



ORIGINAL ARTICLE

Association of Ultrasound Quadriceps Muscle Thickness with Frailty among Hemodialysis Patients

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ABSTRACT

Background: Frailty, an age-related trait linked to poor chronic kidney disease (CKD) outcomes, affects 66.3% of Egyptian patients. Two-thirds of elderly CKD patients frequently feel fatigued with high risk of falling. Ultrasound can be used for objective frailty evaluations. Measurement of Bilateral Anterior Thigh Thickness (BATT) using ultrasound is a promising, simple, cheap and non-invasive tool to predict frailty. The current study aims to Evaluate the ultrasound measurements of BATT in screening for Frailty in hemodialysis patients.

Methods: The cross-sectional study comprised 120 adult end-stage renal disease (ESRD) patients on regular hemodialysis at Zagazig University from November 2023 to April 2024. The FRAIL scale, clinical exams, frailty phenotypic tests, bilateral anterior thigh muscle thickness by ultrasounds and routine labs were measured.

Results: We found gender differences in Frailty (70%) males, (30%) women. Men (45.2%) were more pre-frail than women (13.9%) ($p=0.0009$), but women (83.3%) were frailer. Females with lower bilateral anterior thigh thickness ($36.5\pm4.7\text{mm}$) had higher frailty ratings, slower walking speed and poorer hand grip strength compared to men ($58.1\pm10.4\text{mm}$) ($p<0.0001$). There was a significant positive association between low BATT and Frailty Phenotype score ($P=0.0494$) ($OR=1.096$). While there was significant negative association between low BATT and Walking Speed ($P=0.0437$) ($OR=1.0275$) and Grip strength ($P<0.0001$) ($OR=0.9795$).

Conclusion: Bilateral Anterior Thigh Thickness measurements via ultrasound are effective in screening for frailty in hemodialysis patients. Low BATT correlates with higher frailty and worse physical performance, indicating its utility in early detection.

Keywords: Quadriceps Muscle Thickness, Frailty, Hemodialysis.

INTRODUCTION

A complicated age-related condition, frailty is typified by a decline in physical health and a reduction in functional reserves. Frailty is a powerful predictor of bad clinical outcomes, such as increased hospitalization rates and mortality, and it considerably increases an individual's vulnerability across all stages of chronic kidney disease (CKD) [1].

Frailty in ESRD has a complex pathophysiology. Compared to their non-frail peers, frail patients are probably more prone to experience morbidity and mortality. Numerous frailty screening instruments have been investigated and proven effective in various CKD and ESRD contexts. The focus should be on using any one of the screening techniques to detect frailty if there isn't agreement on the best

one. To address risk factors that could worsen its course, a comprehensive individual assessment should be taken into consideration. All frail ESRD patients should have access to personalized exercise programs, adequate food intake, and social and psychological support. Frailty screening has not yet gained general acceptability, despite attempts to include it in the ESRD population made by the ERBP in 2016 and the Kidney Disease Improving Global Outcomes (KDIGO) in 2015[2].

Regardless of age, frailty is very common among ESRD patients. Patients undergoing hemodialysis (HD) and peritoneal dialysis (PD) have prevalence rates ranging from 30% to 80% and 65% to 72%, respectively [3]. These rates are significantly higher than the 12% rate for patients with kidney disease at an earlier stage [4].

In Egypt, a recent study by Abdelhamid et al. [5] found that nearly 50% of elderly patients with CKD, typically those aged 65 years and older, are at high risk of falls. Furthermore, about two-thirds of these patients experienced fatigue, a symptom often associated with frailty and disability, particularly among those undergoing hemodialysis.

First off, there hasn't been any research done on bilateral anterior thigh thickness in the context of hemodialysis. Second, no research has been done on the connection between frailty and US-derived muscle characteristics in hemodialysis patients. Currently, frailty diagnosis relies on various clinical scoring systems, such as the FRAIL scale, which often include subjective measures. To address this limitation, research is focusing on the use of ultrasound as a more objective and quantitative tool for assessing frailty [6,7]. The wide availability of ultrasonography in hemodialysis units, besides being cheap, non-invasive and easily applicable measure, makes it an attractive tool for frailty screening. In the current study, we aimed to evaluate the application of ultrasound measurements of bilateral anterior thigh thickness (BATT) as a routine screening method for frailty in hemodialysis patients.

