Determinants of Sarcopenia in Elderly Patients with Chronic Kidney Disease

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Introduction. This study was conducted to determine the factors affecting the development of sarcopenias in elderly patients with chronic kidney disease (CKD), in order to provide future clinical reference and guidance in preventing the occurrence of sarcopenias in patients with CKD.

Methods. We included 116 CKD patients admitted to affiliated Hospital of Hebei University for retrospective analysis between September 2019 and March 2022. Fifty-one CKD patients with sarcopenias were selected as the observation group (OG) and 65 CKD patients without sarcopenias were considered as the control group (CG). Clinical baseline data such as age and sex were recorded, venous blood was collected for routine examination, and a multi-frequency body composition analyzer was applied to measure patients' body composition. Grip strength, middle arm circumstances (MAC) and triceps skin-fold thickness (TSF) were also measured. Then, patients' sleep quality, nutritional status and negative psychological status were assessed by using the Pittsburgh Sleep Quality Index (PSQI), Malnutrition inflammation score (MIS), and Self-rating Anxiety/Depression Scale (SAS/SDS), respectively. Differences in test results were compared inter-group, and the factors affecting the occurrence of sarcopenias in CKD patients were analyzed by multiple Logistic regression.

Results. OG patients were older than CG patients, with a higher number of female patients. Their BMI, bone mass, MAC, serum creatinine (Scr), uric acid (UA) and triglyceride (TG) were lower ($P < .05$). According to multiple Logistic regression analysis, age, as well as PSQI, MIS, SAS, and SDS scores were the risk factors for sarcopenias in CKD, while BMI, bone mass, MAC, Scr, UA and TG were protective factors ($P < .05$).

Conclusion. Age, poor sleep quality, poor nutritional status and negative emotions are independent risk factors for sarcopenias in CKD patients, while BMI, bone mass, MAC, UA, TG, and Scr are independent protective factors.

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Original Paper

INTRODUCTION

Chronic kidney disease (CKD) is a common diseases with a prevalence rate, showing a constantly increasing trend.[1] In 2019, the incidence of CKD among adults over 18 years old was about 10%. Worldwide; [2] sixty percent of them would

eventually progress to the end-stage kidney disease (ESKD).[3] Maintenance hemodialysis can effectively remove toxins and maintain the homeostasis of body compositions in ESKD patients.[4] As the renal function deteriorates, patients with ESKD gradually experience muscle weakness, changes in the muscle structure, and a reduction in muscle mass, known as sarcopenias.[5] The incidence of sarcopenias has been reported to be about 7 to 20% in patients with CKD and 40% in ESKD patients.[6] Sarcopenia can lead to motor dysfunction an increase in the risk of fractures, falls, and cardiovascular complications, thereby seriously compromising patients' quality of life.[7] Previous studies have shown that sarcopenias increases the risk of death in patients with liver cirrhosis and heart failure by 6 to 8 folds.[8,9] Therefore, we should pay more attention to sarcopenias in patients with CKD or ESKD to ensure patient safety and to limit harm. However, except for few primary research such as Moorthi RN *et al.*, who investigated the potential factors leading to sarcopenias in patients with CKD, did not provided a definitive and reliable clinical case study.[10] In the face of the increasing prevalence of CKD and frequent occurrence of sarcopenias in these patients, detecting the potential pathogenic factors which could provide a reliable guide for prevention and treatment of patients is required to ensure the safety of patients.

In this study, we aimed to investigate factors related to the occurrence of sarcopenias in CKD patients to fill the gap in the research related to CKD and sarcopenias and provide a reliable foundation for the future studies.

MATERIALS AND METHODS

Patient Information

We included 116 CKD patients admitted to affiliated Hospital of Hebei University for retrospective analysis between September 2019 and March 2022 CKD patients with sarcopenias were as assigned to observation group (OG; n = 51) and those without sarcopenias were assigned to the control group (CG; n = 65). All study participants signed a written informed consent, and this research strictly followed the *Declaration of Helsinki*.

Criteria for Patient Enrollment

All CKD patients, aged above 60, with complete medical records, the ability to walk independently and communicate normally, were enrolled in this study.[11] The exclusion criteria were: central nervous system disease, neuromuscular disorders, long-term bedridden, inability to take care of themselves, liver diseases, severe cardiovascular diseases, malignant tumors, immune deficiency diseases, history of surgery or chemoradiotherapy in the past six months, metal implants in the body, and amputation of limbs.

