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Original article

Noninvasive evaluation of muscle mass by ultrasonography of quadriceps femoris muscle in End-Stage Renal Disease patients on hemodialysis

Alice Sabatino [a], Giuseppe Regolisti [a], Marco Delsante [a], Tommaso Di Motta [b], Chiara Cantarelli [b], Sarah Pioli [c], Giulia Grassi [d], Valentina Batini [e], Mariacristina Gregorini [f], Enrico Fiaccadori [a, b, *]

[a] Acute and Chronic Renal Failure Unit, Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy
[b] Postgraduate School of Nephrology, Parma University, Parma, Italy
[c] Dialysis ASL Parma, Italy
[d] Nephrology and Dialysis South, Cecina-Piombino, Livorno, Italy
[e] Nephrology and Dialysis North, Livorno, Italy
[f] Nephrology and Dialysis, Reggio Emilia, Italy

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SUMMARY

Background & aims: Protein-Energy Wasting (PEW) is a pathological condition of renal patients with advanced Chronic Kidney Disease characterized by a progressive reduction of energy and protein assets. Nutritional status assessment, especially for what concerns muscle mass, is essential for both the identification of patients at risk for the development of PEW, as well as monitoring the effects of nutritional interventions. Ultrasound methods are easily applicable at the bedside for quantitative assessment of skeletal muscle. The present study was aimed at evaluating quadriceps rectus femoris thickness (QRFT) and quadriceps vastus intermedius thickness (QVIT) in patients on chronic hemodialysis.

Methods: This was a prospective observational study. Three groups of adult patients were studied: young healthy subjects, well-nourished hospitalized patients with normal renal function, and End-Stage Renal Disease patients on hemodialysis (ESRD-HD). QRFT and QVIT were measured at two sites bilaterally (8 measures/patient) and were compared between groups, and also between subgroups of ESRD-HD patients stratified on the basis of conventional nutritional status parameters.

Results: We enrolled 35 healthy subjects, 30 hospitalized patients, and 121 ESRD-HD patients on hemodialysis. QRFT and QVIT of ESRD patients on hemodialysis were lower than those of both control groups ($P < 0.001$). After stratifying ESRD patients into subgroups based on nutritional variable cut-offs commonly used to define PEW in this clinical setting (BMI [$\geq$ 23 *vs* <23 kg/m^2], albumin [$\geq$3.8 *vs* <3.8 g/dL]) and malnutrition inflammation score (MIS) status (<6 *vs* $\geq$6), QRFT and QVIT of patients with worse nutritional status were significantly lower than those of well-nourished ESRD-HD patients (P value range: <0.001 to <0.05).

Conclusion: Skeletal muscle ultrasound is a simple and easily applicable bedside technique in the dialysis units, and could represent an adequate tool for the identification of patients with reduced muscle mass.

1. Introduction

End-Stage Renal Disease on chronic hemodialysis (ESRD-HD) is characterized by progressive worsening of nutritional status with a high prevalence of Protein-Energy Wasting (PEW) [1], a pathological condition associated with poor outcome [1]. Thus, the assessment of nutritional status is essential both for preventing PEW in

* Corresponding author. Unità di Fisiopatologia dell'Insufficienza Renale Acuta e Cronica, Dipartimento di Medicina Cinica e Sperimentale, Università degli Studi di Parma, Via Gramsci 14, 43100 Parma. Italy.
E-mail address: enrico.fiaccadori@unipr.it (E. Fiaccadori).

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patients at risk, and for monitoring nutritional support in those with established PEW [2].

In this regard, increasing attention is devoted to the assessment of muscle mass. Skeletal muscle is in fact the largest store of Lean Body Mass (LBM) protein, and its quantitative/qualitative alterations may impact negatively on patients' quality of life and prognosis [3]. In ESRD-HD patients muscle mass is usually assessed by conventional bedside techniques, such as anthropometry, bioimpedance spectroscopy [BIS], or bioimpedance analysis [BIA], which however have some limitations [3]. As a matter of fact, the gold standard imaging techniques such as computerized tomography [CT], magnetic resonance imaging [MRI], and Dual Energy X-ray Absorptiometry [DEXA] are expensive, not easily available at the bedside, and finally may imply exposure to radiation or strong magnetic fields. Conversely, ultrasonography (US) is commonly available in many different clinical settings, can be applied to the evaluation of different skeletal muscle groups, and allows bedside serial measurements of muscle cross-sectional diameter and area [4,5]. Thus, this noninvasive method could represent a good alternative to more sophisticated and expensive techniques. Ultrasonographic measurements of the quadriceps muscle (the single largest skeletal muscle group in the body) are highly correlated to muscle mass as assessed by gold standard methods [6,7]. Specifically, quadriceps femoris muscle thickness best correlates with fat-free mass by DEXA [6], and appears to be as accurate as the quantification of muscle mass by CT or MRI [7,8]. Finally, quadriceps femoris US has been suggested recently as a reliable and easily reproducible method to assess muscle thickness in patients with Acute Kidney Injury (AKI) [9]. The same study also showed that even relevant and rapid fluid shifts caused by renal replacement therapy in edematous patients did not affect US measurements of quadriceps muscle thickness [9].

