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Evaluation of muscle elasticity in patients with end-stage renal disease complicated with sarcopenia by real-time shear wave elastography multipoint measurement

Li Guo[1], Lei Ran[1], YaPu Zhang[1], XiaoHong Guo[1], Jing Li[1], YouLan Gong[1], Xuan Zhou[2*], XiaoXi Wu[3]

1. Department of Nephrology, Affiliated Hospital of HeBei University, HeBei Province, China
2. Department of Ultrasound Diagnostic, Affiliated Hospital of HeBei University, HeBei Province, China
3. Department of Clinical Nutrition, Affiliated Hospital of HeBei University, HeBei Province, China

ABSTRACT

Background: To analyze the value of real-time shear wave elastography (SWE) multi-point measurement in the evaluation of muscle elasticity in patients with end-stage renal disease (ESRD) complicated with sarcopenia.

Methods: We enrolled 169 ESRD patients treated as the research objects from January 2019 to February 2022. According to whether they were complicated with sarcopenia, the patients were divided into sarcopenia group (n=63) and non-sarcopenia group (n=106). The Young's modulus and shear wave velocity (SWV) of muscles in relaxed and contracted states were measured by SWE technology in the two groups.

Results: Logistic regression analysis showed that age and hs-CRP were independent risk factors for sarcopenia in ESRD patients (P<0.05), while BMI, muscle thickness, Young's modulus in stretched state and SWV in stretched state were protective factors for sarcopenia in ESRD patients (P<0.05). BMI, muscle thickness, Young's modulus in extended state, SWV in extended state and Young's modulus in rest state were all negatively correlated with age and hs-CRP (P<0.05), while there was a significant positive correlation between age and hs-CRP (P<0.05). Independent influencing factors were used to construct the prediction model of nomogram. The consistency index (C-index) was 0.845 (95% CI: 0.830~0.857), and the AUC of ROC curve was 0.852 (95% CI: 0.836~0.871), which had good discrimination.

Conclusion: SWE could accurately evaluate the muscle elasticity of ESRD patients, so as to reflect the changes of muscle mass and stiffness of patients, and could provide the important imaging indicator for the prediction of sarcopenia.

Keywords: real-time shear wave elastography, end-stage renal disease, elasticity of muscle, nomogram

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INTRODUCTION

End-stage renal disease (ESRD) was the final stage of chronic kidney disease, which was usually treated by hemodialysis [1]. Hemodialysis was an important means to maintain the life of patients, but there were also corresponding side effects in the treatment, including dialysis imbalance syndrome, metabolic acidosis, hormone imbalance, protein-energy consumption, etc. Thus, the muscle mass and strength of the patients decreased, and then they developed into sarcopenia [2,3]. Sarcopenia not only reduced the mobility of patients with ESRD, affected their daily life, but also greatly increased the risk of disability, cardiovascular complications, and even death [4]. Therefore, early diagnosis and evaluation of sarcopenia were of great significance for the choice of treatment options and the improvement of patients' prognosis.

With the continuous development of ultrasound technology, high frequency ultrasound was widely used in clinical detection due to its advantages of high resolution, safety, non-invasiveness and convenience. A study [5] showed that the high-frequency ultrasound re-evaluation of muscle mass was highly consistent with computerized tomography and MRI, and could be used as a conventional method for clinical screening of sarcopenia. Shear wave elastography (SWE) was a new quantitative evaluation of tissue stiffness in recent years, which had been widely used in the musculoskeletal system [6]. Several studies [7] have shown that SWE technology has a high significance in evaluating the quality of gastrocnemius muscle thickness and stiffness. However, no studies have reported on the evaluation of muscle elasticity in ESRD patients complicated with sarcopenia by SWE technology. In this study, the clinical applica-

* Correspondence to: Xuan Zhou, Department of Ultrasound Diagnostic, Affiliated Hospital of HeBei University, HeBei Province, China. E-mail: hbbdzhouxuan1@163.com

tion value of SWE ultrasound technology in patients with ESRD complicated with sarcopenia was explored by analyzing the relevant influencing factors, in order to provide a corresponding reference for clinical diagnosis and treatment.

MATERIALS AND METHODS

We selected 169 ESRD patients treated as the research objects from January 2019 to February 2022, including 91 males and 78 females. They were treated with hemodialysis. The patients were 52 to 81 years old, and a mean age of (77.49 ± 4.63) years. Inclusion criteria: (1) ESRD diagnostic criteria were met [8]; (2) All patients were tested by SWE; (3) The clinical data were complete. Exclusion criteria: (1) Those with neuromuscular diseases; (2) Those with metabolic diseases affecting skeletal muscle (diabetes, stroke, cognitive impairment, hyperthyroidism, etc.); (3) Those with regular participation in competitive sports or exercise. Patients were divided into sarcopenia group (n=63) and non-sarcopenia group (n=106) according to whether they had sarcopenia. Informed consents were obtained and signed by all patients or family members in the study. The diagnosis of sarcopenia was based on the "2019 Asian consensus on diagnosis and treatment of sarcopenia" [9]: the diagnosis of sarcopenia should be consistent with the decrease of muscle mass and muscle strength; Using bioelectrical impedance detection method, the skeletal muscle index of males was less than 7.0 kg/m^2, and that of females was less than 5.7 kg/m^2, which meant that the muscle mass decreased. Male dominant hand grip strength was less than 28kg, while female dominant hand grip strength was less than 18kg, which meant that muscle strength was reduced. Skeletal muscle index = skeletal muscle mass of limbs (kg)/ height ^{2}(m^2).