Sarcopenias Diagnostic Criteria[12]

The sarcopenias diagnostic criteria were: appendicular skeletal muscle mass index (ASMI) < 7 kg/m^2 in males and < 5.7 kg/m^2 in females indicated by bioelectrical impedance analysis, hand grip strength (HGS) < 26 kg in males and < 18 kg in females, six meters walking test speed < 0.8 m/s. Patients who had one of the above-mentioned criteria were considered as early-stage sarcopenias. Patients meeting two criteria were considered mid-stage sarcopenias, and those who fulfilled all three criteria were classified as severe sarcopenias.

Basic Information on the Subject of the Study

Patients' baseline data, including age, gender, marital status, smoking, alcohol use, and area of residence, were collected and stored as electronic documents.

Specimen Collection and Testing

Blood samples from peripheral vein was collected and sent to laboratory for the examination of blood urea nitrogen (BUN), serum creatinine (Scr), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), hemoglobin (Hb), platelet (PLT), C-reactive protein (CRP), white blood cells (WBC) count, red blood cells count (RBC), and uric acid.

Physical Examination

Patients' body composition was measured with the use of a multi-frequency body composition analyzer (Beijing Xinruikang Technology Co., Ltd.). They were required to remove excess metal accessories and electronic devices before the examination. Patients' height and weight were measured barefoot to calculate body mass index (BMI), calculated with the use of weight (kg) / height (m^2) formula. After disinfection of the electrodes of the instrument by alcohol, each

patient was asked to stand barefoot on the foot electrode, and hold the handle with both hands with slightly extended arms. The patient's basic information (number, sex, age, height) was recorded before initiation of the study. No conversation or activity was allowed during the test, which took about 30 to 60 seconds. Patients' hand grip strength was evaluated by using an electronic grip meter. They were asked to hold the instrument with the hand other than the side with arterio-venous fistula (AVF) (the dominant hand), and with the maximum strength. The test was performed three times and the average of the results was used as the final result, retaining one decimal place. For the measurement of middle arm circumstances (MAC) and triceps skin-fold thickness (TSF), the patient was instructed to relax the upper limb and let it sag naturally. The examiner stood behind the patient and measured the circumference of the mid-arm between the acromion process and the middle point of the ulnar olecranon on the non-AVF side. The skin and the subcutaneous tissue were picked up at the midpoint with the left hand to separate the fat from the muscle, and the thickness of the skinfold was measured at 1 cm below the thumb (MAC = MAC - 3.14 × TSF).

Scored Surveys

The scored surveys were: 1) Pittsburgh Sleep Quality Index (PSQI)[13] with 18 self-rating items and 7 dimensions in which each item scored 0 to 3 points (Higher scores suggest worse sleep quality), 2) Malnutrition Inflammation Score (MIS)[14] which includes four domains of subjective evaluation, BMI, physical examination and laboratory parameters with 10 questions in total, each of which scoring 0 to 3 points (The score is inversely related to nutritional status), and 3. Self-rating Anxiety/Depressive Scale (SAS/SDS)[15] with two scales, each with 20 questions scoring 0 to 4 points according to the frequency of symptoms, (they were used to evaluate patients' depression and anxiety, and the scores are positively associated with the severity of anxiety and depression symptoms). All scored surveys were administered to patients at the 48th hour after admission, one-on-one by the study team, and the results were recorded.

Statistics and Methods

This study used SPSS software version 22.0 for statistical analysis, and the significance level was set as $P < .05$. The descriptive statistics were shown by percentages (%) and (`c ± s), chi-square test and independent sample t test were used for between the group comparison, respectively.

RESULTS

Comparison of the Occurrence of Sarcopenias

Out of 116 patients participating in this study, 56.03% (65 cases) did not have sarcopenias and 43.97% (51 cases) were diagnosed as having sarcopenias at early-stage, mid-stage, and sever sarcopenias at 37.25% (19 cases), 39.22% (20 cases), and 23.53% (12 cases), respectively.

Comparison of Clinical Baseline Data

Comparing the clinical baseline data between OG and CG (Table 1), we found no statistical difference in the number of patients with diabetes mellitus, hypertension and types of kidney disease ($P > .05$), but CG were older and mostly comprised female patients ($P < .05$).

Comparison of Physical Fitness

The inter-group comparison of physical fitness indices revealed no significant difference between OG and CG in triceps skin-fold thickness, fat content, protein content, water and lean body mass ($P > .05$), while BMI, MAC and bone mass were lower in research group ($P < .05$) (Table 2).