No data are currently available on the utilization of quadriceps femoris muscle US in patients with ESRD-HD. Thus, in the present study we performed US measurements to assess the thickness of two out of four muscles constituting the quadriceps femoris (namely, the rectus femoris [quadriceps rectus femoris thickness, QRFT] and the vastus intermedius [quadriceps vastus intermedius thickness, QVIT]) in patients with ESRD-HD. Healthy subjects and hospitalized patients with normal renal function and nutritional status were used as controls.

The specific aims of the study were:

a) to evaluate if QRFT and QVIT are decreased in patients with ESRD-HD in comparison to both healthy subjects and well-nourished hospitalized patients with normal renal function;
b) to evaluate if QRFT and QVIT are different in patients with ESRD-HD when they are stratified based on conventional diagnostic criteria for PEW;
c) to ascertain if a correlation exists between US measures and conventional variables utilized for the evaluation of muscle mass and nutritional status in the same clinical setting;
d) to ascertain if measurements in ESRD-HD are affected by the dialysis procedure itself.

2. Materials and methods

A cross-sectional, prospective observational study was performed in Italy at six Hemodialysis Centers of the National Health System (Parma, Borgo Val di Taro, Livorno, Piombino, Cecina and Reggio Emilia). The study was approved by the local Institutional Review Board (Ref. n° 45737, December 12th, 2015). The procedures were in agreement with the Declaration of Helsinki, and written informed consent was obtained from all the participants.

The following groups of subjects were enrolled:

A – Healthy subjects: We enrolled 35 subjects from the hospital staff. Inclusion criteria were BMI > 18.5 kg/m^2, Subjective Global Assessment (SGA) class A, absence of chronic or acute illnesses.
B – Hospitalized patients with normal renal function: We enrolled 30 hospitalized adult patients with normal renal function from internal medicine wards. Inclusion criteria were BMI > 18.5 kg/m^2, SGA class A and eGFR > 90 ml/min/1.73 m^2 by the CKD-EPI equation. Heart failure, chronic obstructive pulmonary disease, chronic liver disease, chronic use of corticosteroids, malignancy, proteinuria, or diabetes mellitus were considered as exclusion criteria.
C – One hundred twenty-one adult ESRD-HD patients with at least 6-month dialysis vintage. Malignancy or conditions with mandatory immobilization (e.g., amputation) were considered as exclusion criteria.
D – Thirty additional ESRD-HD patients were enrolled for the comparison between US muscle measurements taken at the start and immediately after the end of the dialysis session

2.1. Ultrasonographic technique

QRFT and QVIT were measured by experienced assessors (renal dietician or nephrologists) using B-mode, wall-tracking US systems (Philips HD7xe, Logiq and General Electric) and 7.5 MHz linear array transducers. The transducer was placed perpendicular to the long axis of the thigh with abundant use of contact gel and minimal pressure to avoid compression of the muscle. Measurements were performed in a standardized way at the level of two specific landmarks, the midpoint and the border between the lower third and the upper two-thirds between the superior anterior iliac spine and the upper pole of the patella, as previously described [9]. The right and left quadriceps femoris muscle thickness were measured in both legs with the patient lying in a supine position, with both knees extended but relaxed and toes pointing upwards. Assessors performed two measurements at the level of each landmark (for a total of 8 measurements in each subject) immediately before each hemodialysis session, and the average of the values obtained for each site was used in the analyses. QRFT and QVIT were measured at the internal limit of the muscle. For the comparison between measurements performed before and after hemodialysis, measurements were performed by the same assessor, immediately before and within 15 min after the end of each dialysis session.

2.2. Nutritional status evaluation

ESRD-HD patients were independently evaluated by a different assessor blinded of the US measurements for protein-energy wasting (PEW) by using the International-Society for Renal Nutrition and Metabolism (ISRNM) recommendations [10]. A PEW diagnosis was made accordingly.

In addition, the SGA status was defined [11] and the malnutrition inflammation score (MIS) was calculated [12].

2.3. Demographic and clinical variables

Demographic, clinical and anthropometric data (height, body weight, BMI, triceps skinfold and mid-arm circumference) were collected for all groups. In ESRD patients, dialysis characteristics, chronic comorbidities and laboratory data were also collected.

2.4. Statistical analysis

Based on the data from a previous study [9] we estimated that sample sizes of 43 and 129 in the control and ESRD group would achieve an approximate 80% power to detect a difference of −0.2 cm between the null hypothesis that both groups means are 0.12 cm and the alternative hypothesis that the mean of the control group is 0.14 cm when the estimated common standard deviation is 0.4 cm (i.e. that the effect size of the difference between ESRD-HD and the control group is 0.50) and the significance level is 0.05, using a two-sided two-sample *t*-test.