METHODS

This cross-sectional study involved 120 patients with end-stage renal disease undergoing regular hemodialysis at the nephrology unit of the Internal Medicine Department, Faculty of Medicine, Zagazig University. The study took place from November 2023 to April 2024.

Participants were adults aged 18 years and older who had been receiving regular hemodialysis for at least six months and were able to provide informed consent. Patients were excluded if they had hemodialysis for less than 6 months, declined participation, or were under 18 years old.

In this study, all participants underwent a comprehensive evaluation including a detailed history and completion of the FRAIL scale. The FRAIL scale is a 5-question tool assessing fatigue, resistance, ambulation, illness, and weight loss. It is then assessed in the form of a score ranging from 0 to 5, categorizing health status as frail (3-5), pre-frail (1-2), or robust (0). Fatigue was measured based on responses to tiredness over the past month, while resistance and ambulation were assessed by difficulty with walking and climbing stairs. Illness was scored based on the number of reported illnesses, and weight loss was recorded if there was a 5% or greater decline in body weight over the past year.

Participants also underwent a thorough clinical examination and frailty phenotype (FP) tests. Typical walking aids were allowed, and one of these was a timed walk speed measured more than four meters from a standing start. No walking speed was determined, and a deficit was noted for this component of the pertinent frailty scores if the participant was unable to finish the 4m. A dynamometer was used to assess the patient's bilateral hand-grip strength while the patient's arm was resting at their side, elbow extended, and wrist in the neutral resting position. After discarding the results of a practice grip, each subject was given one summative grip on each hand, during which they were urged to exert all their effort. Although both scores were recorded, the higher of the two was chosen for further examination. In the original Fried frailty phenotypic cohort,

adjusted hand-grip strength was computed as the fold changes from the lowest 20% by gender and BMI [9].

Blood sample was taken before the mid-week dialysis session. Laboratory tests included a complete blood count with emphasis on the total leukocyte count and neutrophil/lymphocyte ratio (NLR), liver and kidney function tests, hemoglobin A1c, fasting blood sugar, lipid profile, serum electrolytes, and parathyroid hormone (PTH) levels. Additionally, participants had an electrocardiogram (ECG) and echocardiography performed.

Consenting individuals' bilateral anterior thigh muscle thickness was assessed by ultrasonography during routine dialysis sessions. With their knees pleasantly supported in a natural resting posture of 10° to 20°, they were sitting at an angle of $\leq 45^\circ$. The total of the bilateral rectus femoris and vastus intermedius antero-posterior depth was used to determine the bilateral anterior thigh thickness. A single transverse plane in the anterior mid-thigh captures the depth of the rectus femoris, vastus intermedius, and subcutaneous tissue. This was defined as half of the measured distance between the femur's lateral epicondyle and greater trochanter. The low muscle mass (LMM) thresholds for males and females were 54.36 mm and 38.53 mm, respectively.

The Institutional Review Board (IRB) at Zagazig University's Faculty of Medicine gave its approval to the study (IRB#: 5 /8-1-2025). Every study procedure complied with the Declaration of Helsinki's and its modifications' ethical guidelines. Prior to enrollment, all individuals provided written informed consent.

STATISTICAL ANALYSIS

The computer was fed data, and IBM SPSS Corp., released in 2013, was used for analysis. IBM SPSS Statistics 22.0 for Windows. N.Y. Armonk: IBM Corp. Percentage and numbers were used to describe qualitative data. The Kolmogorov-Smirnov test was used to check for normality, and the mean and standard deviation were used to represent quantitative data. The median and interquartile range were

used for non-parametric data. The qualitative data analysis test was Chi-Square test for comparison of 2 or more groups. Quantitative data analysis tests between groups were Parametric tests, independent student t test that was used to compare 2 independent groups and One-way ANOVA test that was used to compare >2 independent groups, and non-parametric tests, Mann Whitney test that was used to compare 2 independent groups. The significance of the results was assessed at the 0.05 level.

