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Muscle Mass Loss in Mechanically Ventilated Critically Ill Patients in Intensive Care Unit

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SUMMARY

Background. Muscle mass can be an important predictor for survival in critical illness, and there is no universally acknowledged approach for routinely assessing low muscularity at ICU admission. We aimed to identify patients with low muscularity and investigate whether ultrasound muscle mass measurements changed during the ICU stay.

Materials and methods. We performed a retrospective analysis of the ultrasound data of patients admitted with septic shock and sepsis in the ICU. We included patients who underwent ultrasound measurements of the quadriceps femoris muscle thickness including the rectus femoris and vastus intermedius. Weight and ultrasound measurements were performed on days 1, 3, 5, and 7 of the ICU stay.

Results. The study group comprised 61% (n = 14) males and 39% (n = 9) females with a mean age group of 63.74 ± 10.97 years. The mean APACHE score was 16.0 ± 2.38. The mean admission weight was 62.2 ± 16.6 and the recorded weight on day 7 was 59.4 ± 15.7 wherein the reduction in weight was statistically significant ($p < 0.01$). Muscle mass thickness measurements of rectus femoris reduced from 1.44 ± 0.34 cm on day 1 to 1.22 ± 0.33 cm on day 7 which was statistically significant ($p = 0.002$). Similarly, muscle mass measurements of the vastus intermedius reduced significantly from 1.23 ± 0.48 cm on day 1 to 0.97 ± 0.36 cm on day 7 with $p = 0.035$.

Conclusions. Ultrasound measurements of the quadriceps muscle layer thickness can be used to detect low and reduced muscularity. Strategies involving both adequacies of nutrition and timely rehabilitation and mobility can prove beneficial in lowering muscle loss in hospitalized critically ill patients.

KEY WORDS

Critically ill; mechanical ventilation; muscle mass; quadriceps; ultrasound.

INTRODUCTION

A systemic inflammatory response syndrome (SIRS) is a condition that triggers metabolic disorders in patients admitted to the intensive care unit (ICU). Bed rest, systemic inflammation, and pro-inflammatory response insulin resistance all contribute to muscle loss in critically ill patients (1, 2). Muscle wasting is one of many common outcomes that is faced by patients in ICU, and it contributes to muscle weakening (3, 4). Skeletal muscle is a component of lean body mass, and muscle loss has been linked to longer periods of mechanical ventilation (MV) as well as increased ICU and hospital mortality (5, 6). In recent years, there has been a greater knowledge of the science of muscle wasting and the diagnosis of prolonged functional impairment in survivors after critical illness (7-13). Even after 1 year of discharge complete physical function was not achieved and some patients suffered from physical impairments 5 years after the resolution of critical illness (14, 15). Loss of muscle mass, metabolic and physiological dysregulation of skeletal muscle, skeletal muscle architectural degeneration, and malfunctioning central and peripheral brain impulses all contribute to muscle weakness (7). Given the unstable and debilitated state of patients, obtaining objective and practicable measurements of muscle health at admission and during the course of critical illness is difficult; consequently, nonvolitional approaches and alternative measures are required to assess muscle health (16). The quadriceps muscles, which are a key weight-bearing muscle group, have been studied in most research to demonstrate the correlation between muscle mass and strength among hospitalized patients (17-19). Muscular quantifications that are sensitive enough to identify minor changes over short time periods may aid in the evaluation of therapies to combat muscle atrophy and weakness.

Calorie requirements among critically ill patients shift dramatically throughout their illness, putting them at risk of malnutrition or overfeeding. It's a known fact that malnutrition is linked to a loss of lean body mass (LBM), delayed wound healing, a higher risk of nosocomial infection, and weakened respiratory muscles. Many factors can influence resting energy expenditure (REE). The LBM is one of the most important drivers of REE. In critically ill patients, a measurement of muscle mass and changes in muscle mass could be used to establish an LBM index. According to recent Global Leadership Initiative on Malnutrition (GLIM) Guidelines, muscle mass is a new and unique metric of malnutrition (20). A number of techniques like muscle ultrasound, lean body mass via CT scan, and segmental bioelectrical impedance spectroscopy are now available to assess muscle mass, lean body mass (LBM), or Fat-Free Mass (FFM) in ICU patients at the bedside.