Data are expressed as mean and standard deviation, or median and range for continuous variables, as appropriate. Categorical variables are expressed as frequencies (percentage). To analyze differences in muscle thickness among groups of patients we fitted a linear mixed model with group as main factor (i.e. ESRD-HD patients, hospitalized patients and healthy subjects) and age, gender and BMI as covariates. In further analyses exploring differences in muscle thickness in ESRD-HD patients after stratification based on conventional diagnostic criteria for PEW, we fitted linear mixed models with subgroup as main factor and age, gender and BMI (stratification by serum albumin or MIS) or age and gender (stratification by BMI) as covariates.

The correlation between nutritional variables (BMI, Albumin, MIS score and arm muscle area) and ultrasound was assessed by Pearson's correlation coefficient for parametric data and Spearman correlation coefficient for non-parametric data.

For the comparison between measurements performed before and after the hemodialysis session, a paired *t*-test was used. Data analysis was performed using SPSS (Version 23, Armonk, NY: IBM Corp. USA).

3. Results

3.1. Clinical and demographic variables

Both ESRD-HD patients and hospitalized patients were significantly older compared to the healthy subjects control group; no statistically significant difference was found between ESRD-HD patients and hospitalized patients. Male patients were more prevalent in the ESRD-HD group. BMI values were not significantly different among the three groups (Table 1).

Clinical, metabolic and nutritional variables of the entire ESRD-HD cohort are reported in Table 2. On average, these patients had a fair dietary protein intake (DPI) (1.11 [SD 0.27] g/kg/day], low serum albumin (3.63 [SD 0.39] g/dL), and only a limited number of cases of PEW (14% [17/121]) as diagnosed by the ISRNM criteria.

Table 3 illustrates the clinical and nutritional data of ESRD-HD patients when stratified by variables commonly used for the evaluation of the nutritional status in this clinical setting (BMI, albumin and MIS score status). No difference in DPI was found between subgroups (BMI $\geq$ 23 kg/m^2 *vs* BMI < 23 kg/m^2: 1.08 [SD 0.06] *vs* 1.12 [SD 0.29], $P = 0.40$; albumin $\geq$ 3.8 g/dL *vs* albumin < 3.8 g/dL: 1.09 [SD 0.07] *vs* 1.14 [SD 0.26], $P = 0.30$; MIS score $\geq$ 6 *vs* MIS score < 6: 1.08 [SD 0.25] *vs* 1.14 [SD 0.29], $P = 0.25$). There was no significant difference in inflammatory status as assessed by CRP; on the other hand, predictably, all of the variables used for the assessment of nutritional status were different between the BMI, and MIS subgroups. No differences were found in BMI and arm muscle area when ESRD-HD patients were stratified according to albumin status. Conversely, when patients were stratified according to the MIS score, BMI ($P < 0.001$) and arm muscle area ($P = 0.004$) were significantly different between the subgroups; significant differences between the MIS subgroups were also found in some metabolic variables, namely blood urea nitrogen ($P < 0.001$), serum creatinine ($P = 0.003$), serum transferrin ($P < 0.001$), and albumin ($P < 0.001$).

Table 2
Clinical, metabolic and nutritional variables of ESRD-HD patients.

Variable	All patients ($n = 121$)
Dialysis vintage (years, median [range])	4.1 [0.55–40.3]
Laboratory data	
BUN (mg/dL)	48 (20)
sCr (mg/dL)	8.8 (3.4)
Transferrin (mg/dL)	192 (43)
CRP (mg/L) (median [range])	1.41 [0.0–191.7]
Albumin (g/dL)	3.63 (0.39)
DPI (g/kg/day)	1.11 (0.27)
Cholesterol (mg/dL)	155 (41)
Triglycerides (mg/dL)	158 (90)
Chronic comorbidities	
Diabetes mellitus (%)	30/121 (25)
COPD (%)	11/121 (9)
Peripheral vascular disease (%)	36/121 (30)
Cerebral vasculopathy (%)	25/121 (21)
Coronary artery disease (%)	30/121 (25)
Chronic heart failure (%)	11/121 (9)
Nutritional status	
SGA score	29 (4.7)
MIS score (median [range])	6 [1–22]
AMA (cm^2)	47.9 (13.1)
Body weight (kg)	68.1 (12.4)
BMI	24.9 (4.6)
PEW status (%)	17/121 (14)

AMA, arm muscle area; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DPI, dietary protein intake; MIS, malnutrition inflammation score; PEW, protein energy wasting; sCr, serum creatinine; SGA, subjective global assessment.
Data are expressed as mean (standard deviation), except when differently specified.

3.2. Comparison between US measurements performed before and after the hemodialysis session

Demographic and clinical characteristics of the 30 patients enrolled in this part of the study are shown in the Supplementary Table 1. Figure 1 illustrates the mean muscle thickness for both

Table 1
Demographic and anthropometric data of healthy subjects, hospitalized patients and ESRD-HD patients.