RESULTS

The study included 120 patients, the main causes of ESRD were hypertension (49.2%), diabetes (9.2%) and unknown causes (20%). The average BMI was 26.3 ± 5.6 kg/m². Bilateral Anterior Thigh Thickness (BATT) was low in 55 (45.83%) while the remaining were within normal range according to their age, sex, and BMI. Other demographic data, baseline characteristics and laboratory investigations of the study population are outlined in table 1.

We assessed the impact of gender on the incidence of frailty indicated by different frailty measures (Table 2). Female patients showed higher incidence of frailty indicated by significant difference in different frailty indicators from their male counterparts. Grip strength was significantly lower in females (17.1 ± 4.35 kg) compared to males (32.54 ± 9.56 kg) ($p < 0.0001$), as well as Walking speed (8.39 ± 2.62 s vs. 6.79 ± 3.08 s) ($p = 0.0003$). Females had higher Frailty Phenotype (FP) scores, with a significantly higher proportion scoring 2 (21, 25%) and 4 (18, 21.43%) in males compared to females scoring 2 (1, 2.78%) and 4 (15, 41.67%) ($p = 0.0037$ and $p = 0.0228$, respectively). Overall, more females (31, 86.11%) were frail compared to males (45, 53.57%) ($p = 0.0006$).

On the FRAIL Scale, Frailty severity was higher in females (30, 83.33%) compared to males (39, 46.43%) ($p = 0.0001$), while more males (38, 45.24%) were prefrail compared to females (5, 13.89%) ($p = 0.0009$). Bilateral Anterior Thigh Thickness (BATT) was

significantly lower in females (36.46 ± 4.72 mm) than in males (58.1 ± 10.39 mm) ($p < 0.0001$), with low BATT more common in females (24, 66.67%) compared to males (31, 36.9%) ($p = 0.0025$).

The relation between low BATT and different frailty indices was then assessed. The univariable analysis showed significant association between low BATT and each of Frailty Phenotype (FP) score ($P < 0.0001$), and FRAIL Scale score ($P < 0.0001$). There was a

significant negative correlation between low BATT and each walking speed ($P < 0.0001$) and Grip strength measured ($P < 0.0001$) (Table 3). Upon multivariable analysis, the significant association between low BATT and Frailty Phenotype (FP) score ($P = 0.0494$) (OR=1.096) was maintained, as well as the negative correlation between low BATT and its 2 components: Walking Speed ($P = 0.0437$) (OR=1.0275) and Grip strength ($P < 0.0001$) (OR=0.9795) (Table 4).

Table 1: Baseline Demographic data and Laboratory investigations of the study population.

Age	58.59 ± 12.57
Gender	
• Male	84 (70%)
• Female	36 (30%)
Dialysis Ventage	6.85 ± 4.88
Comorbidities	
• Hypertension	85 (70.83%)
• Diabetes Mellitus	29 (24.17%)
• Chronic lung disease	5 (4.17%)
• Bronchial Asthma	3 (2.5%)
• Congestive heart failure	11 (9.17%)
• Angina Pectoris	7 (5.83%)
• Rheumatoid arthritis	8 (6.67%)
Cause of end stage renal disease	
• Hypertension	59 (49.17%)
• Diabetes Mellitus	11 (9.17%)
• Glomerulonephritis	6 (5%)
• Autosomal dominant polycystic kidney disease	6 (5%)
• Urologic causes	6 (5%)
• Unknown	24 (20%)
• Drug induced	9 (7.5%)
BMI (Kg/m²)	26.33 ± 5.56
• Underweight	11 (9.17%)
• Average	46 (38.33%)
• Overweight	37 (30.83%)
• Obese	26 (20.83%)
Virology status	
• HCV PCR + ve	24 (20%)
• HBV PCR + ve	8 (6.67%)
• Negative HCV and HBV PCR	88 (73.33%)
Laboratory investigations :	
• Hgb (g/dL)	10.64 ± 1.56
• PLT (×10 ³ cells/mcl)	187.93 ± 55.2