Table 1. Comparison of general data between the two groups

Clinical parameters	Sarcopenia group (n=63)	Non-sarcopenia group (n=106)	χ^2/t value	P-value
Age (years)	76.84±4.52	70.48±3.75	9.385	<0.001
Sex			0.001	0.980
Male	34(53.97%)	57(53.77%)		
Female	29(46.03%)	49(46.23%)		
BMI(kg/m^2)	21.35±2.73	23.83±2.64	5.547	<0.001
Marital status			0.407	0.524
Unmarried	7(11.11%)	13(12.26%)		
Married	42(66.67%)	70(65.04%)		
Divorce / Widowhood	14(22.22%)	23(21.70%)		
Monthly household income (yuan)			0.006	0.914
<2000	11(17.46%)	19(17.92%)		
2000~5000	28(44.44%)	47(44.34%)		
>5000	24(38.10%)	40(37.74%)		
Smoking	20(31.75%)	34(32.08%)	0.002	0.967
Drinking	24(38.10%)	40(37.74%)	0.003	0.958
Hypertension	27(42.86%)	45(42.45%)	0.003	0.953
Hyperlipemia	20(31.75%)	34(32.08%)	0.018	0.894
Chronic glomerulonephritis	21(33.33%)	35(33.02%)	0.002	0.962
Dialysis age (months)	54.16±23.72	53.58±22.85	0.150	0.881
Pinnation angle (°)	16.23±2.35	21.36±2.25	13.411	<0.001
Length of muscle bundle (mm)	30.27±3.24	34.57±2.71	8.813	<0.001
Muscle thickness (mm)	10.52±1.31	14.48±2.13	12.675	<0.001
Grip strength (m/kg)	18.78±2.04	24.69±2.13	16.854	<0.001
Walking speed (m/s)	0.68±0.18	0.70±0.20	0.620	0.536
Somatic cell mass (m/kg)	18.25±3.76	31.94±4.85	18.288	<0.001
TC(mmol/L)	4.53±1.23	4.52±1.26	0.003	0.936
TG(mmol/L)	1.62±0.57	1.63±0.61	0.100	0.920
HDL-C(mmol/L)	1.38±0.62	1.39±0.68	0.091	0.928
LDL-C(mmol/L)	3.22±0.75	3.21±0.73	0.081	0.935
hs-CRP(mg/L)	4.52±1.31	3.58±1.27	4.375	<0.001
Hb(g/L)	98.73±25.36	100.27±23.84	0.377	0.707
PAB(mg/L)	243.35±62.97	242.29±61.84	0.102	0.919
Alb(mg/L)	29.94±8.12	30.06±9.09	0.082	0.935

Note: BMI, Body mass index; TC, total cholesterol; TG, triglycerides; HDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; Hb, hemoglobin; Alb, albumin; hs-CRP, high sensitive C-reactive protein; PAB, prealbumin.

Clinical data such as gender, age, body mass index (BMI), marital status, and previous medical history wre collected. After serum was centrifuged from venous blood within 24 h of admission, the data of low-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), hemoglobin (Hb), albumin (Alb), high-sensitivity C-reactive protein (hs-CRP), and prealbumin (PAB) was detected.

First of all, all patients underwent conventional two-dimensional ultrasound scanning. The patients were prone, and their feet were placed outside the test bed. The ankle joint was in a neutral position and relaxed. The maximum dorsal flexion of the ankle joint was contracted. The probe was placed in the thickest area of the medial head of the gastrocnemius muscle of the patient. The thickness of the gastrocnemius muscle, the pinnation angle and the length of the muscle bundle were measured, and the average of the three measurements was taken. Then the SWE mode is switched. After the image was stable, a qualified image was selected to start the Q-box for shear wave elasticity measurement. The system automatically calculated the Young's modulus value, minimum and shear wave velocity (SWV). The average value was taken from the same site five times in the relaxed and contracted states.

