ORIGINAL ARTICLE

Association of SOFA Score with Severity of Muscle Wasting in Critically Ill Patients: A Prospective Observational Study

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Abstract

Background: Muscle wasting is a frequent complication in critically ill patients. This study aimed to evaluate whether muscle wasting occurs in these patients and its association with the severity of the disease.

Materials and methods: This was a prospective, observational study including 50 patients admitted to the multidisciplinary ICU of a tertiary care hospital. Using a linear ultrasound probe, the thickness of the rectus femoris was measured on day 1 of admission and repeated at the same point on day 7. Sequential organ failure assessment (SOFA) scores were calculated daily during the study period. The highest SOFA score during this period was recorded. The mean difference in the thickness of the rectus femoris between day 1 and day 7 was used to predict the occurrence of muscle wasting and the correlation between this difference and the highest SOFA score was analyzed.

Results: The mean thickness of the rectus femoris on day 1 was 1.32 + 0.06 cm and on day 7 was 1.16 + 0.08 cm. The mean difference was found to be 0.16 cm ($p < 0.01$). There was a statistically significant difference in the thickness of the rectus femoris between day 1 and day 7. It was found to have a positive correlation with the highest SOFA score $r = 0.886$ ($p < 0.01$).

Conclusion: This study demonstrates that there is significant muscle wasting in critically ill patients and this positively correlates with the severity of illness. Our study also highlights the role of bedside ultrasound in detecting muscle wasting.

Keywords: Correlation, Critical illness, Intensive care unit, Muscle wasting, Organ dysfunction score, Prospective observational study, Sequential organ failure assessment, Ultrasound.

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Highlights

Muscle wasting is a notorious complication in the critically ill. The more the severity of illness, the higher the chances of wasting.

Introduction

The incidence of muscle wasting, in critically ill patients requiring admission in intensive care units (ICUs) can be up to 2% per day.[1] It adversely affects both immediate and long-term outcomes. Muscle wasting is greatest in patients with multiorgan dysfunction and occurs early (first 10 days).[2] Intensive care units acquired muscle weakness adversely affects recovery and it independently predicts 1 year mortality.[2–4]

Immobilization, inflammation, stress response, infection, nutritional deficiency, inadequate glycemic control, drugs mainly steroids, neuromuscular blocking agents, etc. are the various causes of muscle weakness.[5] Numerous studies have debunked the association of lean body mass depletion and nutritional support.[6] Increasing the nutrition delivery is not found to prevent the decrease in muscle mass.[2]

Ultrasound (USG) is a novel noninvasive tool used for the evaluation of muscle wasting. A systemic review of seven studies suggested the potential and appreciable reliability of muscle USG.[7] B mode ultrasonographic evaluation of rectus femoris is a dependable tool to assess muscle wasting. The USG measurements of muscles have been found to correlate well with magnetic resonance imaging (MRI) and computerized tomography (CT) measurements.[8,9]

Sequential organ failure assessment (SOFA) score is a tool to assess organ dysfunction or failure. Studies have validated the SOFA score, maximum SOFA during ICU stay, and change in the SOFA over a period of time for assessing morbidity in critical illnesses.[10,11] The highest, mean or the total maximum SOFA scores are indicative of cumulative organ dysfunction.[10] A SOFA score ≥2 is indicative of organ dysfunction and confers a mortality of 10%.[12]

In this study, we evaluated muscle wasting in ICU patients by measuring the thickness of the rectus femoris muscle on the day of admission day 1 and day 7, using a USG. The severity of illness in these patients was calculated using daily SOFA scores till day 7. This study aimed to determine the occurrence of muscle wasting in critically ill patients, and if so, its relationship with the severity of

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illness defined by the highest SOFA score during the study period. The primary objective was to assess if rectus femoris (RF) thickness, as measured by ultrasound, on day 1 and day 7 of ICU admission, can be an indicator of muscle wasting. The secondary objective was to determine the relation between muscle wasting and SOFA score.

Materials and Methods

We conducted a prospective, observational study in a multidisciplinary ICU at a tertiary care center in Thiruvananthapuram. The study was carried out between April 2020 and December 2021. All the patients admitted to the ICU, with an expected length of stay of at least 7 days and willing to consent were enrolled in the study. Patients aged <18 years and >65 years, pregnant patients, patients with a history of neuromuscular disorders, bedridden patients, those on long-term corticosteroids, patients with amputated limbs or admitted with burn injury, those referred from other ICUs, unwilling to consent or patients who were shifted out or died within 7 days in the ICU were excluded.

Sampling Technique

All patients meeting the eligibility criteria were included in study.

