Enhanced echo intensity of skeletal muscle is associated with poor physical function in hemodialysis patients—a cross-sectional study

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Abstract

Background: The objective of this study was to evaluate the relationship between ultrasound echo intensity (EI) of skeletal muscle and physical function of patients on maintenance hemodialysis.

Methods: Cross-sectional area (CSA) and mean EI of the right rectus femoris were measured by ultrasound to evaluate the quantity and quality of the muscle, respectively. Physical function was measured by handgrip strength (HGS), gait speed, sit-to-stand 60 s (STS-60) test, and instrumental activities of daily living (IADL) scale.

Results: A total of 107 patients on hemodialysis were included, with women accounting for 37.3% (n = 40), and a mean age of 53.53 ± 12.52 years. Among the patients on hemodialysis, EI was moderately and negatively correlated with HGS ($r = -0.467$, $P < 0.001$), gait speed ($r = -0.285$, $P = 0.003$), and STS-60 ($r = -0.313$, $P = 0.001$). Multiple regression analyses adjusted for CSA showed that the enhanced EI of patients on hemodialysis remained associated with worse HGS ($\beta = -0.207$, $P = 0.047$), lower gait speed ($\beta = -0.002$, $P = 0.001$), less STS-60 ($\beta = -0.136$, $P = 0.049$), and a higher likelihood of dependency in IADL (Odds Ratio: 1.070, 95% CI: [1.033–1.111], $P = 0.001$).

Conclusions: In patients on hemodialysis, enhanced EI in the skeletal muscle measured via ultrasound was correlated with poor physical performance. The combined muscle quality and muscle quantity evaluation provides more information for assessing the level of physical function of the patients.

Introduction

Patients on hemodialysis often suffer from reduced muscle strength and exercise capacity, lowering their autonomy and quality of life and shortening survival time [1]. Decreased muscle mass is one of the main causes of reduced muscle strength and exercise capacity [2, 3]. A recent study showed that muscle quality is decreased significantly at the same time as or before the decrease in muscle mass [4]. Studies of the elderly have also reported that the decline of muscle quality is closely related to the decline in physical function and poor prognosis of patients [5, 6]. Therefore, both the quantity and quality of muscle affects muscle function. Joint evaluation may help formulate intervention measures and improve prognosis.

Muscle quality is a relative new term that refers to the microscopic and macroscopic changes in muscle structure and composition and the level of muscle function from each muscle mass unit [7]. The existing research methods for evaluating muscle quality are mainly measurements of the amount of fat penetrating into the muscle determined through computed tomography (CT), magnetic resonance imaging (MRI), and muscle radiation attenuation by CT. CT measurement of mid-thigh intermuscular adipose tissue predicts usual gait velocity and 6-min walk distance of patients on hemodialysis [2]. However, only a few studies focused on evaluating the muscle quality of patients on hemodialysis are available.

Ultrasound can effectively assess muscle mass and muscle quality with good internal and external consistency [8]. It also has the advantages of bedside operation, convenience, non-invasiveness, and lack of radiation exposure, and is widely studied as a tool in muscle assessment. Echo intensity (EI) is an important indicator for ultrasound assessment of muscle quality. Enhanced EI indicates increased infiltration of fibrotic tissue and/or adipose tissue in the muscle and represents reduced muscle quality [9]. Numerous studies in the elderly have shown that an increase in EI is related to decline of muscle strength and physical function [10-12]. A recent study involving 61 patients with chronic kidney disease (CKD) showed that patients with high EI had low physical function [13]. However, to date, there are no relevant studies evaluating ultrasound derived EI in patients on hemodialysis. Hence, this study clarified the application value of ultrasound EI of skeletal muscle in patients on hemodialysis by evaluating the relationship between ultrasound EI and physical function.