SPSS 23.0 statistical software was used for statistical analysis of the data. The measurement data were tested by normal distribution, and all conformed to normal distribution. The difference between two groups was compared by the t-test, and the χ^2 test was performed to compare the differences in multiple percentages or composition ratios. In multivariate analysis of measurement data, the median is selected as the critical value. The multivariate logistic regression analysis was used to analyze the independent influencing factors for sarcopenia in ESRD patients. Pearson's test was employed for correlation analysis. The nomogram model was constructed according to the influencing factors. The Bootstrap self-sampling method was used for validation. The receiver operating characteristic curve (ROC) and area under ROC curve (AUC), consistency index (C-index) were used to evaluate the discrimination and accuracy of the model. The difference was statistically significant with $P<0.05$.

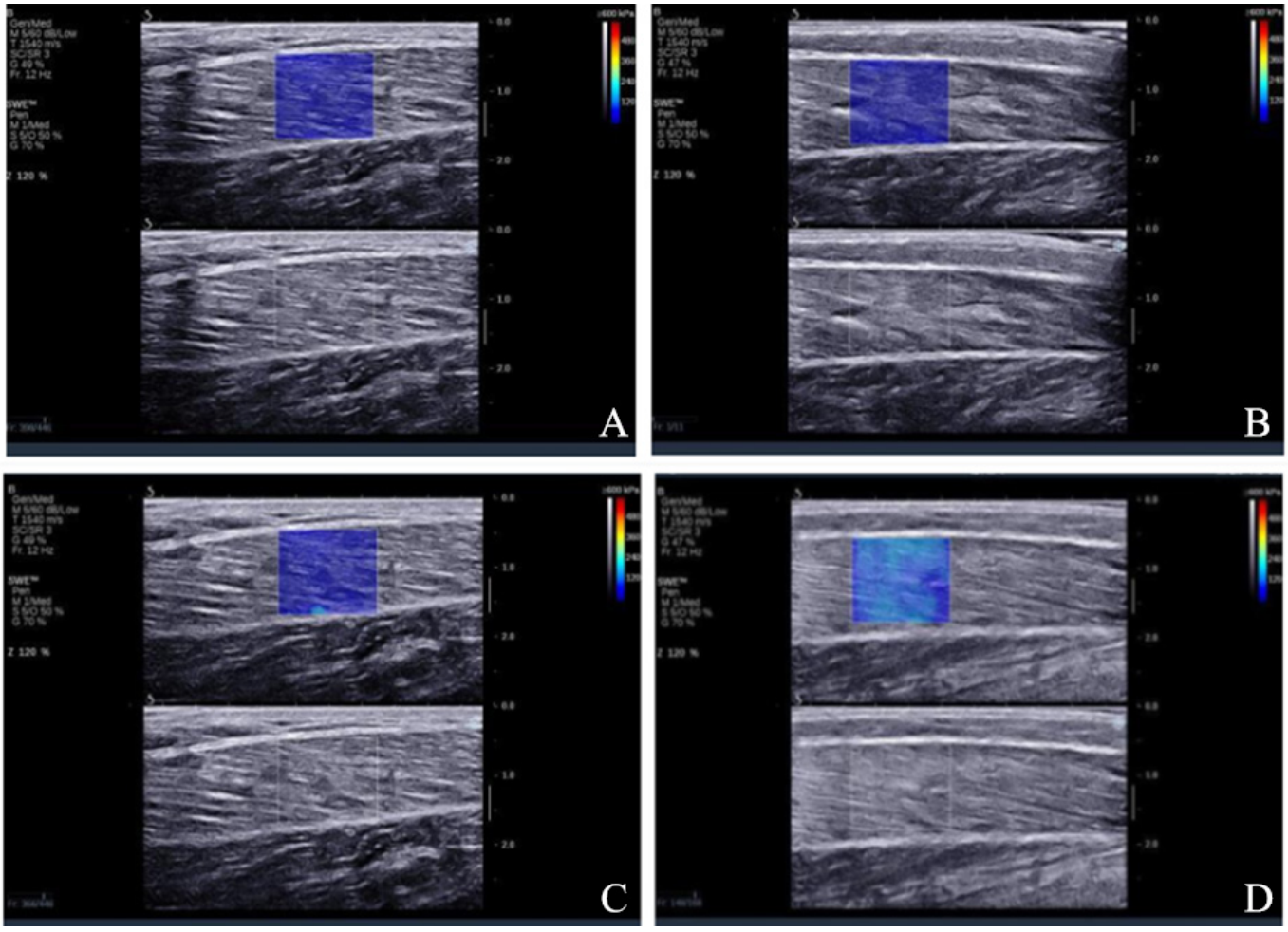

Fig. 1. Comparison of real-time shear wave velocity characteristics of muscles between the two groups (A: resting state of sarcopenia group; B: resting state of non-sarcopenia group; C: stretching state of sarcopenia group; D: stretching state of non-sarcopenia group)

RESULTS

Comparison of general data between the two groups

Comparing the general data of two groups, the age and hs-CRP level in the patients with sarcopenia were significantly higher than those in the non-sarcopenia group (*P<0.05*), and the BMI, pinnation angle, muscle bundle length, muscle thickness, grip strength, and somatic cell mass were significantly lower than those in the non-sarcopenia group (*P<0.05*)(Table 1).

