



Research Article

Relationship between modified Nutrition Risk in the Critically Ill (mNUTRIC) Score and nutrition intake with quadriceps femoris muscle thickness in critically ill patients

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ABSTRACT

Muscle wasting in critical illness is seen from inadequate nutrition intake and stress catabolism. Modified Nutrition Risk in the Critically Ill (NUTRIC) Score is a screening tool that measures starvation, inflammation, disease severity, and organ dysfunction. The relationship between muscle strength and muscle thickness causes the evaluation of muscle thickness is quite relevant. This study aimed to analyze the relationship between modified NUTRIC score and nutrition with muscle wasting in critically ill patients. The study was conducted on 30 patients in the ICU Dr Soetomo Hospital Surabaya. Nutritional intake and thickness of the quadriceps femoris muscle were monitored for one week. There was a relationship between mNUTRIC score with quadriceps femoris muscle thickness on days 3rd, 5th, and 7th. In the comparison between the low-risk group and the high-risk group, it was found that there was a significant difference in the change in the percentage of muscle thickness difference on the 3rd, 5th and 7th-day observation. There is a relationship between protein debt with quadriceps femoris muscle thickness ($p = 0.008$) with a positive correlation with moderate correlation strength ($r = 0.477$) on day 7. In conclusion, the modified NUTRIC Score had a moderate relationship with quadriceps femoris muscle thickness in critical patients from day 3rd until day 7th. The calorie intake has not had a relationship with quadriceps femoris muscle thickness. Protein intake had a moderate relationship with quadriceps femoris muscle thickness only on day 7th measurement in critical patients.



INTRODUCTION

The mortality rate in critically ill patients is slowly falling compared to the last few decades. Improving the functional outcome of patients with critical illness is the focus of clinicians at this time. Muscle wasting is a common problem that occurs in patients in the Intensive Care Unit (ICU). Weakness and loss of muscle mass often contribute to physical and functional limitations (Casaer & Ziegler, 2015).

Muscle wasting occurs early and quickly during ICU treatment and contributes significantly to ICU acquired weakness (ICUAW) in 50-100% of ICU survivors. Decreased skeletal muscle mass is associated with increased mortality, prolonged treatment time with mechanical ventilation, and length of stay (LOS) in the ICU and hospital (Pardo et al., 2018; Z. Puthuchear, 2019). ICUAW is currently recognized as an important factor in patients with “difficult-to-wean” in the ICU, which is associated with prolonged ICU and hospital stay (Formenti, Umbrello, Coppola, Froio, & Chiumello, 2019). Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients (Weijs et al., 2014).

In healthy conditions, muscle mass is maintained through a balance between protein breakdown and synthesis. Muscle wasting is a consequence of catabolic conditions that lead to depression of muscle protein synthesis and an increase in muscle protein breakdown (Gao, Arfat, Wang, & Goswami, 2018). Protein is continuously degraded and replaced (turn over) by a process that is balanced over time. There is a loss of 20-30 g of protein in healthy people without protein intake or a loss of 1% of total body protein per day. During stressful (hypermetabolic) conditions, there is an increase in protein degradation that exceeds the rate of protein

synthesis (Preiser, Ichai, Orban, & Groeneveld, 2014).

Skeletal muscle atrophy occurs in response to various stressors, including decreases in external loading and neural activation, increases in inflammatory cytokines and glucocorticoids, and malnutrition. Immobilization is a catabolic condition for muscle that causes significant loss of muscle mass (Bodine, 2013). A study with 24 healthy patients who performed one-legged knee immobilization using full leg cast showed a reduction in the cross-sectional area of 3.5 ± 0.5 and $8.4 \pm 2.8\%$ following 5 days and 14 days of immobilization. This suggests that even short periods of muscle disuse can cause substantial loss of skeletal muscle mass and strength (Wall et al., 2014).