Methods

Study population

This study screened outpatients on maintenance hemodialysis in our county hospital from July 2020 to August 2020. The inclusion criteria of this study included patients who had undergone more than 3 months of hemodialysis. patients on hemodialysis who could not walk or were completely blind were excluded. We screened a total of 110 patients and excluded 3 patients who could not walk. A total of 107 subjects were eventually enrolled. The research was conducted in accordance with the Helsinki Declaration. This study was also approved by the ethics committee of our hospital. All subjects signed the written informed consent, and then their demographic information, past medical history, and duration of dialysis were collected. Various body measurements and assessments of physical function were performed before hemodialysis. A complete ultrasound examination of the right rectus femoris was also performed after hemodialysis.

Body measurements and assessments of physical function

Measurement of body mass index (BMI)

BMI measurement of individual research subjects was calculated based on body dry weight and the following formula: $BMI (Kg/m^2) = \text{body weight}/\text{height}^2$.

Measurement of handgrip strength (HGS)

HGS of individual subjects was measured before hemodialysis. Patients with internal arteriovenous fistula were subjected to HGS measurement on the non-fistula hand twice to obtain the maximum value.

Patients using tunneled cuffed catheters were subjected to the HGS measurement on the dominant hand twice to obtain the maximum value.

Gait speed

Individual subjects were required to walk independently for a 4-meter distance, followed by recording of the completion time and calculation of the gait speed (meter/second) twice to obtain the maximum value.

Sit-to-stand 60 s (STS-60) test

The number of times an individual patient stood up and sat down on a chair within 60 seconds was calculated. This STS-60 test assessed the strength and endurance of muscles of the lower limbs of the tested subject [14]. The patient was asked to complete the sit down-stand up-sit down movement as many times as possible within 60 seconds by holding his/her hands in front of the chest and starting from the sitting position. The number of STS-60 movements was recorded at the end of the test.

Dependence in IADL

Physical function was also measured using the instrumental activities of daily living (IADL) scale [15, 16]. The IADL scale included 8 items: ability to shop on the street, do outdoor activities, cook meals, do household activities, wash clothes, use the telephone, take medications, and handle personal finances. The evaluation of the results of each item were divided into 3 levels: completion with no assistance, completion with partial assistance, and completion with full assistance. The IADL scale of individuals with any item which needed assistance (including partial or full assistance) was characterized as impaired IADL, otherwise IADL was characterized as intact.

Ultrasound measurement

A portable ultrasound machine with a 60-mm width curvilinear transducer (2–5 MHz, S II, SonoSite, USA) was used to gain enough ultrasound window to cover the whole width of the rectus femoris muscle. All ultrasounds were standardized by the default machine settings (depth, gain, and focus). One experienced pain physician who had been practicing musculoskeletal ultrasound more than 10 years obtained all the images.

B-mode 2D ultrasonography of the right rectus femoris was taken immediately once hemodialysis was finished. The patient would lie in the supine position at a 45° angle, with the rectus femoris muscle relaxed. A line at the midpoint between the anterior superior iliac spine and the superior patellar border was marked. The ultrasound transducer was placed perpendicular to the longitudinal axis of the thigh,

overlying the line. Minimal pressure was applied to avoid muscle distortion. In the transverse ultrasound image, the rectus femoris muscle was confirmed and the muscle epimysium boundary was identified as an oval circle wrapping around the muscle fibers. Two images from the same point for each person were saved.

Ultrasound images were transferred to the computer for measurements using Image J software (National Institute of Health, USA). The whole rectus femoris muscle within its epimysium was circled as the region of interest for cross sectional area (CSA) and mean EI measurement (Figure 1). The software returned measures of CSA and the mean EI, which was expressed as a value between 0 (black) and 255 (white) (Figure 1). The average CSA and mean EI values of two images for the same patient were analyzed.

