression analysis of sarcopenia.

	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR (95% CI)	p-Values	OR (95% CI)	p-Values
Age	1.07 (1.02–1.12)	0.008		
Dialysis duration	1.12 (1.02–1.21)	0.014	1.10 (1.00–1.21)	0.047
MQSGA	1.31 (0.98–1.72)	0.051		
DM	5.09 (1.28–20.3)	0.021	7.64 (1.70–34.3)	0.008
P	0.11 (0.03–0.47)	0.003	0.13 (0.03–0.67)	0.014
ALB	0.88 (0.75–1.02)	0.098		
Pre-ALB	0.98 (0.98–1.00)	0.009		

Note: ALB, albumin; pre-ALB, pre-albumin.

besides, indicators such as dialysis duration, calcium and phosphorus levels were not analyzed in their study.

Dialysis duration was closely related to the development of sarcopenia in MHD patients mainly because MHD patients had several pathological states such as hormone imbalance, malnutrition, loss of ATP and glycogen, oxygen transportation disorder caused by anemia, metabolic acidosis, electrolyte disturbance, lifestyle changes and muscle atrophy,^{4,13} all of which were closely related to the development of sarcopenia. Thus, longer dialysis duration was associated with higher sarcopenia incidence.

Our study found that compared with non-sarcopenic patients, the fasting plasma glucose levels of sarcopenic patients were significantly higher, and that diabetes was an independent risk factor for sarcopenia. Previous studies have reported that insulin resistance was related to the development of uremic myopathy, and higher incidence with higher severity of uremic myopathy in diabetic patients undergoing dialysis was found, mainly

because insulin resistance would not only inhibit the release of insulin, reduce the use of glycogen as energy resource, increase hepatic glycogen production, but will also reduce the glycogen uptake of liver and/or skeletal muscle and damage glycogen metabolism within the cells.¹⁴ Besides, insulin resistance could also increase the degradation of muscle protein through the UPS pathway.¹⁵

The development of sarcopenia was often closely related to malnutrition.^{9,16} Protein-energy wasting (PEW) of CKD patients had an incidence of about 18–75%, manifesting as the reduction of proteins in the circulating system and the loss of body weight and muscle mass.¹⁷ MQSGA includes subjective and objective scores, its role in the evaluation of nutritional status of hemodialysis patients has been widely validated. It is recommended by KDOQI to be used in the evaluation of the nutritional status of adult hemodialysis patients.^{8,18,19} Our study found that traditional indicators of nutritional status such as BMI, TSF, MAC, MAMC and ALB, as well as TCH, TG, HDL and LDL, were not closely related to sarcopenia. However, we found that the MQSGA scores of sarcopenia group were higher than those of non-sarcopenia group, indicating that the patients with sarcopenia had poorer nutritional status. Besides, we found that the serum pre-albumin levels of sarcopenia group were significantly lower than those of non-sarcopenia group, and that pre-albumin was a sensitive early indicator of malnutrition, as well as an independent risk factor predicting the death of MHD patients.^{20,21}

BIA is also widely used to evaluate the nutritional status of hemodialysis patients, among which PA and