The causes of muscle wasting during critical illness can be seen from two main perspectives, namely inadequate nutritional intake and catabolism due to stress. Striated muscles are the body's largest protein and amino acids reserves that can be mobilized to maintain and overcome critical illness conditions. It is hoped that the intake of nutrients and protein can reduce the risk of muscle wasting due to the use of the body's protein and amino acid reserves (Pardo et al., 2018; Z. A. Puthuchear et al., 2013). Stress-induced catabolism is a process related to the degree of inflammation (which is closely related to disease severity) that requires nutritional screening that takes into account the severity of the disease and the metabolic conditions. The Nutrition Risk in the Critically Ill (NUTRIC) Score is a screening tool that considers this aspect and has been validated in critical patients (Lee & Heyland, 2019; Rahman et al., 2015). This scoring system represents a model that measures starvation, inflammation, disease severity, and organ dysfunction factors that can affect nutritional status at ICU admission and have implications for patient outcomes (Heyland, Dhaliwal, Jiang, & Day, 2011).



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Table 1. Modified NUTRIC Score variables

Variable	Range	Points
Age	<50	0
	50-<75	1
	≥75	2
APACHE II	<15	0
	15-<20	1
	20-28	2
	≥28	3
SOFA	<6	0
	6-<10	1
	≥10	2
Number of Comorbidities	0-1	0
	≥2	1
Days from hospital to ICU admission	0-<1	0
	≥1	1

Source: Rahman et al, 2015

Patients with high scores (5–9) are associated with worse clinical outcomes (mortality, ventilation). These patients are most likely to benefit from aggressive nutritional therapy. Patients with low scores (0-4) have a low risk of malnutrition. The Modified NUTRIC Score has been validated in predicting 28th-day mortality. Patients with a maximum score of 9 have a mortality of up to 53%. There was no mortality in patients with a NUTRIC score of 0 or 1. The odds of mortality at 28 days were multiplied by 1.4 (95% CI, 1.3e1.5) for every point increase on the NUTRIC score. Higher NUTRIC scores are also significantly associated with higher 6-month mortality ($p < 0.0001$) (Rahman et al., 2015).

Manual muscle strength measurement in a standardized manner has been shown to be beneficial in patients, but it requires a conscious and cooperative patient condition which is not usually possible in the ICU. The relationship between muscle strength and muscle thickness leads muscle thickness evaluation relevant enough as it reflects muscle the strengthness

(Formenti et al., 2019; Pardo et al., 2018). Monitoring muscle mass in critical patients is expected to detect patients at risk and predict the outcome that occurs due to decreased skeletal muscle mass in critically ill patients. In addition, monitoring muscle mass during treatment in the ICU can help doctors to evaluate the success of nutritional interventions during treatment (Pardo et al., 2018; Parry et al., 2015) It was reported that there was a loss of 12.5% cross-sectional area (CSA) or cross-sectional area of the rectus femoris after 7 days of ICU treatment. This illustrates that muscle wasting occurs early and quickly in critical patients (Pardo et al., 2018; Z. A. Puthuchearry et al., 2013).

Accurate assessment of body composition and lean mass is a challenge. Anthropometric measurements such as tricipital skin-fold thickness and upper arm circumference cannot accurately measure sarcopenia in critically ill patients because of subcutaneous edema in critical patients (Martín, Monares Zepeda, & Lescas Méndez, 2017; Pardo et al., 2018).



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The quadriceps femoris muscle can document muscle wasting because it's easiest to describe and evaluate even in conditions of massive muscle loss. The quadriceps femoris muscle is important in the remobilization process because it functions for simultaneous hip flexion and knee extension (Formenti et al., 2019; Pardo et al., 2018).

To evaluate the anatomy of the thigh and leg muscles, several examination techniques can be used, such as computerized tomography (CT), magnetic resonance imaging (MRI) or ultrasonography (USG). CT and magnetic resonance imaging (MRI) can accurately estimate muscle mass. However, these methods cannot be performed quickly, require high costs, provide unnecessary radiation exposure, and risky transportation makes these techniques inapplicable in ICU patients (Martín et al., 2017; Pardo et al., 2018). Ultrasound can be used as a valid and practical measurement tool for documenting muscle mass (Pardo et al., 2018). Ultrasound can measure and estimate muscle thickness and volume with good accuracy. In addition, ultrasound measurements can be performed non-invasively, instantaneously, and can be repeated. Ultrasonography measurement of quadricep muscle thickness shows good intra and inter-observer reliability (Pardo et al., 2018). Parameters obtained from ultrasound examination can help doctors monitor lean mass changes dynamically and guide doctors in evaluating nutritional intake in intervening in muscle wasting in critical patients in the ICU.