	Healthy subjects ($n = 35$)	Hospitalized patients ($n = 30$)	ESRD-HD ($n = 121$)	ANOVA
Age (SD)	41 (10.0)[a]	63 (17.2)[c]	67 (16)	<0.001
Gender (male) %	15/35 (43%)[b]	16/30 (53%)[c]	79/121 (65%)	0.046
Height, cm (SD)	170 (9)[c]	169 (10)[c]	166 (9)	0.050
Weight, kg (SD)	70.5 (16.6)	75.4 (16.2)[b]	68.1 (12.4)	0.037
BMI (SD)	24.3 (4.6)[c]	26.4 (4.8)[c]	24.9 (4.6)	0.16

BMI, body mass index; ESRD, end-stage renal disease.
Data are expressed as mean (standard deviation). Gender is reported as percentage of males.
[a] $P < 0.001$ *vs* ESRD.
[b] $P < 0.05$ *vs* ESRD.
[c] Non-statistically significant *vs* ESRD, post-hoc multiple comparisons with Dunn's test.

Table 3
Clinical and nutritional data of ESRD-HD patients stratified by BMI, albumin and MIS score status.

	BMI < 23 kg/m^2 (n = 47)	BMI ≥ 23 kg/m^2 (n = 74)	P	Albumin < 3.8 g/dL (n = 71)	Albumin ≥ 3.8 g/dL (n = 50)	P	MIS score < 6 (n = 51)	MIS score ≥ 6 (n = 70)	P
Age	65 (18)	68 (14)	0.33	70 (18)	62 (18)	0.003	59 (15)	72 (15)	<0.001
Gender male (%)	68 (32/47)	64 (47/74)	0.61	59 (42/71)	74 (37/50)	0.09	61 (31/51)	69 (48/70)	0.37
Laboratory data									
BUN (mg/dL)	48 (16)	47 (21)	0.79	44 (14)	53 (22)	0.05	57 (21)	41 (16)	<0.001
sCr (mg/dL)	8.9 (2.6)	8.7 (3.3)	0.69	8.5 (3.7)	9.2 (3.9)	0.28	9.9 (3.8)	7.9 (2.8)	0.003
Transferrin (mg/dL)	187 (19)	196 (42)	0.29	187 (21)	201 (44)	0.08	215 (38)	176 (39)	<0.001
CRP (mg/L)	1.2 [0.0–114.0]	1.4 [0.06–191.7]	0.39	1.6 [0.05–192]	1.3 [0.03–15.2]	0.22	1.55 [0.05–20.2]	0.98 [0.02–192]	0.51
Albumin (g/dL)	3.6 (0.1)	3.6 (0.4)	0.62	3.4 (0.2)	4.0 (0.1)	<0.001	3.8 (0.3)	3.5 (0.42)	<0.001
DPI (g/kg/day)	1.08 (0.06)	1.12 (0.29)	0.40	1.09 (0.07)	1.14 (0.26)	0.30	1.14 (0.29)	1.08 (0.25)	0.25
Nutritional status									
SGA score 1 (well-nourished)	68 (32/47)	93 (69/74)	<0.001	77 (55/71)	92 (46/50)	0.05	94 (48/51)	76 (53/70)	0.007
SGA values	27.5 (0.7)	30.4 (3.6)	0.003	28.6 (11.3)	30 (3.8)	0.16	32 (3)	28 (5)	<0.001
MIS score	7 [1–22]	5 [1–16]	0.004	7 [1–22]	5 [1–15]	<0.001	4 [1–5]	8 [6–22]	<0.001
AMA (cm^2)	40 (0.9)	52.9 (12.6)	<0.001	47.6 (6.1)	48.5 (11.1)	0.53	51.4 (11.5)	45.3 (13.6)	0.004
BMI	20.5 (0.2)	27.6 (3.6)	<0.001	24.9 (4.9)	24.8 (4.1)	0.89	26.6 (4.3)	23.6 (4.4)	0.003
PEW status (%)	34 (16/47)	1 (1/74)	<0.001	24 (17/71)	0 (0/50)	<0.001	4 (2/51)	21 (15/70)	0.007

AMA, arm muscle area; BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; DPI, dietary protein intake; MIS, malnutrition inflammation score; PEW, protein energy wasting; sCr, serum creatinine; SGA, subjective global assessment.
Data are expressed as mean (standard deviation) or median (range).

measurements. No significant difference was found between measurements performed before and after the end of the hemodialysis session. Weight change was −2.25 kg (−0.5 to −3.6). We divided patients into 2 groups based on the median of intradialytic weight-loss (<−2.25 kg and >−2.25 kg) in order to assess whether the amount of fluid removed could have influenced US measurements; no difference was found between these subgroups (Supplementary Table 2).