Comparison of muscle SWE characteristics between the two groups

At rest, the gastrocnemius images of both groups were dark blue and evenly distributed. In the stretched state, the image of the sarcopenia group showed blue mixed with a little green, which was unevenly distributed, while that of the non-sarcopenia group showed blue-green and unevenly distributed (Figure 1).

Table 2. Comparison of SWE data of muscle between the two groups in the resting state and stretching state

Clinical parameters	Sarcopenia group (n=63)	Non-sarcopenia group (n=106)	t-value	P-value
Resting state				
Young's modulus value (kPa)	11.46±2.14	15.27±2.35	10.018	<0.001
SWV(m/s)	2.23±0.17	3.04±0.53	11.189	<0.001
Stretching state				
Young's modulus value (kPa)	23.63±2·57	30.62±2·61	16.107	<0.001
SWV(m/s)	4.28±0.62	5.14±0.87	6.538	<0.001

Note: SWV, shear wave velocity.

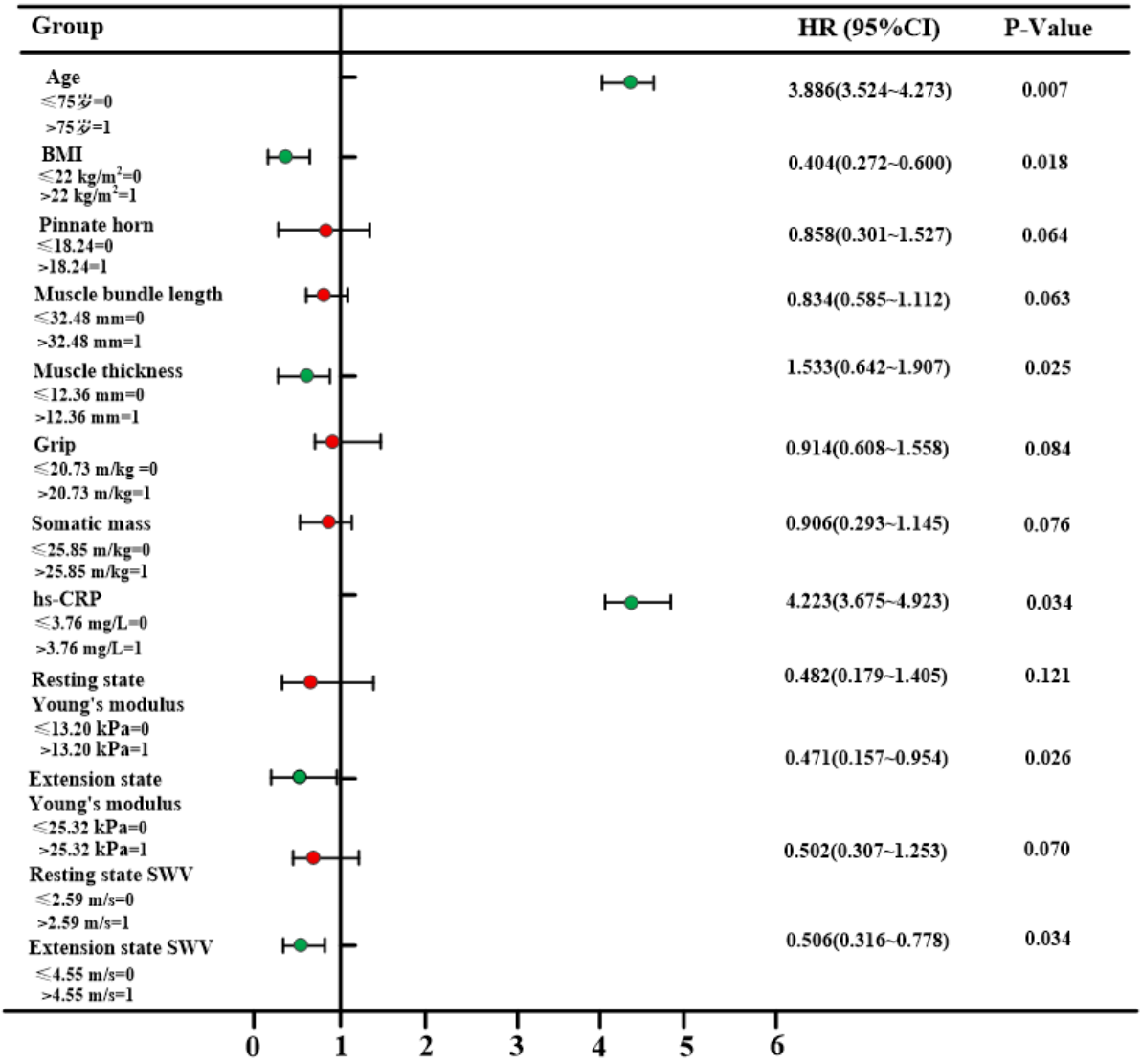

Fig. 2. Multivariate Logistic regression analysis of forest plots

Comparison of SWE data of muscle between the two groups in the resting state and stretching state

When the gastrocnemius was in a resting state and a stretching state, the Young's modulus and SWV of the sarcopenia patients were significantly lower than those of the non-sarcopenia patients (*P<0.05*) (Table 2).