Therefore, clinicians need to prevent muscle wasting, know the factors that influence it, and quantify patients who are at high risk for muscle wasting. Modified NUTRIC score as a scoring system which is expected to represent patients at high risk of complications and mortality. This study aimed to investigate whether there was a relationship between

nutritional intake and modified NUTRIC score with quadriceps femoral muscle thickness in critically ill patients.

METHODS

The research was conducted in the Intensive Care Unit (ICU) of Dr. Soetomo hospital Surabaya during January-April 2020 that sampled patients aged between 18 to 65 years old. The research protocol was approved under the number 1683/KEPK/XI/2019 by the Committee on Institutional Ethics and Research Development (RSUD Dr. Soetomo, Surabaya, Indonesia). The sampling technique was consecutive sampling; patients who met the inclusion and exclusion criteria will be collected until the required sample size was fulfilled.

We selected the patients aged between 18 and 65 years old, and the patient's family stated readiness to include the patient in the research. This research sample was taken consecutively from the population that met the inclusion criteria. We excluded patients with deformities, lesions, fractures, and amputations of the lower extremities that were impossible to measure, patients with neuromuscular disease or critical illness neuropathy, patients with a history of chronic kidney disease, patients with a history of previous liver disease (cirrhosis of the liver, acute liver failure, or hepatoma) and palliative patients. After the subject meets the inclusion and exclusion criteria, the subject will be grouped into high-risk (5-9) and low-risk (0-4) patients based on the modified NUTRIC Score during ICU admission.

Measurement started with collecting the general characteristics data of the subjects who met the inclusion and exclusion criteria who had agreed and signed the informed consent. General characteristics data include patient identity, clinical data, and supporting data. General patient characteristics were collected: gender, weight, height, body mass index, diagnosis, and



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comorbidities were recorded. Bodyweight was measured by weighing the patient. The patient's height was measured with a measuring tape.

Then we obtained the clinical data from recording vital signs (blood pressure, MAP, pulse, rectal temperature, respiratory rate, and GCS). The Modified NUTRIC Score was calculated when the patient entered the intensive observation room. APACHE II Score and SOFA Score were also be measured.

Nutritional data was recorded daily, total daily calorie intake (kcal / day), and daily protein intake (g / day). Provision of calories and protein is given based on the ideal body weight obtained from measuring height using a measuring tape. Calorie debt is calculated based on the difference in calorie needs based on the predictive formula of ideal 25 kcal / kg / day and the amount of calorie intake given. Protein debt was calculated based on the difference in protein needs based on the predictive formula of 1.2 grams / kg of ideal body weight / day with the amount of calorie intake given.

The quadriceps femoris muscle thickness was measured by ultrasonography on the 1st, 3rd, 5th, and 7th day of ICU treatment. The examination was carried out with an ultrasound machine using a 12 Mhz linear transducer. Each examination was carried out on both feet at the midpoint of the upper part of the patella and the superior anterior iliac spine. Measurements were taken of the rectus femoris and vastus intermedius muscle for 3 times and the measurement results are the average of the examination. The difference in thickness of the quadriceps femoris muscle during the first week was obtained from the difference in measurement at the time of examination with the first-day examination.

This research data was presented in the form of tables, graphs or diagrams and text or writing that clarifies the graph diagram. The research data were tabulated and analyzed by computer

software with the Kolmogorov Smirnov normality test and Pearson or Spearman Correlation test with SPSS. Data of patients who dropped out of the study due to death on day 3 and 7 were also analyzed.