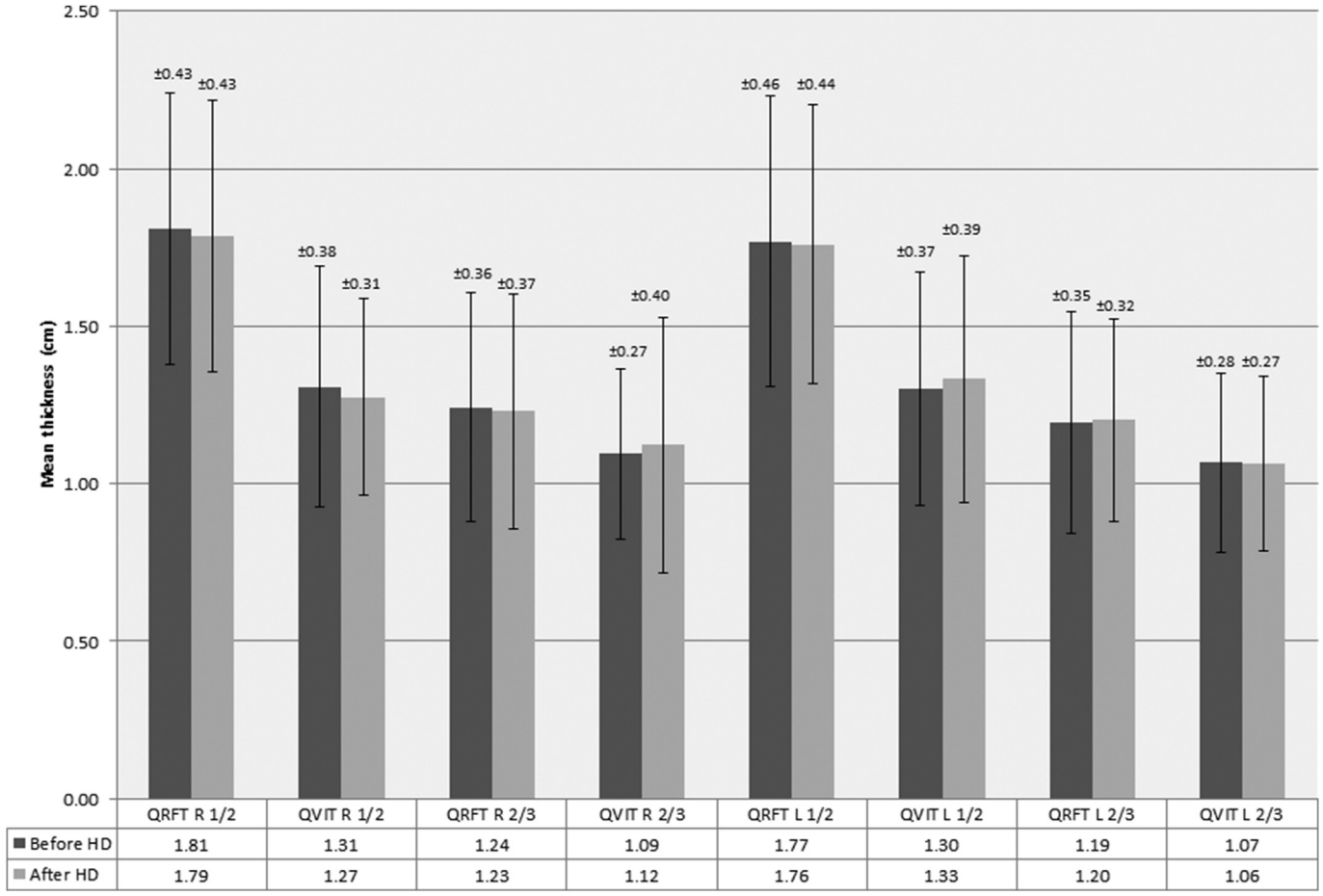


Fig. 1. Comparison between US measurements performed before and after the HD session. Data are expressed as mean and standard deviation. No significant difference was found between measurements. HD, hemodialysis; US, ultrasound.

3.3. Ultrasonographic measurements of muscle thickness

Figure 2 illustrates the values of QRFT and QVIT in ESRD-HD patients, hospitalized patients and healthy subjects. All of the measures of muscle thickness were significantly lower at all sites in ESRD-HD patients compared with the two control groups. After adjusting for gender, age and BMI, QRFT and QVIT of ESRD-HD patients remained significantly lower as compared to the control groups.

Patients with a BMI < 23 kg/m^2 showed decreased quadriceps muscle thickness at all of the explored sites compared to well-nourished patients. The differences in QVIT were greater than the differences in the QRFT, but all differences achieved statistical significance (Fig. 3A). At multivariable analysis, the adjusted differences in muscle thickness between the MIS subgroups were highly statistically significant (Fig. 3C). Conversely, no differences were found in muscle thickness between patients with serum albumin < 3.8 g/dL compared to those with serum albumin ≥ 3.8 g/dL (Fig. 3B).