Age	58.59 ± 12.57
• TLC (×10³ cells/mcl)	6.81 ± 1.61
• Neutrophil count (×10³ cells/mcl)	4.04 ± 1.25
• Lymphocyte count (×10³ cells/mcl)	1.7 ± 0.55
• NLR	2.59 ± 1.14
• Na (mEq/L)	137.2 ± 2.54
• K (mEq/L)	4.59 ± 0.52
• Ca (mmol/L)	8.86 ± 0.44
• Phosphorus	5.67 ± 1.1
Parameters	N = 120
• Parathormone hormone (pg/mL)	376.61 ± 246.21
• Fasting blood sugar (mg/dL)	70.78 ± 6.17
• HbA1c (g/dL)	5.28 ± 0.8
• Albumin (g/dL)	3.97 ± 0.5
Bilateral Anterior Thigh Thickness (BATT)	
• Normal measured BATT	65 (54.16%)
• Low BATT	55 (45.83%)

N, Number; BMI, body mass index; HCV, hepatitis c virus; PCR, polymerase chain reaction; + ve, positive; HBV, hepatitis b virus; Hgb, hemoglobin; PLT, platelet; TLC, total leukocytic count; NLR, neutrophil leuokocytic ratio; Na, sodium; K, potassium; Ca, calcium; HbA1c, glycated hemoglobin; BATT, bilateral anterior thigh thickness.

Table 2: Effect of gendre on frailty.

	Male patients (N =84)	Female patients (N = 36)	P. Value
Frailty phenotype			
• Prevalent Fracture	26 (30.95%)	10 (27.78%)	0.7307 ^[X]
• Weight loss	36 (42.86%)	17 (47.22%)	0.659 ^[X]
• Endurance	61 (72.62%)	31 (86.11%)	0.1111 ^[X]
• Low physical activity	71 (84.52%)	34 (94.44%)	0.1343 ^[X]
• Grip strength measured (Kg)	32.54 ± 9.56	17.1 ± 4.35	<0.0001* ^[MWU]
• Low Grip strength	29 (34.52%)	26 (72.22%)	0.0001* ^[X]
• Walking Speed (4.5m/Sec)	6.79 ± 3.08	8.39 ± 2.62	0.0003* ^[MWU]
• Slow Walking	34 (40.48%)	28 (77.78%)	0.0001* ^[X]
• Frailty Phenotype (FP) score			
- 0	10 (11.9%)	2 (5.56%)	0.292 ^[X]
- 1	8 (9.52%)	2 (5.56%)	0.4752 ^[X]
- 2	21 (25%)	1 (2.78%)	0.0037* ^[X]
- 3	12 (14.29%)	4 (11.11%)	0.6426 ^[X]
- 4	18 (21.43%)	15 (41.67%)	0.0228* ^[X]
- 5	15 (17.86%)	12 (33.33%)	0.0637 ^[X]
• Frailty Phenotype Frail	45 (53.57%)	31 (86.11%)	0.0006* ^[X]
FRAIL Scale			

	Male patients (N =84)	Female patients (N = 36)	P. Value
• Fatigue	68 (80.95%)	35 (97.22%)	0.019* ^[X]
• Resistance	60 (71.43%)	34 (94.44%)	0.0048* ^[X]
• Ambulation	32 (38.1%)	31 (86.11%)	<0.0001* ^[X]
• Illnesses number			
- 1	19 (22.62%)	8 (22.22%)	0.9623 ^[X]
- 2	44 (52.38%)	13 (36.11%)	0.1036 ^[X]
- 3	13 (15.48%)	8 (22.22%)	0.377 ^[X]
- 4	5 (5.95%)	3 (8.33%)	0.6352 ^[X]
- 5	3 (3.57%)	4 (11.11%)	0.1081 ^[X]
• Illnesses score	3 (3.57%)	5 (13.89%)	0.0381* ^[X]
• FRAIL Scale score			
- 0	10 (11.9%)	2 (5.56%)	0.292 ^[X]
- 1	8 (9.52%)	2 (5.56%)	0.4752 ^[X]
- 2	21 (25%)	1 (2.78%)	0.0037* ^[X]
- 3	12 (14.29%)	4 (11.11%)	0.6426 ^[X]
- 4	18 (21.43%)	15 (41.67%)	0.0228* ^[X]
- 5	15 (17.86%)	12 (33.33%)	0.0637 ^[X]
• Frailty Severity			
- Frail	39 (46.43%)	30 (83.33%)	0.0001* ^[X]
- Prefrail	38 (45.24%)	5 (13.89%)	0.0009* ^[X]
- Robust Health	7 (8.33%)	1 (2.78%)	0.2673 ^[X]
Bilateral Anterior Thigh Thickness (BATT)			
• Measured BATT	58.1 ± 10.39	36.46 ± 4.72	<0.0001* ^[w.t]
• Low BATT	31 (36.9%)	24 (66.67%)	0.0025* ^[X]