Analysis of independent risk factors for complicated sarcopenia

The multivariate logistic regression analysis was performed if the patients were complicated with sarcopenia as the dependent variable (No=0, Yes=1), and the indicators with statistical differences in the univariate analysis as the independent variable. The results showed that age and hs-CRP were independent risk factors for sarcopenia in ESRD patients (*P<0.05*), while BMI, muscle thickness, Young's modulus in the stretching state and SWV in the stretching state were protective factors for sarcopenia in ESRD patients (*P<0.05*) (Figure 2). The colinearity diagnostic analysis was performed on the screened variables. The results showed that the variance inflation factor (VIF) was less than 10, indicating that the variables were independent of each other and there was no colinearity (Table 3).

Correlation between influencing factors of sarcopenia and SWE parameters

Pearson correlation test was used to analyze the correlation between independent risk factors and the correla-

Table 3. Colinearity diagnostic coefficient of variables

Variables	Rongcha	VIF
Age	0.945	2.013
BMI	0.963	1.045
thickness of muscle	0.946	3.291
hs-CRP	0.937	2.876
Young's modulus in the stretching state	0.929	3.019
SWV in the stretching state	0.925	4.765

Note: BMI, Body mass index; hs-CRP, high sensitive C-reactive protein; SWV, shear wave velocity.

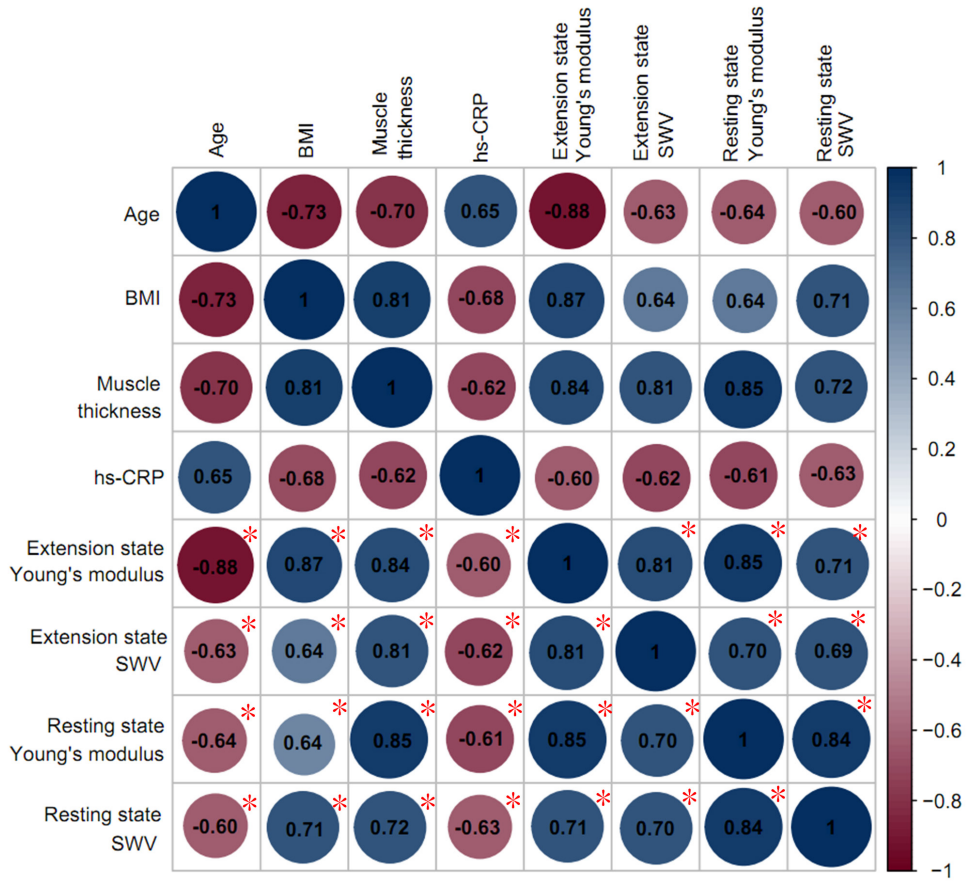

Fig. 3. Correlation between factors of sarcopenia in end-stage renal disease patients (data in the figure are r values, *P<0.05) (BMI, Body mass index; hs-CRP, high sensitive C-reactive protein; SWV, shear wave velocity.)

tion between influencing factors and SWE parameters (Figure 3). BMI, muscle thickness, Young's modulus in extended state, SWV in extended state and Young's modulus in rest state were all negatively correlated with age and hs-CRP (P<0.05), while there was a significant positive correlation between age and hs-CRP (P<0.05).