Comparison of Laboratory Indexes

According to the results of laboratory indices (Table 3), there was no significant differences between OG and CG in BUN, PLT, CRP, WBC, RBC, LDL, HDL, and Hb ($P > .05$); however, t Scr, TG and uric acid were lower in OG ($P < .05$).

Comparison of Scoring Indicators

There was a significant difference between the two groups in PSQI, MIS, SAS and SDS scores, with higher scores in the research group as compared to the control group ($P < .05$) (Table 4).

Analysis of Factors Affecting the Occurrence of Sarcopenias in CKD Patients

Multiple logistic regression analysis was performed on potential risk factors to determine whether the patient had sarcopenias as the dependent variable (Table 5). The results revealed

Table 1. Comparison of Clinical Baseline Data

Factors	CG (n = 65)	OG (n = 51)	t/χ^2	*P*
Age	63.51 ± 2.58	68.92 ± 4.70	7.849	< .001
Gender				
Men/Women	40/25	14/37	13.350	< .001
Smoking				
Yes/No	34/31	25/25	0.124	.725
Drinking				
Yes/No	36/29	28/23	0.002	.959
Place of residence				
Urban/Rural	55/10	42/9	0.107	.744
Nationality				
Han Nationality/Minority	62/3	50/1	0.605	.437
Diabetes				
Yes/No	39/26	33/18	0.269	.604
Hypertension				
Yes/No	25/40	20/31	0.007	.934
Type of Disease				
Chronic Glomerulonephritis	12	10	0.127	.998
Diabetic Nephropathy	22	16		
Hypertensive Kidney Injury	19	16		
Interstitial Nephropathy	8	6		
Other	4	3		

Note: $\alpha = 0.05$.

Table 2. Comparison of Physical Fitness

Factors	CG (n = 65)	OG (n = 51)	t/χ^2	*P*
BMI	25.51 ± 4.67	22.11 ± 5.19	3.691	< .001
Fat content, kg	15.32 ± 3.85	14.62 ± 3.92	0.961	.339
Bone mass, kg	3.30 ± 0.34	2.86 ± 0.41	6.291	< .001
Protein, kg	9.05 ± 1.95	8.86 ± 2.70	0.438	.662
Moisture, kg	36.61 ± 5.36	35.59 ± 7.69	0.837	.405
Lean body mass, kg	46.42 ± 5.11	45.34 ± 4.93	1.144	.255
MAC, cm	23.40 ± 3.37	19.13 ± 3.24	6.866	< .001
TSF, mm	11.99 ± 1.98	12.23 ± 3.14	0.500	.618

Note: $\alpha = 0.05$.

Table 3. Comparison of Laboratory Indices

Factors	CG (n = 65)	OG (n = 51)	t/χ^2	*P*
BUN, mmol/L	26.50 ± 4.89	26.88 ± 4.58	0.427	.670
Scr, mg/dL	10.72 ± 1.34	9.56 ± 1.98	3.727	< .001
TG, mmol/L	1.77 ± 0.32	1.46 ± 0.17	6.248	< .001
LDL, mmol/L	2.21 ± 0.61	2.13 ± 0.72	0.645	.520
HDL, mmol/L	1.24 ± 0.20	1.22 ± 0.25	0.477	.635
Hb, g/L	115.02 ± 14.55	117.58 ± 14.01	0.953	.343
PLT, $\times 10^9$/L	174.43 ± 32.99	171.27 ± 25.71	0.561	.576
CRP, mg/L	5.99 ± 1.53	6.08 ± 1.28	0.337	.737
WBC, $\times 10^9$/L	4.62 ± 0.88	4.60 ± 0.74	0.130	.897
RBC, $\times 10^{12}$/L	7.57 ± 1.52	7.85 ± 1.34	1.034	.304
Uric Acid, μmol/L	435.09 ± 69.67	401.14 ± 58.24	2.789	.006

Note: $\alpha = 0.05$.

Table 4. Comparison of Scoring Indicators

Factors	CG (n = 65)	OG (n = 51)	t/χ^2	*P*
PSQI	8.37 ± 3.81	9.92 ± 2.94	2.392	.018
MIS	5.85 ± 2.09	9.63 ± 2.67	8.518	< .001
SAS	40.25 ± 4.62	44.14 ± 4.88	4.375	< .001
SDS	45.43 ± 7.62	48.10 ± 5.37	2.117	.036

Note: $\alpha = 0.05$.