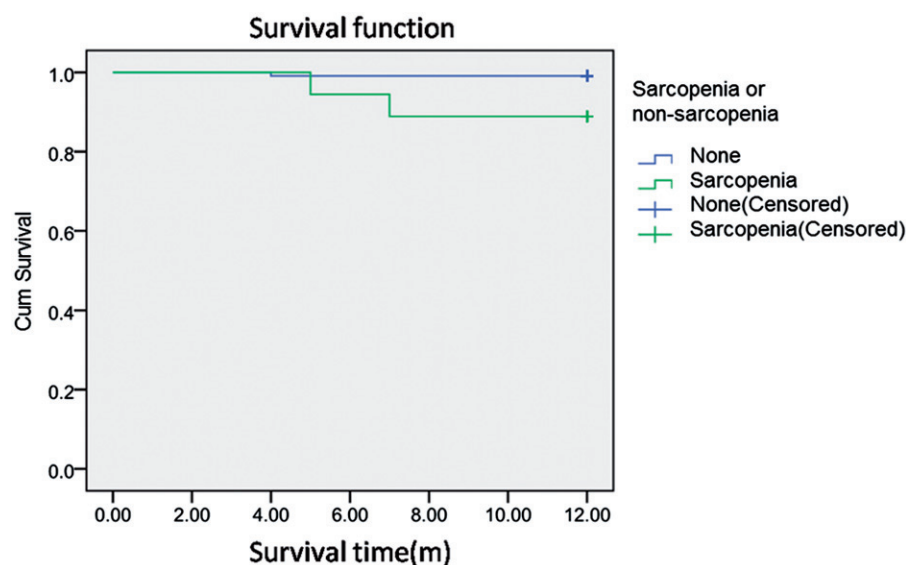


Figure 3. The influence of sarcopenia on survival rates.

FFM are the main indicators reflecting the nutritional status, the lower the PA and FFM are, the higher the FM and FM% are, and the worse the nutritional status is.^{22,23}

To further evaluate the nutritional status of sarcopenic patients, we once again analyzed the BIA indicators which reflected nutritional status and found that indicators of LBM, LM% and PA, as well as FFM and FFMI of the sarcopenia group were all lower than those of the non-sarcopenia group, while indicators of FM and FM% were higher; in addition, vector analysis also found that patients of the sarcopenia group were all distributed in the malnourished and emaciated section, which further demonstrated that the development of sarcopenia was closely related to malnutrition.

Normalized protein catabolic rate (nPCR), often used for the estimation of dietary protein intake, is one of the common indicators reflecting the nutritional status of MHD patients. However, in our study, nPCR were not significantly different between the sarcopenic group and the non-sarcopenic group. This is mainly because nPCR also has its limitations as an indicator, evaluating patients' dietary protein intake, although nPCR of most patients have a correlation with dietary protein intake, nPCR may overestimate the protein intake of patients with actually lower intake (<0.8 g/kg), while underestimate patients with high dietary protein intake (>1.2 g/kg).²⁴

Hyperphosphatemia is commonly seen in MHD patients and is closely related to the risks of vascular calcification and cardiovascular death. However, our study found that the serum phosphorus level of sarcopenic group was lower than that of non-sarcopenic group, while the comparisons of serum calcium, 25(OH)

Vitamin D and PTH, as well as the medication compliance of phosphate binders, calcitriol and calcimimetics between the two groups showed no significant difference. The possible reason is that high-protein diet is the main source of dietary phosphorus, and uremic patients are often accompanied with the loss of appetite and even anorexia. The reduction of food intake will certainly lead to the decrease of patients' serum phosphorus, malnutrition and protein-energy consumption, and eventually causing the development of sarcopenia.^{25,26}

Previous studies suggested that micro-inflammatory state was one of the reasons for MHD patients to develop sarcopenia,²⁷ while our study found no significant difference between the patients' hsCPR of the two groups, which might be partly explained by the fact that all patients in our center were under high-flux dialysis and ultra-pure water.

It is reported that sarcopenia would cause an increased mortality rate in uremic patients.⁴ However, few studies regarding the influence of sarcopenia on the mortality risk of MHD patients was reported. After a one-year follow-up, we found that the mortality rate of the sarcopenia group was 11.1% and the one-year survival rate of the sarcopenia group was 88.9%, which were significantly lower than those of the non-sarcopenia group, thus further demonstrating that sarcopenia is a risk factor for the mortality of MHD patients.

The limitations of our study are the small sample size due to its nature as a single-center cross-sectional study. In addition, the period of follow-up was only one-year. Thus, larger-scale multi-center cohort studies are needed to further clarify the incidence and possible influence factors of sarcopenia, and to conduct long-term

follow-ups for further investigation of its influence on the mortality risk.

Declaration of interest

The authors declare that they have no competing interests.

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