Construction of the model

The independent influencing factors of the above ESRD patients complicated with sarcopenia were included to construct a line graph prediction model. The results are shown in Figure. 4. The scores of age > 75 years, BMI ≤ 22 kg/m², muscle thickness ≤ 12.36 mm, hs-CRP > 3.76

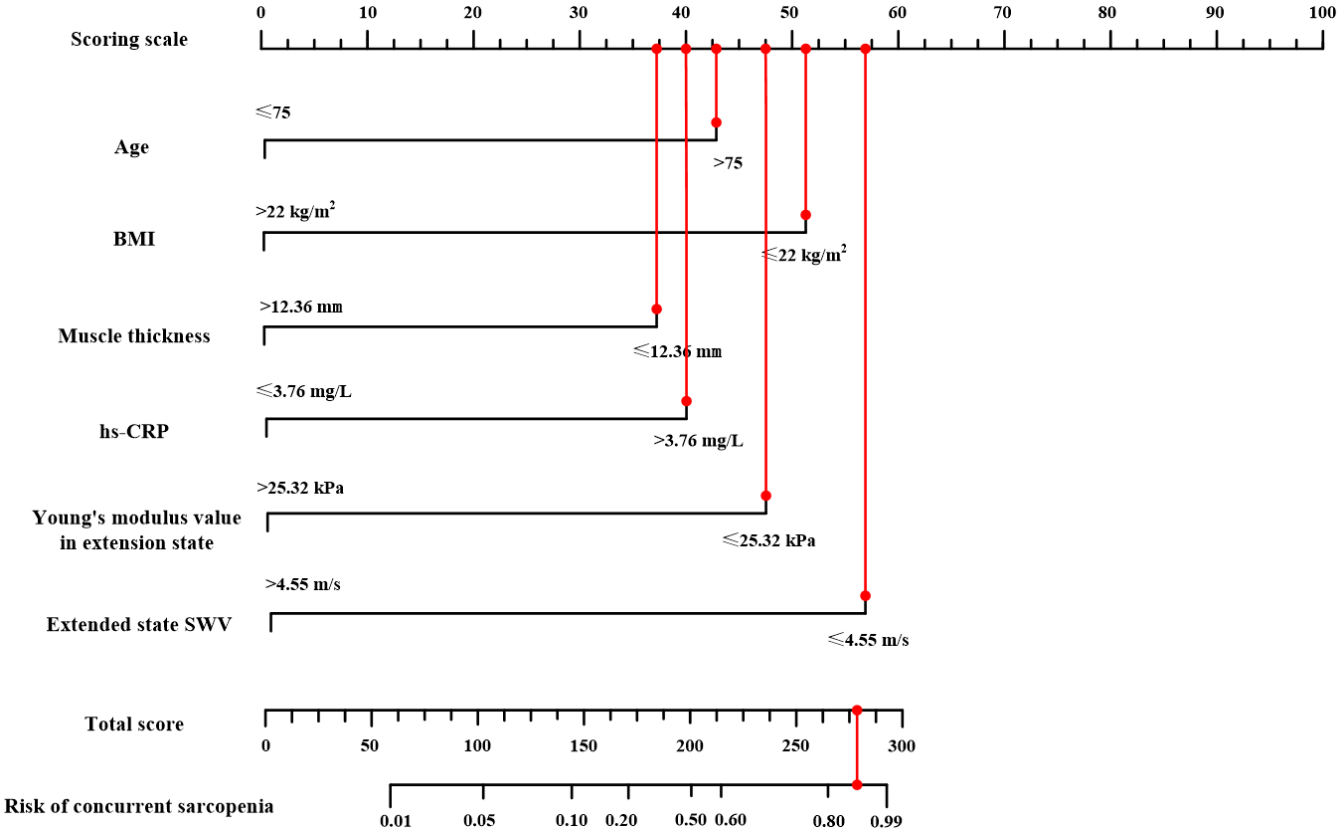

Fig. 4. Prediction model of nomogram in end-stage renal disease patients with sarcopenia