Statistical analysis

Continuous data are presented as mean $\pm$ standard deviation, and categorical data are presented as a percentage. For continuous data, one-way ANOVA was used to compare two groups when normal distribution was fulfilled; otherwise, the non-parametric Wilcoxon rank sum test was performed. For categorical data, the chi-square test was performed. The association of EI with physical function was examined using Pearson's correlation analysis. Multiple linear regression (continuous outcomes) and logistics regression (dichotomous outcomes) were performed to assess the independent association of EI and CSA with physical function. The two model methods were as follows: Model 1—only adjusted for EI and CSA; Model 2—further adjusted for age, gender, and dialysis duration. All statistical analyses were performed using MedCalc Software (Version 18.2.1 MedCalc Software Ltd, Belgium). $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

A total of 107 patients on maintenance hemodialysis were enrolled in this study. Patients were 37.3% female ($n = 40$), mean age was 53.53 ± 12.52 years, average dialysis duration was 2.97 ± 2.32 years, and average BMI was 21.43 ± 3.77 kg/m². In addition, 15.9% of the patients had diabetes ($n = 17$), 93.5% of the patients had hypertension ($n = 100$), and 26.2% ($n = 28$) of the patients had dependency in IADL.

As shown in Table 1, no significant differences in age, BMI, prevalence of hypertension, or duration of hemodialysis were found between males and females. However, the prevalence of diabetes in the male group was higher than in the female group ($P = 0.018$). In terms of physical function, male patients on hemodialysis had significantly stronger HGS than the female patients ($P < 0.001$) while no significant differences in gait speed, STS-60 completion time, or dependency in IADL were found between males and females ($P > 0.05$). In terms of ultrasound parameters of the rectus femoris, the EI value of the male group was significantly lower than in the female group, and the CSA of the male group was significantly higher than the female group ($P < 0.001$).

Relationship between muscle quality and physical function

As shown in Figure 2, the EI of the overall patient population on hemodialysis was negatively correlated with HGS ($r = -0.467$, $P < 0.001$), gait speed ($r = -0.285$, $P = 0.003$), and STS-60 ($r = -0.313$, $P = 0.001$).

Comparison of physical function with muscle quality (EI) and muscle quantity (CSA)

Further multiple linear regression analyses and logistic regression analyses were performed to assess the relationship between EI, CSA, and physical function. As shown in Table 2, Model 1 adjusted for the EI and CSA, and Model 2 further adjusted for age, gender, and dialysis duration. Enhanced EI was associated with worse HGS ($\beta = -0.207$, $P = 0.047$), lower gait speed ($\beta = -0.002$, $P = 0.001$), less STS-60 ($\beta = -0.136$, $P = 0.049$), and a higher likelihood of dependency in IADL in Model 1 (OR: 1.070; 95% CI: [1.030–1.111], $P = 0.001$), but was only associated with dependency in IALD ($P = 0.001$) in Model 2. Except for STS-60, increased CSA was a significant predictor of better HGS, higher gait speed, and lower IALD disability in both Model 1 and Model 2 in patients on hemodialysis.

Discussion

This study was the first to report the relationship between ultrasound derived EI of the skeletal muscle and physical function in patients on hemodialysis. Our results showed that high EI was closely related to low physical function including HGS, gait speed, STS-60, and IADL disability in patients on hemodialysis.

The pathophysiological mechanisms of decreased muscle quality include muscle fiber reduction, mitochondrial dysfunction of myocytes, intramuscular fat infiltration, and increased fibrosis [17]. The existing assessment methods of muscle quality mainly include CT, MRI, and ultrasound. Although CT and MRI directly evaluate the degree of intramuscular fat infiltration, they are expensive and require patients go to a specific place or have a certain degree of radiation, which affects patient compliance with the examination. Numerous studies in the elderly have confirmed the close relationship between ultrasound derived EI and physical function. However, in the field of kidney diseases, only one small-scale study of stages 3–5 CKD pre-dialysis patients has reported that EI is moderately and negatively correlated with the STS-60 test, the incremental shuttle walk test (ISWT) ($n=61$), and peak oxygen consumption (VO_2 peak) results ($n = 32$), but not with the gait speed and HGS ($n = 29$); EI was not correlated with any index of physical function when the CSA was corrected [13]. In this study, EI was moderately and negatively correlated with HGS, gait speed, and STS-60 in patients on hemodialysis. Moreover, after adjusting for muscle area, high EI in patients on hemodialysis remained associated with worse HGS, low gait speed, reduced STS-60, and IADL disability. Thus, this is the first report showing the value of ultrasound derived EI in muscle evaluation of patients on hemodialysis.