N, Number; P value, probability value; BATT, bilateral anterior thigh thickness.

Table 3: Univariable analysis between low BATT and frailty indices.

	Unstandardized Coefficients		OR	Test value	P. Value	95.0% Confidence Interval for B	
	B	Std. Error				Lower Bound	Upper Bound
Frailty Phenotype score	0.1833	0.023	1.2012	7.9692	<0.0001*	0.1377	0.2288
FRAIL Scale score	0.2046	0.0288	1.227	7.1152	<0.0001*	0.1477	0.2616
Walking Speed	-0.0811	0.0131	1.0845	-6.1831	<0.0001*	0.0551	0.107
Grip strength measured	-0.0298	0.0032	0.6545	-9.4037	<0.0001*	-0.0361	-0.0235

B, Unstandardized beta; Std. Error, standard error; P value, probability value; OR, odds ratio.

Table 4: Multivariable regression analysis between low BATT and frailty indices.

	Unstandardized Coefficients		OR	Test value	P. Value	95.0% Confidence Interval for B	
	B	Std. Error				Lower Bound	Upper Bound
Frailty Phenotype (FP) score	0.0917	0.0462	1.096	1.986	0.0494*	0.0002	0.1832
FRAIL Scale score	0.0351	0.0549	0.9655	0.6394	0.5238	-0.1439	0.0737
Walking Speed	-0.0271	0.0133	1.0275	-2.0393	0.0437*	0.0008	0.0535
Grip strength measured	-0.0207	0.004	0.9795	-5.1346	<0.0001*	-0.0286	-0.0127

B, Unstandardized beta; Std. Error, standard error; P value, probability value; OR, odds ratio.

DISCUSSION

Relevant markers for the diagnosis of PEW are muscle mass. Now, the gold standard for determining body composition is Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). However, these procedures are costly, not always feasible or accessible in clinical settings, technically complex, and expose patients to excessive radiation, at least in the case of CT. Body composition has also been evaluated using other techniques such as bio-impedance analysis (BIA) and dual-energy X-ray absorptiometry (DEXA). However, because fluid state can confuse these approaches, they may be imprecise [10].

Additionally, ultrasound has demonstrated good agreement with bioimpedance and CT assessments of the thickness of the mid-thigh quadriceps. Crucially, there have been no discernible changes in the thickness of the quadriceps femoris muscle before and after dialysis, suggesting that fluid overload has no discernible effect on outcomes. According to recent studies, measurements of quadriceps size obtained by ultrasound are linked to mortality and muscular function in hemodialysis patients [11].

In the context of common hemodialysis patients, the objectives of this study were to: 1) investigate the relationship between BATT and measures of muscle function as indicated by the frailty phenotype; and 2) evaluate the relationship between muscle size and frailty using common frailty tools [11].

Facilitate this assessment, a study of 223 hemodialysis patients found that ultrasound-measured BATT variably correlated with frailty depending on the assessment tool used (e.g., Frailty phenotype, clinical Frailty Scale), highlighting tool-dependent associations [8].

The Comprehensive Geriatric Assessment (CGA) is the gold standard for diagnosing frailty. Due to financial and practical constraints, this is rarely utilized in clinical and/or research settings; instead, several frailty screening and diagnostic instruments have been put forth. These include the Edmonton Frail Scale (EFS), the Frailty Index (FI), and the Frailty Phenotype (FP), which focuses on the physical elements of frailty. BATT exhibits good inter-rater reliability.