Sample Size Calculation[13]

Alpha error 0.05, Beta error 0.2
$r = 0.4$ (Correlation between thickness of rectus femoris muscle and SOFA score)
The standard normal deviate for $\alpha = Z\alpha = 1.960$
The standard normal deviate for $\beta = Z\beta = 0.842$
$C = 0.5 * \ln [(1+r)/(1-r)] = 0.424$
Total sample size $= N = [(Z\alpha + Z\beta)/C]$ ^2 + 3 = 47
Required sample size = 47
Hence sample size is taken as 50
Based on the study by Katari et al. [14]

Study Procedure

An Institutional ethics committee approval was obtained before commencing the study. An informed written consent was taken from all participants in the study. On day 1 of ICU admission, in the supine position, a straight line was drawn from the anterior inferior iliac spine to the patella on the right leg and the 2/3rd point was measured using a caliper and marked with a permanent marker.[15] Measurement was recorded at the same point every time using a portable ultrasound set (GE Logiq®) with a high-frequency linear transducer (5–10 MHz), and the thickness of rectus femoris was measured. A transducer was placed perpendicular to the long axis of the muscle (i.e., perpendicular to the major axis of the limb) and the transverse view of the anterior thigh was obtained with no pressure on the skin by the same observer.[14] In B mode, the thickness of the rectus femoris muscle (measured in centimeters from the internal borders of the rectus femoris muscle to the external border of the same) was measured. The measurements were repeated on day 7 by the same investigator exactly at the point previously marked. Day 1–Day 7 (Δ thickness) difference was calculated. All patients received the standard amount of calories and proteins prescribed in our ICU.

Sequential Organ Failure Assessment score was calculated for these patients on admission and every day till day 7. The highest SOFA score for each patient was compared with the Δ thickness to look for the correlation between wasting and severity of illness.

Table 1: Percentage distribution of sample according to age and gender

	Count	*Percent*
Age		
≤40	6	12.0
41–50	5	10.0
51–60	15	30.0
61–70	24	48.0
Mean ± SD	56.4 ± 9.7	
Sex		
Male	33	66.0
Female	17	34.0

Table 2: Descriptive statistics for height and ideal body weight

	Mean ± SD	*Median (IQR)*	*Minimum*	*Maximum*
Height	168.9 ± 8.2	169 (163.5–176.25)	153.0	182.0
Weight	63.5 ± 9.2	65.11 (56.04–71.7)	46.0	76.9

Outcomes

Primary outcome: Muscle wasting on day 7, as measured by the difference in rectus femoris thickness between day 7 and day 1.

Secondary outcome: To determine whether an association exists between the difference in rectus femoris thickness and the highest SOFA score.

Data Collection and Analysis

Data was collected in Microsoft Excel software.

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD respectively. Rectus femoris thickness between day 1 and day 7 was compared using Paired *t*-test. Karl Pearson correlation was used to find out the relationship between the difference in rectus femoris thickness and highest SOFA score. Pearson correlation coefficient ranges between −1 and 1, −1 means the perfect negative correlation, 0 means no correlation, and 1 means the perfect positive correlation.[14] For all statistical interpretations, $p < 0.05$ was considered the threshold for statistical significance. Statistical analyses were performed using SPSS, version 20.0. Microsoft Word and Excel were used for graphs and tables.

Results

This prospective study was done on 50 patients, of whom 33 were males and 17 were females. The majority were in the age-group 61–70 years (48%). Mean ± SD was 56.4 ± 9.7 (Table 1).

The mean height of the study population was 168.9 ± 8.2 cm (range 153–182 cm). The mean ideal body weight was 63.5 ± 9.2 kg (range 46 and 76.9 kg) (Table 2).

About 36 patients in the sample (72%) received mechanical ventilation while 14 (28%) did not receive mechanical ventilation (Fig. 1).

The mean rectus femoris thickness on day 1 was 1.32 ± 0.06 cm and on day 7 was 1.16 ± 0.08 cm. The mean difference in the thickness of the rectus femoris on day 1 and day 7 was 0.16 cm. The difference was statistically significant ($t = 11.99$, $p < 0.01$) (Table 3).