Table 5. Analysis of Factors Affecting the Occurrence of Sarcopenias in CKD Patients

Factors	β	S.E.	Wald χ^2	*P*	OR	95% CI
Gender	-0.153	0.384	0.162	.681	0.851	0.409 to 1.871
Age	0.852	0.184	27.633	.000	2.342	1.760 to 3.621
BMI	-3.041	0.421	44.662	.000	0.043	0.021 to 0.116
Bone mass	-0.156	0.381	12.164	.000	0.814	0.410 to 1.871
MAC	-0.298	0.048	42.706	.000	0.789	0.614 to 0.877
Scr	-0.621	0.154	16.662	.000	0.594	0.242 to 2.118
TG	0.915	0.184	24.153	.000	0.797	0.534 to 3.810
UA	-0.005	0.001	7.991	.006	0.642	0.534 to 0.940
PSQI	0.342	0.241	22.214	.000	1.762	0.841 to 3.718
MIS	0.994	0.372	16.853	.000	2.657	1.201 to 5.881
SAS	0.523	0.271	6.087	.012	1.716	1.106 to 2.584
SDS	0.834	0.364	5.145	.023	2.298	1.120 to 4.681

Note: $\alpha = 0.05$.
Abbreviations: β, regression coefficient; S.E., standard error; OR, odds ratio; 95% CI, 95% confidence interval.

that sex was not an independent risk factor for the occurrence of sarcopenias in CKD patients ($P > .05$). Combining the β values of the factors, we know that age, PSQI, MIS, SAS, and SDS scores are risk factors for the development of sarcopenias in CKD ($P < .05$, $\beta > 0$, positive effect); i.e., the higher these indicators, the greater the impact on the development of sarcopenias in CKD patients and the higher level of these indicators will have greater impact on the development of sarcopenias in CKD patients. In contrast, BMI, bone mass, MAC, uric acid, TG, and Scr were protective factors ($P < .05$, $\beta < 0$), i.e., the smaller these indicators are, the lower the likelihood of sarcopenias in CKD patients.

DISCUSSION

Sarcopenias originally refers to the decline of muscle mass and function with increasing age. In recent years, Sarcopenias has been recognized in clinical practice as a progressive and extensive skeletal muscle disorder that may lead to adverse outcomes such as falls, fractures, and physical disability.[16] And sarcopenias can occur for a variety of reasons, including malignant tumors, chronic diseases, and malnutrition.[17] However, in patients with CKD, the impaired kidney function and retention of uremic toxins can lead to decreased appetite and protein intake, and increased protein-energy expenditure.[18] Meanwhile, the possibility of developing sarcopenias significantly increases due to chronic inflammation and metabolic acidosis in patients with CKD. Therefore, it is essential to fully understand the factors associated with the development of sarcopenias in CKD patients in order to provide preventive and therapeutic strategies.

According to the findings of this study, the probability of sarcopenias in CKD patients approached 43.97%, emphasizing the high incidence of sarcopenias in this group of patients. Mid-stage and severe sarcopenias made up 39.22% and 23.53% of them, respectively, which was much more than early-stage sarcopenias. It is clear that sarcopenias has a high incidence and also develops rapidly, making it a major problem. In previous studies, we observed that the prevalence of sarcopenias in CKD was about 20 to 40%,[19] which is consistent with our research results. The comparison of the clinical baseline data between sarcopenias and non-sarcopenias groups showed that patients with sarcopenias were older and with a higher proportion of females ($P < .001$), suggesting that the older and female patients are more likely to develop sarcopenias ($P < .001$). It was established that age was the primary pathologic cause of sarcopenias.

as muscle and mass strength decrease at a rate of 1 to 2% per year after the age of 50, attaining a cumulative reduction of roughly 40% by the age of 70.[20] Age-related declines in nutrient ingestion, absorption, and digestion leads to the situation where the intake of nutrients can no longer meet the needs of the body, resulting in the reduction of motor neurons and degeneration of the muscle fibers.[21] In addition, the higher incidence of sarcopenias in women compared with men may be due the lack testosterone secretion in women which can decrease the number of muscle fibers and myoblasts,[22] so men generally have more muscle mass than women under the same conditions.