Non-invasive measurement of skeletal muscle mass as well as quality parameters of intramuscular glycogen content (IMGC), intramuscular adipose tissue (IMAT), and muscle size using a muscle-specific ultrasound-based technique have been proposed in recent studies (21). Muscle mass from ultrasound has been validated using gold standard procedures such as MRI/CT scan (22). In the ICU, a recent study found good inter-rater and intra-rater reliability for muscle mass ultrasound in critically ill patients (23). Furthermore, research has also indicated that enhanced ultrasound-guided muscle mass has been linked to improved functional handgrip strength following a focused ICU diet intervention (24). This enables a better understanding of the link between skeletal muscle amount and quality, as well as malnutrition and outcome risk (12, 13).

Evidence indicates that numerous factors may cause considerable daily fluctuations in energy expenditure amongst critically ill individuals (25, 26). Indirect calorimetry is a standard used to measure caloric needs in critically ill patients at the bedside, and its use has been strongly suggested by the European Society for Clinical Nutrition and Metabolism (ESPEN) and American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines (27, 28) to optimize nutritional support for better clinical outcome. Despite the fact that measured LBM has been demonstrated to be an essential determinant of REE, no previous research has looked into the association between estimated LBM and REE using ultrasound-based muscle thickness measurement. This present study was taken up with the following objectives:

1. To study muscle mass loss in a period of 7 days from ICU admission in ventilated patients with sepsis and septic shock.
2. Relationship of weight and muscle mass loss.
3. Correlation with comorbidities.
4. Correlation with APACHE score.

MATERIALS AND METHODS

The study is taken up to retrospectively compare whether the body weight measurements correlated with muscle mass measured by ultrasound. Institutional Ethical Committee S. L. Raheja Hospital, Mumbai approval was obtained for the study (ECR/70/Inst/MH/2013/RR-19 – Date of approval: October 13, 2021).

We performed a retrospective observational study in mechanically ventilated critically ill septic shock patients receiving artificial nutrition at the tertiary care hospital. Patients were included and excluded from this study when they met the criteria as depicted in (**figure 1**). Informed consent is not applicable.

Measurement of body weight

The body weight of each patient was checked at admission and thereafter every alternate day to coincide with the measurements by the ultrasound. The weight of each of the patients was checked using a hospital bed using a Hill-Rom HR900 Accella™ bed with an inbuilt weighing scale.

Measurement of muscle mass

An ultrasound for skeletal muscle measurements was done using a Siemens ACUSON X300™ (Siemens Health Care, Germany) machine. Muscle thickness measurements were done using B-mode of USG using 5.0–13.0 MHz (megahertz) linear array probe. All measurements were taken by a doctor who was trained in using bedside USG in ICU and was certified. The measurements were done as per the method described by Gruther *et al.* (3). The thickness of the major muscles of the lower limbs, including the rectus femoris and vastus intermedius, was assessed. The patient was placed in a supine position with legs extended and toes facing the ceiling before the measurements were taken. Using a permanent marker pen, a straight line was drawn from the anterior inferior iliac spine to the superior border of the patella. A midpoint of this line was marked, and a linear probe was placed gently and absolutely perpendicular to the skin. A semicircle-shaped