In addition to muscle quality, muscle quantity is also an important indicator for muscle evaluation of patients. A wealth of evidence from multiple studies has shown that muscle size is closely related to the physical function of patients on hemodialysis [2, 3, 18]. When we further corrected for factors such as age, gender, and the duration of dialysis, only CSA was related to the level of physical function of the patients. Thus, in the clinical setting, the combined evaluation of muscle quantity and muscle quality may provide more information for accurately assessing muscle strength and physical function in patients [19].

Interestingly, analysis of the ultrasound parameters of the rectus femoris showed that the CSA of the male group was significantly higher than in the female group, and the EI value of the male group was significantly lower than in the female group. These phenomena are consistent with our expectations. Male muscles are stronger, with larger CSA of the rectus femoris muscle. In addition, the proportion of body fat in the females was generally higher than that of males. Thus, the EI value of the female skeletal muscle was higher.

Loss of muscle quantity and quality in patients on hemodialysis may be related to factors such as increased oxidative stress, accumulation of uremic toxins, reduced exercise activities, and malnutrition [20, 21]. Exercise training is an effective way to improve muscle function. In patients with CKD, ultrasound measurement of CSA has been used to effectively assesses muscle mass gain after exercise intervention [22]. Impendence movement reduced the accumulation of fat in the muscles of the elderly [23]. However, there is still a lack of research on the improvement of muscle quality through exercise in patients on hemodialysis. In addition, further research is needed to verify whether EI can be used as an evaluation index of the improvement of muscle quality.

Ultrasound-based evaluation of muscle quantity and quality of patients on hemodialysis provided more information for assessing the level of physical function in patients. The ultrasound method has the advantages of simplicity, convenience, non-invasiveness, and without radiation exposure. It has important clinical value and wide application prospects in the muscle evaluation of patients on hemodialysis.

This study had some limitations: First, no standardized measurement method for EI is currently available, and the measurement of EI is also affected by different machine parameters. Thus, EI values may differ between different studies and are not comparable. Second, this was a cross-sectional study, and therefore it is impossible to clarify the etiological inference of the decline in muscle quality represented by EI and the decreased physical function of patients on hemodialysis. In addition, this study was carried out in a single dialysis center in China, and the generalization of our conclusions requires international, multi-center studies.

Conclusion

The present study revealed that enhanced US-derived EI was correlated with poor physical performance in patients on hemodialysis. The combined muscle quality and muscle quantity evaluation provides more

information for assessing the level of physical function of the patients.

Abbreviations

El: Echo intensity; CSA: Cross-sectional area; HGS: Handgrip strength; STS-60: Gait speed, sit-to-stand 60 s; IADL: Instrumental activities of daily living; CT: computed tomography; MRI: magnetic resonance imaging; CKD: chronic kidney disease; BMI: Body mass index; ISWT: incremental shuttle walk test; SD: Standard deviation; SE: Standard error.

Declarations

Ethics approval and consent to participate

The study protocol complied with the Helsinki Declaration standards and was approved by the Ethics Committee of the People's Hospital of Menghai County (approval number 2020-SNK-001) and Shanghai Jiao Tong University Affiliated Sixth People's Hospital (approval number 2020-175). All subjects signed the written informed consent.

Consent for publication

Not Applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JZW and HQL contributed to the conception of the study, performed statistical analysis and wrote the initial manuscript draft. JZW, SRR and LXS participated in study coordination, performed the recruitment, took the measures and collected the data. DSC and NSW contributed to the conception of the study, supervised the study, helped to interpret the results and corrected the draft. All authors read and approved the final manuscript.