3.4. Correlation between conventional nutritional variables and quadriceps muscle thickness assessed by US

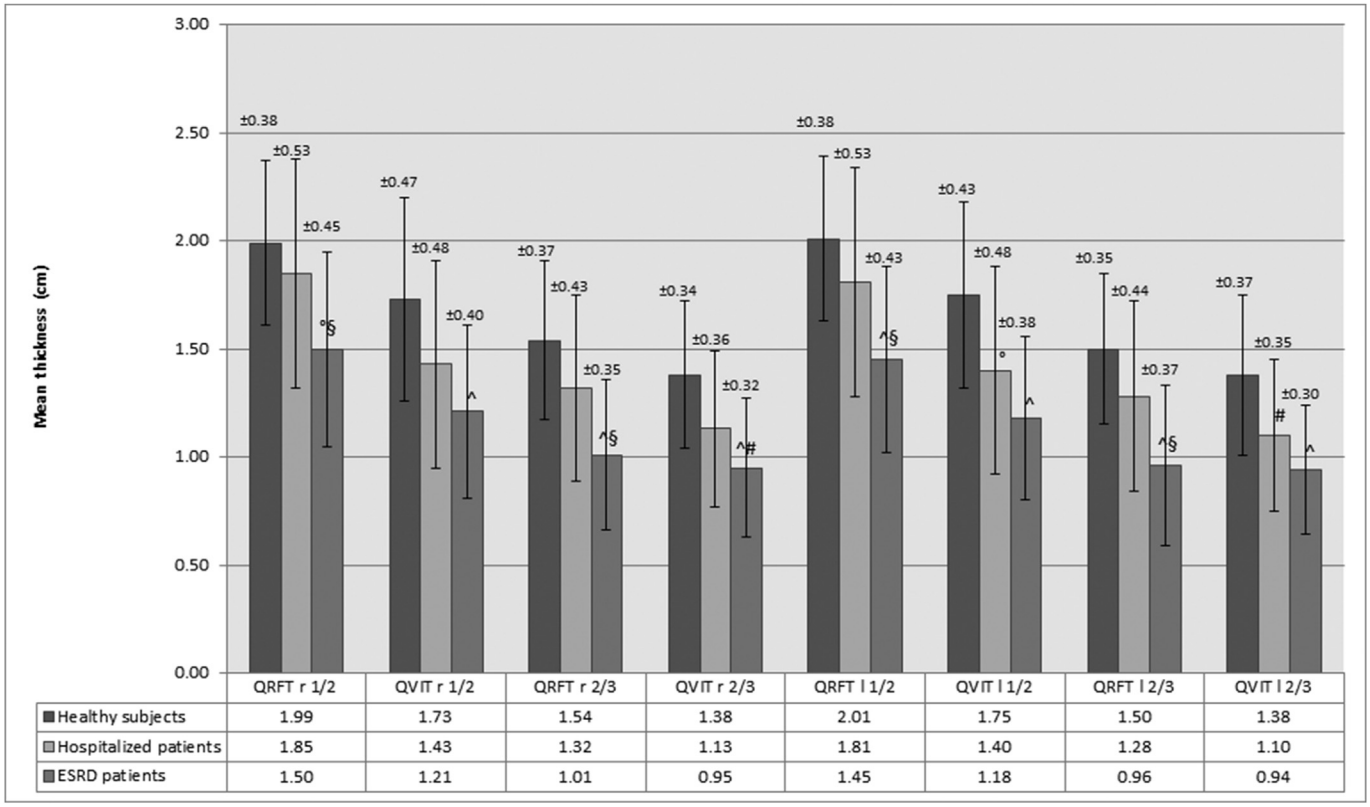
Muscle ultrasonographic indexes were significantly and negatively correlated with the MIS score ($r = -0.37$ to -0.47, $P < 0.001$ for all sites of measurement). BMI ($r = 0.19$–0.36, $P = 0.04$ to $P < 0.001$ for all sites of measurement), albumin ($r = 0.19$–0.27, $P = 0.03$ to $P = 0.003$ for all sites of measurement), and arm muscle area ($r = 0.24$–0.36, $P = 0.005$ to $P < 0.001$ for all sites of measurement) had a weaker though significant positive correlation to quadriceps muscle thickness as assessed by US.

4. Discussion

The main finding of this study is that ESRD-HD patients had lower quadriceps muscle thickness, as assessed by US measurements, in comparison to both younger healthy subjects and well-nourished age-matched hospitalized patients with normal renal function without acute or chronic comorbidities known to negatively influence nutritional status. This finding is unchanged even after adjusting for sex, age and BMI.

Our findings confirm recent data obtained in patients with chronic kidney disease (CKD) on conservative treatment, indicating that the prevalence of sarcopenia as assessed by DEXA was higher among patients with lower eGFR values and ≥60 years old [13]. Moreover, our findings are in agreement with the results of another study performed with MRI, reporting that the volume of quadriceps muscle was significantly lower in ESRD-HD compared to controls [14].