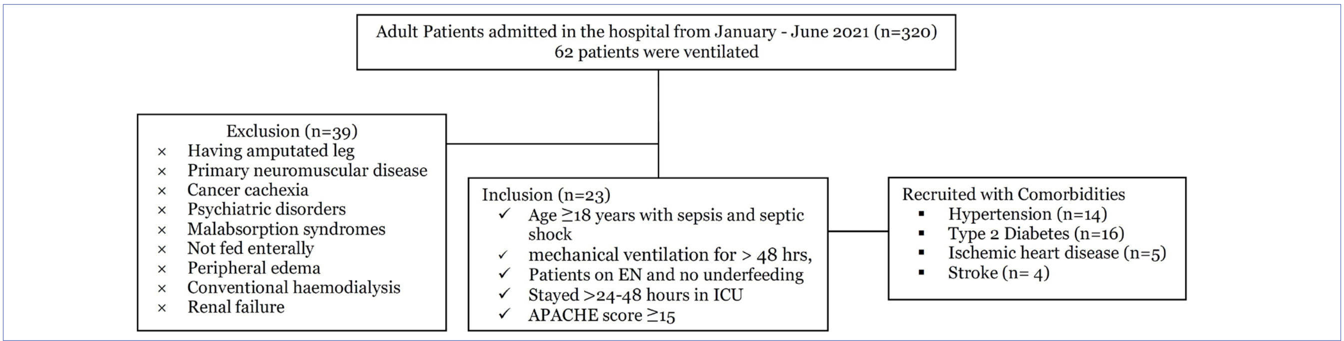

Figure 1. Patient enrolment criteria.

muscle observed in between the skin and subcutaneous tissue and femur bone indicated the rectus femoris muscle. A smaller muscle placed just above the bone and below the rectus femoris was the vastus intermedius (**figure 2**).

Measurements taken were as below:

1. Vertical distance of rectus femoris muscle.
2. Vertical distance of the vastus intermedius.
3. Distance between the upper border of the rectus femoris muscle and the upper border of the femur bone was taken to identify the quadriceps femoris muscle thickness.

Measurements were taken on days 1, 3, 5, and day 7 (**figure 3**). Energy estimations were performed by indirect calorimetry and continuous enteral feeds were planned accordingly. Patients were enterally fed within 24hrs after admission and the adequacy of protein and energy was maintained at 50-70% of the prescribed values from day 2.

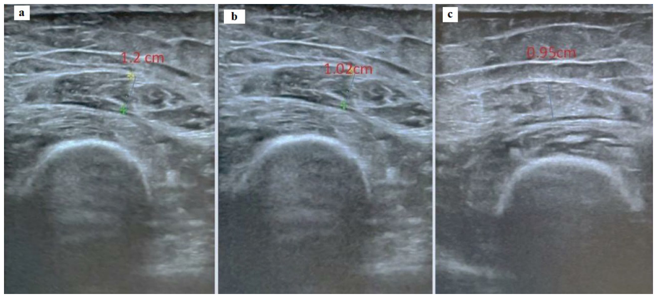

Figure 3. Representative ultrasound sonography image of muscle mass measurement.
(**a**) Day 1; (**b**) Day 5; (**c**) Day 7.

Statistical analysis

The collected data were analyzed with IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). To describe the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables, and the mean and SD were used for continuous variables. Normality of data was ascertained by plotting histograms. All the continuous data were normally distributed. Data were presented to find the significant difference between the bivariate samples in paired groups, the paired sample t-test was used. For the multivariate analysis, repeated measures of ANOVA were used with Bonferroni correction to control the type I error on multiple comparisons. Pearson correlation coefficients were determined to assess the correlation between muscle diameters and various other variables on admission. In all the above statistical tools the probability value 0.05 is considered a significant level.

RESULTS

All hospitalized patients between January 2021 and June 2021, admitted to the ICU with sepsis and septic shock, were included in the study.