In addition to other indicators of fitness, body mass index was found to be associated with sarcopenias ($P < .001$). BMI is the primary index that is frequently used in clinical settings to assess patients' nutritional status. Research suggests that a BMI < 21.0 kg/m^2 is a moderately important predictor of declining muscle mass, walking speed, and hand grip strength.[23] In addition, it was shown in this study that BMI of the experimental group was lower than that of the control group which is consistent with the findings of previous studies ($P < .001$).[24] Furthermore, lower MAC and bone mass were determined in the research group compared with the control, suggesting that MAC and bone mass are also potential factors affecting sarcopenias. MAC, which is frequently used to evaluate protein storage, can also reflect muscle mass and is often used to assess the nutritional status of individuals. A decrease in MAC by more than 10% compared with the median of the control population can be considered as an indicator of muscle wasting.[25] Calcium and phosphorus metabolism disorders are frequently observed in patients with CKD, and the low bone mineral density is one of the most prevalent clinical characteristics in these patients. Hemodialysis will also increase the risk of bone loss and fracture in this group of patients.[26] Hence, a decrease in bone mass is also a key factor that affects patients' mobility, which indirectly increases the risk of sarcopenias.

It was also found that uric acid, TG and Scr were lower in the research group compared with the control group ($P < .001$), indicating that low uric acid, TG and Scr may be potential risk factors for the development of sarcopenia. As a metabolite of purine, uric acid is generally excreted by the kidneys. Under normal conditions, uric acid can help prevent sarcopenias, because it is used as an antioxidant and a scavenger of singlet oxygen and free radicals.[27] However, the loss of renal excretory function in CKD patients leads to abnormally elevated uric acid levels, which accelerate the rate of muscle wasting to some extent.[28] In a previous study, we also found a positive correlation between uric acid levels and hand grip strength,[29] supporting the potential link between uric acid and sarcopenia. However, disorders of lipid metabolism are prevalent in sarcopenic patients.[30] We hypothesize that this is why OG's TG is even lower than CG's. The concentration of Scr, a product of muscle metabolism, is directly related to muscle mass.[31] Serum creatinine is also an indicator of renal function, decreased blood creatinine levels are normal in patients with CKD.[32]

PSQI, MIS, SAS and SDS scores were higher in the research group compared with the control group ($P < .001$), which suggests poor sleep quality and nutritional status as well as a more serious deleterious psychological status in patients of the research group. Inadequate sleep duration and quality of sleep will reduce the secretion of growth hormone and insulin-like growth factor-1, increase cortisol content and insulin resistance, and inflammatory cytokine levels, which can lead to decreased muscle mass by inhibiting protein synthesis pathway and down-regulating of skeletal muscle signal expression.[33] Moreover, because of the complications caused by the disease, CKD patients generally have more severe negative emotions, which are typically represented by loss of interest, psychomotor disorders, lack of appetite and reduced physical activity.[34] This can also lead to apraxia, muscular atrophy, and further acceleration of the progression of sarcopenia. Finally, the direct correlation between muscle mass and nutritional status is well established in the clinic,[35] so we have not gone into too much details.

Finally, through multivariate logistic regression analysis, we found that age, BMI, bone mass, MAC, UA, TG, Scr, PSQI, MIS, SAS, and SDS scores were correlates of the development of sarcopenia in CKD patients, which once again illustrates the correlation between sarcopenia and age, BMI, bone mass, MAC, uric acid, TG, Scr, as well as PSQI, MIS, SAS, and SDS scores. The insignificant correlation between sarcopenia and gender may be due to the small sample size in this study or sampling error; thus,

we plan to run another study with larger sample size cases for verification analysis in the future.

Since the relationship between CKD and sarcopenia has not been identified comprehensively, there may still be some other potential factors which have not been addressed in this study. Finally, we should also conduct a longer follow-up survey on the participants of this study to confirm their subsequent progression of sarcopenias.

CONCLUSION

Age, PSQI, MIS, SAS, SDS score, BMI, bone mass, MAC, uric acid, TG, and Scr are relevant factors affecting the occurrence of sarcopenias in CKD patients. The findings suggest that sleep quality, nutritional status, psychological status, renal function, lipids, and bone health in elderly patients with CKD should be taken into consideration in order to reduce the possibility of sarcopenias in these patients.

ETHICAL APPROVAL

The study protocol was approved by the Ethics Committee of Affiliated Hospital of Hebei University (NO. 20210424).

CONFLICT OF INETEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

Xiaoxi Wu and Lei Wang conceived and designed the project, Jianmin Zhang and Lei Ran wrote and revised the paper.Yapu Zhang generated the data.Li Guo analyzed the data.Youlan Gong modified the manuscript.Jianmin Zhang and Lei Ran made the same contribution.All authors gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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