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Tables

Table 1

Patient characteristics, ultrasound measurements and physical performance in both sexes

	Men (n=67)	Women (n=40)	P
Age (yr)	54.79±13.39	51.42±10.74	0.179
BMI (kg/m ²)	21.81±3.73	20.78±3.79	0.172
EI	58.21±16.59	69.26±12.93	< 0.001
CSA (cm ²)	6.91±1.55	5.46±1.20	< 0.001
Ethnicity			0.126
Han, n (%)	20 (29.9)	9 (22.5)	
Dai, n (%)	20 (29.9)	21 (52.5)	
Hani, n (%)	14 (20.9)	6 (15.0)	
Other, n (%)	13 (19.4)	4 (10.0)	
Hypertension, n (%)	63 (94.0)	37 (92.5)	0.758
Diabetes, n (%)	15 (22.4)	2 (5.0)	0.018
Primary disease			0.104
Chronic glomerulonephritis, n (%)	10 (14.9)	11 (27.5)	
Diabetic nephropathy, n (%)	14 (20.9)	2 (5.0)	
Hypertensive nephropathy, n (%)	9 (13.4)	5 (12.5)	
Obstructive nephropathy, n (%)	9 (13.4)	3 (7.5)	
Other or unknown, n (%)	25 (37.3)	19 (47.5)	
Dialysis duration (yr)	3.06±2.54	2.82±1.93	0.607
Physical performance measures			
HGS (kg)	31.27±9.81	21.37±4.36	< 0.001
Gait speed (m/s)	0.97±0.19	0.93±0.14	0.252
STS-60 (repetitions)	30.12±8.44	28.85±7.99	0.445
Dependency in IADL, n (%)	19 (28.4)	9 (22.5)	0.507

BMI, body mass index; EI, echo intensity; CSA, cross-sectional area; HGS, handgrip strength; STS-60, sit-to-stand 60 s; IADL, instrumental activities of daily living. Values are presented as mean (SD) for continuous values, and n (%) for categorical values.

Table 2

Comparisons of physical function with muscle quality (EI) and muscle quantity (CSA) in all patients on hemodialysis.

	Model 1		Model 2	
	β (SE)	P	β (SE)	P
HGS (kg)				
EI	-0.207 (0.047)	<0.001	-0.090 (0.047)	0.061
CSA	2.527 (0.479)	<0.001	1.393 (0.483)	0.005
Gait speed (m/s)				
EI	-0.002 (0.001)	0.028	-0.002 (0.001)	0.130
CSA	0.030 (0.010)	0.003	0.030 (0.011)	0.009
STS-60 (repetitions)				
EI	-0.136 (0.049)	0.006	-0.081 (0.051)	0.119
CSA	0.892 (0.497)	0.075	0.747 (0.522)	0.156
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Dependency in IADL				
EI	1.070 (1.030–1.1112)	0.001	1.086 (1.033–1.141)	0.001
CSA	0.569 (0.376–0.860)	0.008	0.438 (0.255–0.755)	0.003

Multiple linear regression for continuous outcomes and logistic regression for dichotomous outcomes. Model 1: EI + CSA; Model 2: model 1 + sex + age+ dialysis duration. HGS, handgrip strength; EI, echo intensity; CSA, cross-sectional area; STS-60, sit-to-stand 60 s; IADL, instrumental activities of daily living.

Figures

Figure 1

Representative ultrasound image of a relaxed rectus femoris. Rectus Femoris cross-sectional area is outlined by the dotted line. The histogram analysis for computerized quantitative grayscale analysis is illustrated at the lower right corner of the image. RF, rectus femoris; VL, vastus lateralis; VI, vastus intermedius

Figure 2

Correlation between echo intensity and physical function in all patients. a. HGS; b. Gait speed; c. STS-60. HGS, handgrip strength; STS-60, sit-to-stand 60 s