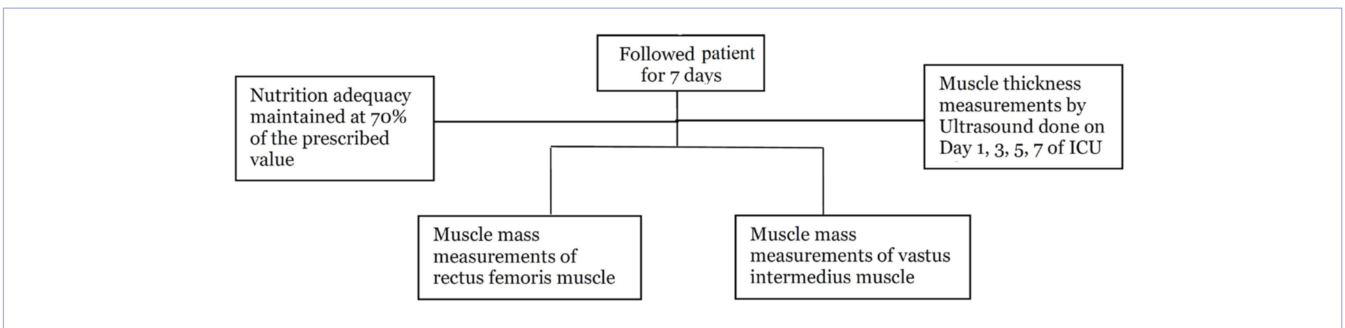

Figure 2. Muscle mass measurement timeline.

During the study period, 320 patients were admitted to the ICU. Of the 62 patients who were ventilated, of which 23 were eligible for inclusion with sepsis and septic shock, 39 were excluded. The study group consisted of 61% (n = 14) males and 39% (n = 9) females with a mean age group of 63.74 ± 10.97 years. Among the 23 patients with septic shock, 61% (n = 14) had hypertension, 70% (n = 16) had type 2 diabetes mellitus, 22% (n = 5) had ischemic heart disease, and 17% (n = 4) had a stroke. Among the patients included, 16 and 7 patients had 2 and 3 comorbidities respectively. The mean APACHE score was 16.04 ± 2.38. The mean weight at admission was 62.2 ± 16.6 and the recorded weight on day 7 was 59.4 ± 15.7 wherein the reduction in weight was statistically significant ($p < 0.01$) as depicted in **table I**.

The muscle mass thickness measurements of the rectus femoris (muscle mass 1) reduced from 1.44 ± 0.34 cm on day 1 to 1.22 ± 0.33 cm on day 7 which was statistically significant ($p = 0.002$) (**table I**). Similarly, the muscle mass measurements of the vastus intermedius (muscle mass 2) reduced significantly from 1.23 ± 0.48 cm on day 1 to 0.97 ± 0.36 cm on day 7 with $p = 0.035$ (**table I**). The comparison of rectus femoris muscle mass on day 1 and between days by repeated measures with ANOVA showed the F-value = 8.833 ($p = 0.002$) which indicates a statistically significant difference between muscle mass on day 1 and the following days. A similar comparison was done with the repeated measurements of the vastus intermedius muscle with F-value = 6.661 ($p = 0.010$) showing a statistically significant reduction in the thickness of the muscle. This reveals that critical illness leads to significant muscle loss, with the rectus femoris muscle loss of around 15% and the vastus intermedius loss of approximately 25% by day 7. There was no significant correlation between APACHE scores and the muscle mass thickness of rectus femoris, vastus intermediate, or both combined.

All the patients who were included in the study were also monitored for adequacy of energy and protein through enteral feeding.

Tables II and **III** demonstrate the correlation between various parameters with the diameter of rectus femoris and vastus intermedialis at different time periods. There was a significant positive correlation of only weight on admission with rectus femoris diameter on day 1 ($r = 0.811$, $p < 0.001$), day 5 ($r = 0.682$, $p = 0.001$), and day 7 ($r = 0.552$, $p = 0.022$). However, weight showed a significant positive correlation with vastus intermedialis diameter on day 1 only ($r = 0.725$, $p < 0.0001$). No other parameter showed a significant parameter with muscle diameter at any time point.

DISCUSSION

In this study on 23 critically ill patients with sepsis, we investigated whether ultrasound-based quadriceps muscle thickness reduced after admission to the ICU. This measurement is a good indicator of muscle mass. Our study revealed that the muscle mass thickness measurements of the quadriceps femoris reduced from 2.63 ± 0.80 cm on day 1 to 2.16 ± 0.62

Table I. Patients characteristics with weight and muscle mass measurements.