Hemodialysis patients' ultrasound-derived quadriceps muscle mass has been verified against CT and BIA and is unaffected by volume overload. Our results support and expand upon those of Matsuzawa and colleagues, who discovered a correlation between walking speed and grip strength and the cross-sectional area of the rectus femoris [11].

Our study population included 84 males and 36 females; significant gender differences were observed in frailty parameters. Females had significantly lower grip strength (17.1 ± 4.35 kg vs. 32.54 ± 9.56 kg, $p < 0.0001$) and slower walking speed (8.39 ± 2.62 s vs. 6.79 ± 3.08 s, $p = 0.0003$), with more females exhibiting low grip strength (72.22% vs. 34.52%, $p = 0.0001$) and slow walking (77.78% vs. 40.48%, $p =$

0.0001). Females had higher frailty scores, with more scoring 4 on the Frailty Phenotype (41.67% vs. 21.43%, $p = 0.0228$) and being frail (86.11% vs. 53.57%, $p = 0.0006$). On the FRAIL Scale, fatigue (97.22% vs. 80.95%, $p = 0.019$), resistance (94.44% vs. 71.43%, $p = 0.0048$), ambulation (86.11% vs. 38.1%, $p < 0.0001$), and illness score ($p = 0.0381$) were worse in females. Frailty severity was higher in females (83.33% vs. 46.43%, $p = 0.0001$), while more males were prefrail (45.24% vs. 13.89%, $p = 0.0009$). Females also had lower Bilateral Anterior Thigh Thickness (BATT) (36.46 ± 4.72 mm vs. 58.1 ± 10.39 mm, $p < 0.0001$) with more low BATT cases (66.67% vs. 36.9%, $p = 0.0025$). The same prevalence of frailty among females was reported by Anderson, et al. [8].

Like our results, Lee and Son [12] discovered that the pooled prevalence of frailty among hemodialysis patients with ESRD was 46%, with diabetes mellitus, advanced age, and female sex increasing the risk of frailty. Anderson et al. [8] discovered that ultrasound-derived low muscle mass (LMM) was more prevalent in males than in their earlier research. The study discovered that LMM decreased walking speeds in both sexes (males $\beta = -0.115$; 95% C.I. -0.258 to -0.013; $p = 0.03$, females $\beta = -0.152$; 95% C.I. -0.300 to -0.005; $p = 0.04$), but not in females ($\beta = -1.88$; 95% C.I. -5.41 to 1.64; $p = 0.02$). In contrast to female odds (OR = 5.16; 95% C.I. 0.22 to 124; $p = 0.31$), sarcopenia increases frailty risks in males (OR = 9.86; 95% C.I. 1.8 to 54.0; $p = 0.01$). Anderson et al. [8] proposed that testosterone shortage and its reduction with age may explain this disparity since it protects against sarcopenia and frailty.

Our results are in line with those of Simó-Servat et al. [13], who found AUCs of 0.78 for predicting sarcopenia using FFM, handgrip strength, and thigh muscle thickness (TMT) and correlations between SARC-F and FFM ($R = -0.4$, $p < 0.002$) and hand-grip strength ($R = -0.5$, $p < 0.0002$). However, using the SARC-F, the Short Physical Performance Battery (SPPB), and the Timed Up and Go (TUG) to

classify groups according to frailty levels, we did not identify significant differences in BATT ($p > 0.05$).

Among the many drawbacks of our study is its cross-sectional design, which makes it impossible to determine causality or monitor changes in frailty over time. Conducted at a single center, the findings may not be generalizable. Future research should employ a longitudinal, multi-center approach to validate our findings and assess BATT's broader applicability in frailty screening.

CONCLUSION

Our study suggests that ultrasound measurements of BATT could be effective for non-invasive frailty screening in hemodialysis patients. Low BATT correlates with increased frailty, as evidenced by higher FP and FRAIL Scale scores, reduced walking speed and lower grip strength. This method could improve early frailty detection and management, potentially enhancing patient outcomes and care.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

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