RESULTS

There were 30 patients undergoing treatment in the Intensive Care Unit (ROI) Dr. Soetomo Hospital Surabaya. The basal characteristics of the subjects (table 1) showed that the male subjects were more than female subjects (63.3% vs 37.7%). The age group with the most patients is the 31-45-year-old group at 50%. Most of the patients (16 subjects) have normal body mass index (53.3%). There were 5 patients (16.7%) with undernutrition body mass index and 2 subjects (6.7%) with obese body mass index. The most common diagnosis was intraabdominal infection in 7 subjects (23.3%), pneumonia in 6 subjects (20%), multiple trauma in 5 subjects (16.7%), traumatic brain injury in 5 subjects (16.7%), subjects with other sepsis. 4 subjects (13.3%) and heart failure in 3 subjects (10%). Of the 30 subjects, 14 subjects (46.7%) had an APACHE II Score with a range of 11-20. Most of the subjects (76.7%) had SOFA scores ranging from 2-7, there were 2 subjects with SOFA scores >11. Furthermore, 22 of 30 subjects or 73.3% had an mNUTRIC Score in the range 0 to 4, and there were 8 subjects (26.7%) with an mNUTRIC Score ≥ 5 .

The average change of the quadriceps femoris muscle thickness difference in the third day there was a change in the percentage difference of $-2.751 \pm 0.443\%$ in the low-risk mNUTRIC group (0-4) and the highest increased on the seventh day of $-3.867 \pm 0.847\text{cm}$. In the high-risk group (≥ 5) there was a change in the percentage difference in muscle thickness of $-4.315 \pm 0.661 \text{ cm}$ on the third day of observation and to -7.103 ± 0.787 on the



Table 2. Characteristics of research subject

Variables	Amount	Percent (%)
Sex		
1. Female	11	37.7%
2. Male	19	63.3%
Age group		
1. 17-30	4	13.3%
2. 31-45	15	50%
3. 46-60	7	23.3%
4. >60	4	13.3%
BMI		
1. <18,5	5	16.7%
2. 18.5-24.9	16	53.3%
3. 25.0-29.9	7	23.3%
4. >30	2	6.7%
Diagnosis		
1. Intraabdominal infection	7	23.3%
2. Pneumonia	6	20.0%
3. Multiple Trauma	5	16.7%
4. Brain Injury	5	16.7%
5. Sepsis	4	13.3%
6. Heart Failure	3	10.0%
APACHE II Score		
1. 1-10	5	16.7%
2. 11-20	14	46.7%
3. 21-30	9	30.0%
4. >30	2	6.7%
SOFA Score		
1. 2-7	23	76.7%
2. 8-11	5	16.7%
3. >11	2	6.7%
mNUTRIC Score		
1. 0-4	22	73.3%
2. ≥ 5	8	26.7%

day of observation. Based on the statistical test, it was found that the significance was $p = 0.000$ on the three observation days. From these results, it can be concluded that there is a significant difference in the quadriceps femoris muscle thickness between low-risk and high-risk groups.

There is a relationship between the mNUTRIC score and the quadriceps femoris muscle

thickness percentage difference on day 3,5,7 with a significant value of $p = 0.000$. These results indicate that the correlation between the mNUTRIC score and the quadriceps femoris muscle thickness percentage difference on days 3,5,7 is significant. The Spearman correlation value of -0.637 on the 3rd day indicates a negative correlation with a strong correlation between the mNUTRIC score and the quadriceps femoris muscle thickness percentage difference.



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The spearman correlation value of -0.591 on the 5th day indicates a negative correlation with moderate correlation strength between the mNUTRIC score and the quadriceps femoris muscle thickness percentage difference on the 5th day. The spearman correlation value of -0.696 on the 7th day indicates that there is a negative correlation with a strong correlation between the mNUTRIC score and the quadriceps femoris muscle thickness percentage difference on the 7th day.

From the correlation analysis of the APACHE II Score and the quadriceps femoris muscle thickness percentage difference at day 3,5,7, it was found that a significant value was obtained with $p < 0.050$, which indicates that the relationship between the two variables is significant. From the correlation analysis between the SOFA Score and the percentage of

thickness difference at day 3,5,7, a significant value was obtained with $p < 0.050$, which indicates that the relationship between the two variables is significant.

In this study, a significance value of $p > 0.05$ indicates that there is no significant relationship between calorie debt on day 3,5,7 and the percentage of muscle thickness difference on day 3,5,7. And $p = 0.96$ which indicates that the correlation between calorie debt and protein debt with the quadriceps femoris muscle thickness percentage difference on the 3rd and 5th day with the change in the quadriceps femoris muscle thickness percentage difference ($p > 0.050$). On the 7th day, there was a significant relationship between total calorie debt for 7 days with the quadriceps femoris muscle thickness percentage difference ($p = 0.008$).