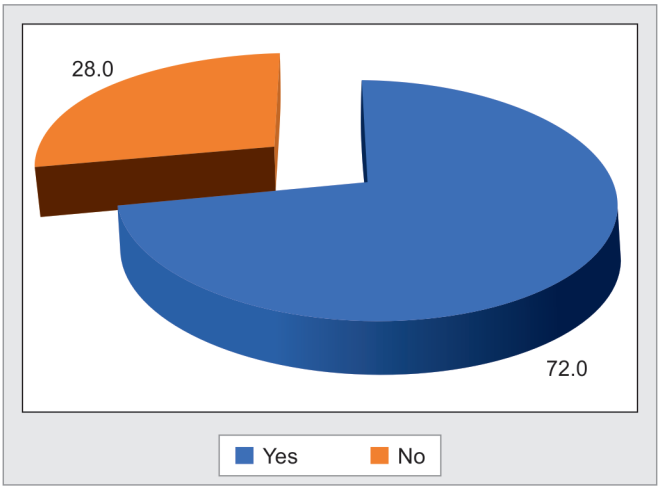

Fig. 1: Percentage distribution of sample according to use of ventilation

Table 3: Comparison of rectus femoris thickness on day 1 and day 7

RFT	*Mean*	*SD*	*N*	*Mean difference*	*Paired t*	*p*
Day 1	1.32	0.06	50	0.16	11.99	$p < 0.01$
Day 7	1.16	0.08	50			

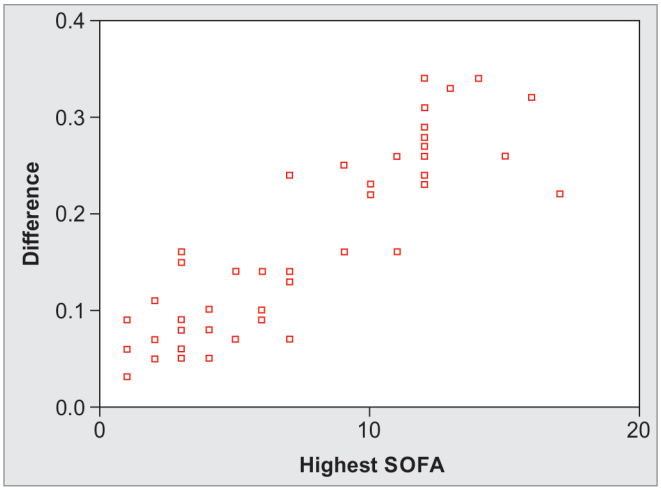

Fig. 2: Scatter diagram showing relation between difference in rectus femoris thickness and highest SOFA score $r = 0.886$, $p < 0.01$

There was a statistically significant positive correlation between the highest SOFA score during the study period and the difference in rectus femoris thickness ($r = 0.886$, $p < 0.01$) (Fig. 2).

Discussion

This study included 50 patients, all of whom stayed in the ICU for at least 7 days and received the standard prescribed nutrition as per the ICU protocol. The mean age-group of the sample was 56.4 ± 9.7 years and 48% of them were between 60 and 65 years. Males constituted 66% of the population and females accounted for 34%. The mean height was 168.9 ± 8.2 cm and median height was 169 (163.5–176.25) cm. The mean ideal body weight was 63.5 ± 9.2 kg and the median ideal body weight was 65.11 (56.04–71.7) kg. During the study period, 72% of the sample was on invasive ventilation. The highest SOFA score was 17. This study showed a significant difference in rectus femoris thickness between day 1 and day 7, indicating the occurrence of muscle wasting and there was a positive correlation between the wasting and the highest SOFA score during the study period. The mean RF thickness on day 1 was 1.32 ± 0.06 and on day 7 was 1.16 ± 0.08. The mean difference was 0.16 cm which was statistically significant ($p < 0.01$). This established the occurrence of muscle wasting in the critically ill population. It was found to have a positive correlation with the highest SOFA score during the study period ($r = 0.886$, $p < 0.01$).

In the study by Katari et al.,[14] on day 3, the RF thickness was 1.26 ± 0.41 as compared to 1.37 ± 0.41 on day 1 ($p < 0.001$). On day 7, the thickness was 1.22 ± 0.47. This difference was highly significant ($p < 0.001$). The mean RF thickness difference in the same study was 0.149 cm and was statistically significant. Puthucheary et al.[16] in their study found that RF thickness underestimated muscle wasting, while rectus femoris cross-sectional area (CSA) had a better correlation with muscle wasting. A study by Pardo et al.[17] showed that the median thickness on admission was 1.72 cm (95% CI, 1.62; 2.13) and 1.45 cm on day 7 (95% CI, 1.24; 1.665), which corresponded to a 16% significant variation in muscle thickness [– 0.32 cm (95% CI, – 0.43; – 0.2), $p < 0.01$]. They continued the study up to 21 days and the median thickness reduced to 1.3 cm on day 21 [95% CI, 0.80; 1.48] which signaled a total loss of 24% of muscle thickness [– 0.6 cm, (95% CI, -0.76; – 0.42), $p < 0.01$]. The difference in the muscle thickness on admission between our study participants and the above can be attributed to the physical difference in the population. Arai et al.[18] found that the thickness of the rectus femoris had the discriminative power to assess sarcopenia at the area under the curve (AUC) of 0.84 (95% CI, 0.74–0.94).