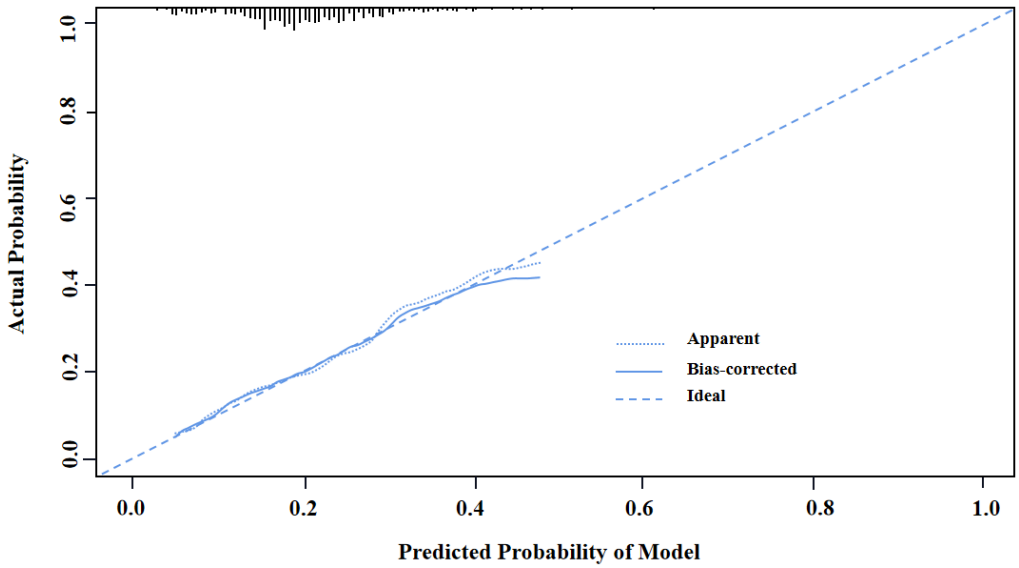

Fig. 5. Calibration evaluation of the nomogram model in end-stage renal disease patients with sarcopenia

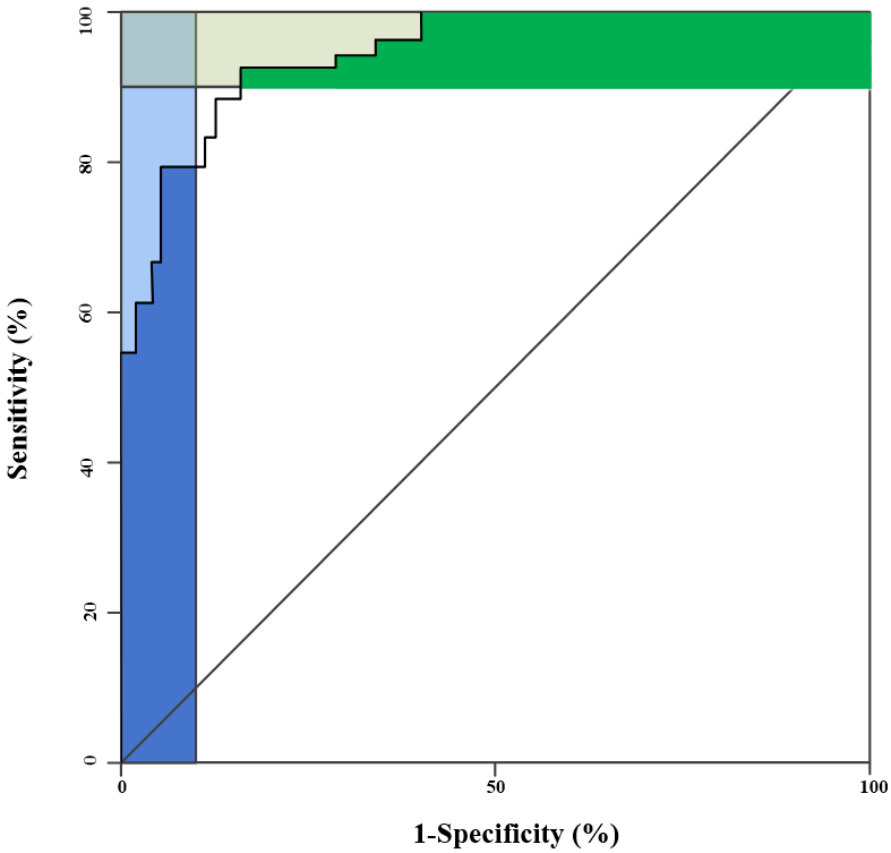

Fig. 6. Discriminant evaluation of the nomogram model in end-stage renal disease patients with sarcopenia

mg/L, Young's modulus value ≤ 25.32 kPa in the stretched state, and SWV ≤ 4.55 m/s in the stretched state were 42.64, 14.23, 30.40.18, 48.06, and 57.65, respectively. The probability corresponding to the total score (227.95) was the probability of the nomogram model predicting ESRD patients complicated with sarcopenia (84.82%).

Model evaluation

The C-index of the prediction model was calculated as 0.845 (***95% CI:*** 0.830~0.857), and the AUC of the ROC curve was 0.852 (***95% CI: 0.836~0.871***). The above results suggested that the risk prediction model had good discrimination (Figure 5). The calibration curve of the prediction model was drawn. The results showed that the prediction probability curve of the model had a good fit with the reference probability, and there was no significant difference in the Hosmer-Lemeshow test results (***P>0.05***), indicating that the model had a high accuracy (Figure 6).