Table 3. Characteristics of the quadriceps femoris muscle thickness difference.

	Low Risk	High Risk	P Value
Day 3	-2.751 ± 0.443	-4.315 ± 0.661	$p = 0.000$
Day 5	-3.485 ± 1.051	-5.315 ± 0.705	$p = 0.000$
Day 7	-3.867 ± 0.847	-7.103 ± 0.787	$p = 0.000$

Comparative analysis with paired T test for the difference of day 3rd, Mann-Whitney test for the difference of day 5th and 7th.

Table 4. The correlation test results of the mNUTRIC Score and quadriceps femoris muscle thickness percentage difference.

	Day 3	Day 5	Day 7
mNUTRIC Score	r: -0.637; p 0.000	r: -0.591; p 0.001	r: -0.696 ; p 0.000
APACHE II Score	r: -0.581; p 0.001	r: -0.479; p 0.007	r: -0.635 ; p 0.000
SOFA Score	r: -0.498; p 0.005	r: -0.413; p 0.023	r: -0.410; p 0.024

Spearman correlation test with $p = 0.05$ was significant



Table 5. Results of the correlation test of total calorie debt with the quadriceps femoris muscle thickness.

	Quadriceps femoris muscle thickness percentage difference		
	Day 3	Day 5	Day 7
Calorie debt	r: -0.079; p 0.676	r: -0.159; p 0.403	r: 0.322; p 0.83
Protein debt	r: 0.263; p 0.160	r: -0.039; p 0.840	r: 0.477; p 0.008

Spearman correlation test with $p = 0.05$ was significant

DISCUSSION

Ultrasonography (USG) muscle examination is a convenient non-invasive tool for evaluating muscle mass loss in critically ill conditions. A study by Pardo et al. Measuring the quadriceps femoris muscle thickness in 29 patients treated for more than 7 days in the ICU, showed that patients lost up to 16% of muscle at the first week of ICU and 24% at the 21st day of treatment (Pardo et al., 2018). In this study, the average loss of quadriceps femoris muscle was -3.168% on day 3, -3.973% on day 5, and -4.730% on day 7. The results of this study differed from previous studies due to several aspects. In this study, patients had a better severity rate than in previous studies. The average APACHE II score was 18, which was estimated to have average intra-hospital mortality of 25% for non-operative patients and 12% for postoperative patients. This is different from the study of Pardo et al., where the patient is in a more severe condition (an estimated 44% mortality) so that he receives aggressive therapy such as muscle relaxants, which makes the patient prone to muscle wasting.

There is a significant correlation between the high-risk mNUTRIC group (≥ 5), compared with low risk group (0-4) with the difference in muscle thickness on days 3rd, 5th, and 7th. Overall the correlation of these factors has a strong correlation strength. This is consistent

with Puthuchery, et al. The study showed a greater reduction in the cross-sectional area of the rectus femoris in patients with multi-organ failure on day 7 than patients with single organ failure. On the third day of examination, there was also a significant difference between the two groups of patients with multiorgan failure with one organ failure, where muscle mass loss occurred prematurely in critical patients (Z. A. Puthuchery et al., 2013).

The severity of muscle wasting is directly related to the severity of the disease, where more organ failure (SOFA > 2) is associated with increased muscle loss (Z. A. Puthuchery et al., 2013). This is consistent with the results of this study where there was a significant correlation between the APACHE II Score and the SOFA Score with the percentage of muscle loss on days 3rd, 5th, and 7th. From the analysis, it was found that there was a correlation with moderate and strong correlation strength between APACHE II Score and SOFA Score with percentage difference in muscle thickness. The increase in disease severity was indicated by an increase in the APACHE II Score and SOFA Score and was correlated with changes in the quadriceps femoris muscle thickness.

In this study, it was found that calorie intake was given slowly and increased gradually. Overall, the nutrition given was 39% (9.91 ± 5.14 cal/kg body weight/day) on the second day of treatment. On day 3 the mean calorie intake



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was increased gradually to 62.4% (15.61 ± 5.18 cal / kkBBI / day). On the next day of treatment, calorie intake was increased gradually until it reached 87.6% of the daily requirement and reached 100% of the requirement within five days of treatment.