Lower limb muscles are prone to early atrophy. Studies have shown a greater decrease in the thickness of the lower limbs within the first 5 days of admission to the ICU as compared to the upper limbs.[19] Rectus femoris is easy to identify and measure compared to quadriceps. A systematic review showed that the most common method of assessing musculature using USG in the literature is muscle layer thickness (MLT), and not CSA.[20] The advantage of MLT is that it can be obtained easily at the bedside.[21] Another flaw highlighted by the review was the inconsistency in the landmarks for measuring the RF thickness.[20] The majority of the studies measured the distance between the anterior superior iliac spine (ASIS) and the patella, but we measured it between the anterior inferior iliac spine (AIIS) and patella as it fell in the midline. There was no consensus on the site of measurement also. Some measured at midpoint, some at 2/3rd. We preferred the 2/3rd point and the measurement on day 7 was also done at the exact same point. Pardo et al. showed that the 2/3rd point was more accurate than the midpoint.[17]

SOFA ≥ 2 signifies multiorgan dysfunction. We found that there was a significant positive correlation between the highest SOFA score and a decrease in RFT. Pearson correlation value was 0.886, $p < 0.01$. This shows that the more the severity of the illness, more the occurrence of muscle wasting or muscle wasting increases with each organ involvement. Even though 72% of the study population was mechanically ventilated, the effect of ventilation on wasting was not studied. Similarly, many of the patients were on vasopressors and renal replacement therapy. Whether this had any predominant contribution to muscle wasting is yet to be studied.

Clinically significant muscle wasting has not been defined. Critically ill patients develop muscle wasting but the cut-off value beyond which it becomes significant is not known. There is a scarcity

of data in this aspect. Bloch et al. classified those with more than 9.24% muscle loss as clinically significant.[22]

Most of the studies have utilized CSA or MLT as a measure of wasting. Puthucheary et al. opined that CSA is superior to MLT.[16] The limitation of CSA is that it is technically difficult to obtain a full view of CSA with conventional linear frequency probes. Another parameter that can be used is muscle echogenicity. Parry et al. showed that muscle echogenicity scores increase in quadriceps muscle.[23] Muscle depth, compared between obese, overweight, and normal weight populations using ultrasound was used as a measure of muscle wasting. Muscle depth loss was found to be comparable but not statistically significant.[24]

Many studies have shown the occurrence of muscle wasting in the critically ill. Studies comparing SOFA scores and muscle wasting are limited in the literature. This study conveys that by daily calculation of SOFA score, we can predict the chances of muscle wasting early. Higher the SOFA score, more the muscle wasting. In such patients, targeted interventions to prevent muscle wasting can be adopted. Those include early goal-directed mobilization, early muscle stimulation, adequate pain control, optimizing tissue oxygenation, minimizing the use of drugs causing muscle weakness, early enteral nutrition, correction of electrolyte disturbances, etc. Annetta et al. opined that "immobilization and inflammation rather than inadequate nutritional support might be major determinants of loss of muscle".[25] Inactivity and inflammatory states favor muscle protein breakdown proteolysis.[26]

Limitations

This study was done on 50 patients. Studies with large sample sizes are needed before reaching a conclusion. As it is an observational study, it's subject to a high risk of bias. Our study measured rectus femoris thickness only. Evidence of the superiority of CSA, even though limited, is there. Combining CSA and MT would be more accurate. Including quadriceps in the assessment may give additional information. The consequence of muscle wasting is long-term morbidity; hence a longer study period might be required to analyze clinically significant outcomes. The effect of mechanical ventilation, vasopressors, and renal replacement therapy was not studied. Organ-specific SOFA scores need to be studied to identify whether any factor predisposes to more wasting. We considered day 1 of admission as the baseline for rectus femoris thickness. Day 1 of admission might not be the same as day 1 of illness. Other ultrasonographic parameters like pennation angle, and echogenicity might provide a better diagnostic value.

Conclusion

This study demonstrates that there is the occurrence of significant muscle wasting in the critically ill population and the muscle wasting positively correlates with the SOFA score which defines the severity of illness. This study also highlights the role of bedside ultrasound in detecting muscle wasting.

Take-home Message

This study underscores the fact that muscle wasting is a reality in the critically ill and supplementing the higher amounts of protein in the diet may not alleviate the problem as it is the severity of illness which is the contributing factor. Even before wasting becomes obvious, we can detect wasting using bedside ultrasound.

Ethics Committee Approval

The questionnaire and methodology for this study were approved by the Human Research Ethics Committee of KIMSHEALTH (KIMS/IHEC/CCM-02/2021).

Reporting Checklist: STROBE

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