DISCUSSION

The sarcopenia was a syndrome caused by continuous loss of skeletal muscle mass, strength and function. It could lead to patients' difficulty in standing, slow walking, easy falling and fracture, and even lead to heart and lung failure as well as death [10,11]. Due to the failure of their own renal function, ESRD patients were prone to changes in muscle structure, muscle strength reduction and muscle atrophy, which greatly increased the risk of sarcopenia [12]. Once ESRD patients were complicated with sarcopenia, their living ability will be further reduced, which will have a very negative impact on the treatment prognosis. Therefore, it was necessary to make early diagnosis, early detection, and early treatment of ESRD patients complicated with sarcopenia.

SWE was one of the ultrasonic elastography techniques. The shear wave propagation speed was mainly reflected by Young's modulus, which could accurately evaluate the stiffness and quality of muscle tissues. At present, SWE technology is widely used in the evaluation of skeletal muscle system. Studies have shown [13] that SWE could objectively and quantitatively reflect the degree of skeletal muscle damage at the site, which is of important diagnostic value for muscle-related degenerative diseases. Previous studies [14] have shown that the SWE technology could be used to evaluate skeletal muscle changes in the population with sarcopenia, but few studies have reported on the evaluation of skeletal muscle in ESRD patients complicated with sarcopenia. In this study, the stiffness of gastrocnemius muscle at resting and in stretching state was assessed by SWE in ESRD patients complicated with sarcopenia and patients with ESRD alone. The SWE images showed uniformly

distributed blue images in the resting state in both patients with and without sarcopenia, suggesting that the muscle stiffness of the two groups was low in the resting state. When the muscle was in the stretching state, the image of the sarcopenia patients was only mixed with a small amount of green and unevenly distributed, and the blue-green image of the non-sarcopenia patients, suggesting that the muscle structure of the sarcopenia patients had been altered. In the sarcopenia patients, the muscle contraction capacity might be reduced, elasticity might be poor, and the muscle stiffness might be significantly lower than that of patients in the non-sarcopenia group. From the SWE data of the two groups, the Young's modulus and SWV in the stretching state of the two groups were higher than those in the resting state, suggesting that there were differences in the stiffness of the muscles in different states. When the muscles were stretched, the structure had been altered, the tension had increased, and the stiffness had increased. In addition, this study also found that the Young's modulus and SWV at the resting and stretching states were significantly lower in patients with sarcopenia than those in patients without sarcopenia. Studies have shown [15] that SWV was one of the indicators reflecting muscle quality. The smaller SWV was, the greater the risk of sarcopenia was. This suggested that the skeletal muscle of patients with ESRD complicated with sarcopenia had functional damage, and the contraction force was reduced. The muscle could not produce the same strength as that of patients with non-sarcopenia, resulting in muscle weakness and reduced muscle stiffness.

The occurrence of sarcopenia was closely related to the prognosis of patients with ESRD. Therefore, it was also crucial to explore the relevant influencing factors and to prevent and treat it early. In this study, age, hs-CRP, and BMI, muscle thickness, Young's modulus in the stretching state, and SWV in the stretching state were found to be independent risk factors for ESRD patients complicated with sarcopenia by multivariate logistic regression analysis, while BMI, muscle thickness, Young's modulus in the stretching state, and SWV in the stretching state were protective factors in ESRD patients complicated with sarcopenia. Studies [16] have shown that the gradual decline in all aspects of body function with increasing age and the degeneration and loss of motor neurons were important influencing factors in the development of sarcopenia, while those with too low BMI had less muscle density and were more prone to muscle atrophy in the treatment of ESRD [17]. The increase of hs-CRP level in the organism often predicts the occurrence of inflammatory reactions in the organism. The increase of inflammatory cytokines could damage the quality of skeletal muscle fiber bundles, resulting in the weakening of skeletal muscle elasticity and the decrease of muscle thickness, which was directly related to muscle mass. The smaller the thickness, the worse the muscle mass [18], with a higher risk of complicating sarcopenia. In addition, the correlation analysis in this study found that there was a significant direct correlation between the Young's modulus value in the stretching state, the SWV in the stretching state, the Young's modulus value in the resting state, and the SWV in the resting state and various influencing factors in ESRD patients, which suggested that the SWE detection technology could directly or indirectly reflect the muscle quality and strength, and could provide accurate and effective information for the diagnosis of sarcopenia. The limitations of this study were that the etiology of sarcopenia was multiple and the skeletal muscle changes caused by ESRD might be different from those caused by other diseases.

In summary, age, hs-CRP, BMI, muscle thickness, Young's modulus in the stretching state, and SWV in the stretching state were independent influencing factors for end-stage renal disease patients complicated with sarcopenia. SWE could accurately evaluate the muscle elasticity of ESRD patients, so as to reflect the changes of muscle mass and stiffness of patients, and provide important imaging indicators for the prediction of sarcopenia.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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