When ESRD-HD patients were stratified for different indexes of nutritional status, muscle mass, as estimated by US measurement of quadriceps muscle thickness, was significantly decreased in malnourished patients. Adopting the ISRNM cut-off values for BMI clearly identified patients with reduced quadriceps muscle thickness and other altered nutritional variables, such as arm muscle area, SGA and MIS score. Similarly to the BMI, patients in the subgroup of the worse MIS score (≥6) had lower quadriceps muscle thickness, arm muscle area, BMI and SGA score, but also lower albumin and total transferrin levels. However, since albumin, transferrin, BMI and the SGA are part of the MIS, these results were not unexpected. On the other hand, stratification of ESRD-HD patients based on albumin cut-off values did not reveal significant differences in quadriceps muscle thickness, BMI or arm muscle area



	QRFT r 1/2	QVIT r 1/2	QRFT r 2/3	QVIT r 2/3	QRFT l 1/2	QVIT l 1/2	QRFT l 2/3	QVIT l 2/3
Healthy subjects	1.99	1.73	1.54	1.38	2.01	1.75	1.50	1.38
Hospitalized patients	1.85	1.43	1.32	1.13	1.81	1.40	1.28	1.10
ESRD patients	1.50	1.21	1.01	0.95	1.45	1.18	0.96	0.94

Fig. 2. Ultrasound measurements of QRFT and QVIT of ESRD-HD, healthy subjects and hospitalized patients. Data are expressed as mean (standard deviation). $P < 0.001$ adjusted for age, sex and BMI. °$P < 0.01$, ^$P < 0.001$ *vs* healthy subjects; #$P < 0.05$, §$P < 0.001$ *vs* hospitalized patients. Post-hoc pairwise comparisons by Sidak's test based on estimated marginal means in the mixed linear model. BMI, body mass index; ESRD-HD, end-stage renal disease; QRFT, quadriceps rectus femoris thickness; QVIT; quadriceps vastus intermedius thickness.