Variable	Day 1	Day 3	Day 5	Day 7	P-value
Age, mean ± SD, years	63.74 ± 10.97				
Male/Female, n (%)	14/9 (61/31%)				
Comorbidities present					
Hypertension, n (%)	14 (61)				
Type 2 Diabetes Mellitus, n (%)	16 (70)				
Ischemic Heart Disease, n (%)	5 (22)				
Stroke, n (%)	4 (17)				
Body Weight mean ± SD, Kg	62.2 ± 16.6	60.8 ± 16.5	60.0 ± 16.2	59.4 ± 15.7	0.0005
Height mean ± SD, cm	160.11 ± 7.73				
APACHE II score	16.04 ±2.38				
Serum creatinine mean ± SD, mg/dL	2.32 ± 1.89				
Muscle Ultrasound thickness					
Rectus femoris (centimetres), mean ± SD	1.44 ± 0.34	1.35 ± 0.34	1.29 ± 0.33	1.22 ± 0.33	0.002
Vastus intermedius (centimetres), mean ± SD	1.23 ± 0.44	1.11 ± 0.38	1.01 ± 0.34	0.97 ± 0.34	0.010
Total quadriceps femoris (centimetres), mean ± SD	2.63 ± 0.80	2.43 ± 0.59	2.28 ± 0.63	2.16 ± 0.62	0.016

Table II. Correlation of various parameters with rectus femoris diameter at different time periods.

Parameters	Day 1		Day 5		Day 7	
	Pearson correlation	P-value	Pearson correlation	P-value	Pearson correlation	P-value
Age (years)	-0.271	0.211	-0.232	0.286	-0.053	0.830
APACHE score	0.305	0.157	0.133	0.544	0.260	0.282
HTN	0.251	0.248	0.117	0.594	0.330	0.168
DM	0.094	0.669	-0.040	0.856	0.039	0.875
Stroke	0.262	0.227	0.236	0.278	0.259	0.285
Weight on admission	0.811	**< 0.0001**	0.682	**0.001**	0.552	**0.022**

Table III. Correlation of various parameters with vastus intermedius diameter at different time periods.

Parameters	Day 1		Day 5		Day 7	
	Pearson correlation	P-value	Pearson correlation	P-value	Pearson correlation	P-value
Age	-0.072	0.744	0.082	0.718	-0.007	0.977
APACHE score	0.119	0.588	0.020	0.930	-0.058	0.818
Hypertension	0.127	0.565	0.269	0.227	0.276	0.268
Diabetes	0.287	0.185	0.083	0.712	0.090	0.721
Stroke	-0.038	0.862	0.191	0.394	0.203	0.420
Weight on admission	0.725	**< 0.0001**	0.195	0.410	0.218	0.417

cm on day 7 which was statistically significant ($p = 0.016$). Studies have also indicated similar results that lower limb muscles are more prone to early atrophy than upper limb muscles, as evidenced by a greater decrease in thickness within the first five days of ICU admission (29). Secondly, few studies have investigated subject groups using ultrasound and set the standard values of the quadriceps muscle layer thickness at ICU admission. At ICU admission, a quadriceps muscle layer thickness of 2.0 cm can be set as a cut-off value indicating low muscularity (30). Although the patients' quadricep measurements indicated that it was above the cut-off on day 1 our study revealed a marked reduction by day 7. In critically ill patients, early enteral feeding and mobility are indicated, and individualized therapy could avoid additional muscle loss (31-33). Although early enteral nutrition was provided and adequacy of 70% of the prescribed goals was maintained, we did not track the functional impairments and methods of mobilization among the study population. Secondly, another limitation is that this was a *post-hoc* examination of discharged patients. As a result, prospective studies should be carried out to confirm these findings.

CONCLUSIONS

In conclusion, we looked retrospectively at how the quadricep muscle had changed over time and identified that ultrasound measurements of the quadriceps muscle layer thickness and the rectus femoris muscle can be used as indications of low muscularity.

Ultrasound muscle mass evaluation during ICU admission can be a useful tool for detecting reduced muscularity.

FUNDINGS

None.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

SS: conceptualization, design. SS, RC, SR, AB, EM, KP: data acquisition, analysis, and interpretation. RC, SS: drafting. SS, RC, SR, AB, EM, KP: critical revision. All the authors have approved the final manuscript.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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