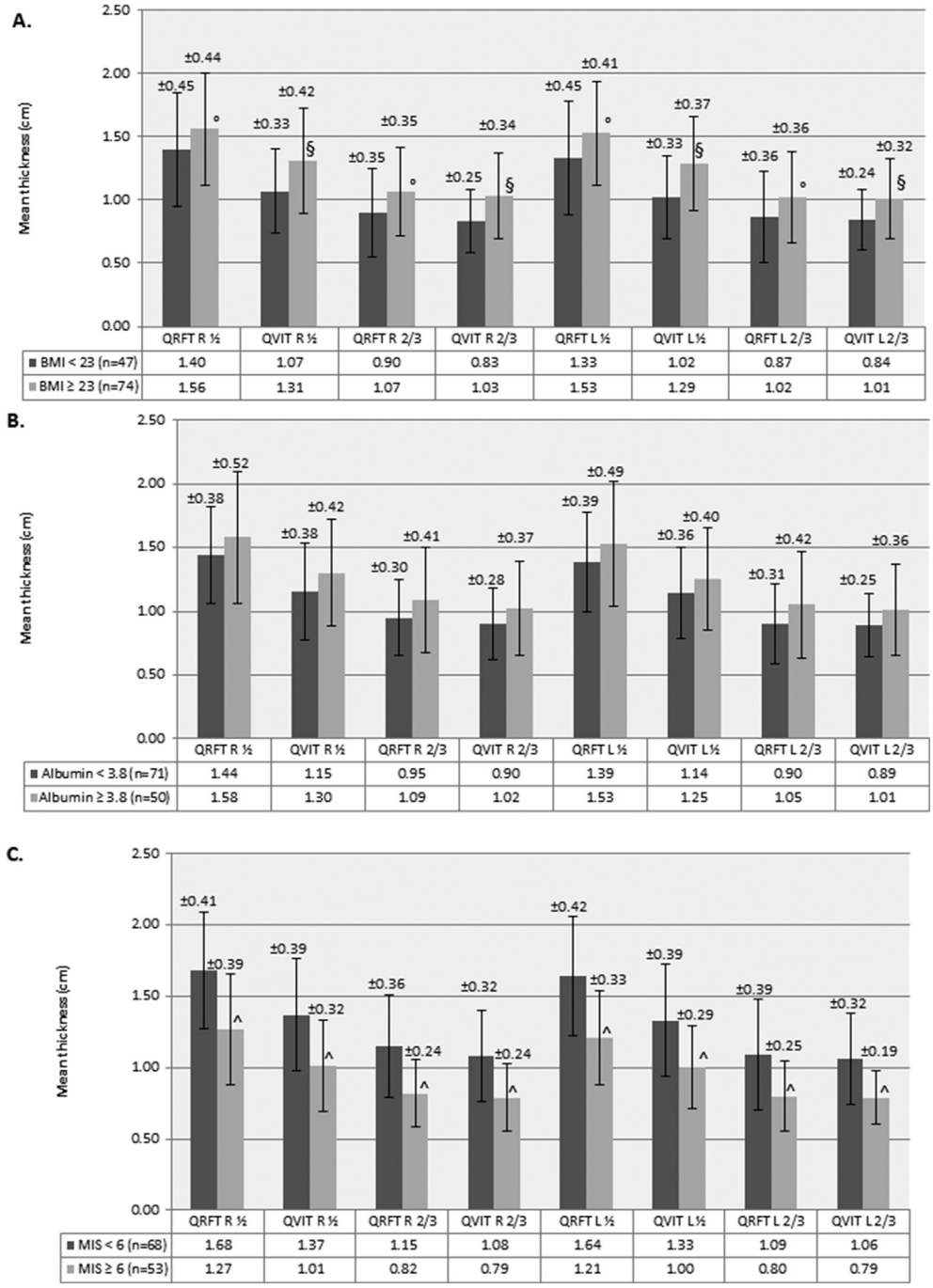


Fig. 3. (A–C). QRFT and QVIT of ESRD-HD patients stratified based on BMI, albumin and MIS score status. Data are expressed as mean and standard deviation. BMI, Body mass index; ESRD, End-stage renal disease; MIS, Malnutrition inflammation score; QRFT, Quadriceps rectus femoris thickness; QVIT, Quadriceps vastus intermedius thickness. A.ESRD patients stratified by BMI. $P < 0.01$, adjusted for age and gender. °$P < 0.01$, §$P < 0.001$ *vs* BMI < 23. Post-hoc pairwise comparisons by Sidak's test based on estimated marginal means in the mixed linear models. B. ESRD patients stratified by albumin. No significant difference between groups, analysis adjusted for age, gender and BMI. C. ESRD patients stratified by MIS score. $P < 0.01$, adjusted for age, gender and BMI. ^$P < 0.001$ *vs* MIS < 6. Post-hoc pairwise comparisons by Sidak's test based on estimated marginal means in the mixed linear models.

reinforcing the poor value of albumin for nutritional status evaluation in ESRD-HD patients, since this variable is known to be also influenced by the inflammatory status typical of ESRD-HD patients [15,16].

We found low to moderate statistically significant correlations between muscle thickness measured by US and other nutritional variables (MIS, arm muscle area, albumin and BMI), with the strongest correlation being found between US measurements and the MIS score. A partial explanation for this finding may reside in the fact that the MIS score is a composite of different nutritional variables, while other variables assessed in this study do not directly reflect (e.g., albumin and BMI), or measure (e.g., arm muscle area) muscle mass. Although BMI was found to be significantly correlated ($r = 0.69$, $P < 0.0001$) with total body muscularity,

as assessed by US measurements of muscle thickness at 9 body sites [17], a lower correlation with the muscle mass of one single limb may be expected.

As in our study on patients with AKI [9], we were able to confirm that US measurements of the quadriceps femoris muscle seems not to be influenced by rapid fluid shifts, even in chronically hyperhydrated patients.

Even despite we are not aware of other studies investigating US measurements of quadriceps muscle thickness in ESRD-HD, it is important to address the limitations of the present study. First of all, no validation of US against a gold standard technique such as CT or MRI was obtained in our ESRD-HD patients. However, the US method for the evaluation of quadriceps femoris muscle has been validated in other clinical settings, such as COPD and coronary artery disease patients [7,18]. Secondly, since this was planned as an observational cross-sectional study, we could not explore the prognostic value of quadriceps muscle thickness in ESRD-HD. Nevertheless, a recent study in a different clinical setting, suggested that reduction in the rectus femoris area measured by US could represent an independent risk factor for hospital readmission and longer hospitalization [19]. Thirdly, in addition to PEW, other factors are known to negatively affect muscle mass, with the most relevant being the level of physical activity [20], a variable not taken into account in our study. Literature data indicate that a sedentary lifestyle is predominant in hemodialysis patients [21–24], and this could represent an important factor contributing to the reduced muscularity found in our study. Nevertheless, the stratification of our ESRD-HD patients into groups based on other nutritional parameters confirmed the lower muscularity in those with worse nutritional status. In addition, the prevalent sedentary lifestyle, and consequently lower muscularity, adds to the increased risk for sarcopenia of ESRD patients. Lastly, we choose two different control groups, young healthy subjects and well-nourished hospitalized patients with normal renal function. Statistical analysis performed by adjusting for sex and age plus BMI, confirmed the differences observed between ESRD-HD patients and control subjects.

The potential for US evaluation of skeletal muscles in ESRD-HD makes it possible to foresee its application to other important research topics. In a recent study in patients with Chronic Kidney Disease on conservative treatment (i.e. not yet started on dialysis), an increase in the area of the rectus femoris muscle measured by US was demonstrated in patients undergoing a physical exercise program compared to sedentary patients matched by age and comorbidities [25]. Together with the early identification of patients in risk for PEW, the ability to directly measure the effectiveness of nutritional interventions and of physical activity intervention programs aimed at improving muscle trophism and mass, could strongly support a more extensive application of muscle US in renal patients.

In conclusion, quadriceps muscle US is a simple technique, easily applicable at the bedside in dialysis units, and suitable for the identification of ESRD-HD patients with reduced muscle mass. Since US is widely available in the Nephrology setting, has a low cost, does not require dedicated staff (radiologists), is non-invasive, and does not provide radiation exposure, it could become a particularly useful tool for bedside evaluation of muscle mass. This could allow an early identification of patients at risk for PEW, as well as a close monitoring of nutritional and rehabilitative interventions aimed at increasing lean body mass.

Statement of authorship

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Conflicts of interest

Authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.05.004.

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