The appropriate calorie intake is a key factor in critically ill patients. Nutrition starts with a small amount and is gradually increased until it reaches the recommended target calorie needs. In this study, the calorie intake was given slowly and gradually increased. From this study, there was no relationship between calorie debt and muscle changes during the first week. This is in accordance with the research of Pardo et al., which showed no correlation between calorie or protein definitions and muscle mass in the first week of treatment (Pardo et al., 2018). In this study, a consensus formula was used to determine daily calorie and protein needs which could cause differences in calorie needs between actual patient needs and the intake given.

It is recommended to provide a daily protein intake of 1.2 to 2.0 grams/kg/day in critically ill conditions. (McClave et al., 2016; Singer et al., 2019). However, this target is difficult to achieve in clinical practice. From this study, an average protein intake of 1.12 g/kg/day was reached by 43.4% of patients on the 7th day of care. In this study, the results show that there is a relationship between protein intake and the quadriceps femoris muscle thickness. This is consistent with the results of a study in 119 critically ill patients who compared the amino acid intake of 0.8 g/kg/day with 1.2 g/kg/day with parenteral nutrition. Higher amino acid administration was significantly associated with antebrachial muscle thickness by ultrasound evaluation (Ferrie, Allman-Farinelli, Daley, & Smith, 2016). Another study on 60 critical patients who received protein intake intervention (average 0.75 g/kg/day) found that there was less loss of quadriceps muscle

thickness on discharge than the standard group in the intervention group (Fetterplace et al., 2018). The two studies are in accordance with the results of this study where on the 7th day, there was a significant and positive correlation with moderate strength correlation between total calorie debt for seven days with the percentage difference from the change in the thickness of the femoral quadriceps muscle ($p = 0.008$). The similarity of the results of this study compared to previous studies is because the average amount of protein intake given is relatively the same. This suggests that protein supplementation is associated with muscle mass loss in critically ill patients, according to clinical guidelines.

The weakness in this study is that measurement of the quadriceps femoris muscle thickness was only performed in the first seven days of treatment. Long-term measurements of the quadriceps femoris muscle thickness are expected to describe better changes in the metabolic conditions of critical patients. Long-term monitoring is expected to observe improvement or to worsen metabolic conditions. Changes in metabolic conditions lead to changes in muscle measurement parameters that can be used to predict prognosis in critically ill patients.

A study of 280 ultrasound examinations of quadriceps thickness performed on 29 critically ill patients showed that examination of quadriceps muscle thickness revealed good intra-and inter-observer reliability. It was found that Intra-observer reliability's ICC was 0.74 [95% CI 0.63; 0.84] and Inter-observer reliability's ICC was 0.76 [95% CI, 0.66; 0.86] at the "midpoint" site. (Pardo et al., 2018). In this study, only one researcher performed an ultrasound examination. This is intended to avoid inter-observer subjectivity.

The use of an indirect calorimeter is expected to be able to determine caloric requirements more precisely. Calorie requirements changes



can provide a rough idea of the metabolic state of the patient. An indirect calorimeter is expected to reduce the energy deficit and observe the relationship of better caloric and protein intake with loss of muscle mass in critical patients.

Another weakness of this study only measures the quadriceps femoris muscle thickness and not measuring the cross-sectional area of the muscles. One study showed the measuring of the cross-sectional regions as a replacement parameter of muscle strength versus muscle thickness. The difficulty of obtaining a complete picture of the rectus femoris muscle is a major concern in cross-sectional areas using a conventional high-frequency linear probe (Z. A. Puthuchear et al., 2017).

This study is expected to increase clinician's attention to muscle mass loss in the ICU, monitor nutritional protocols and exercise interventions to maintain muscle mass. Nutrition monitoring in the ICU with clinical, biological, and technical examinations is expected to prevent and detect nutrition-related early complications. The Modified NUTRIC Score can be used to predict the risk of complications due to critical illness, including loss of muscle wasting. Functional recovery in critically ill patients is one of the focuses in future studies

CONCLUSION

Modified NUTRIC score has a moderate relationship with the quadriceps femoris muscle thickness in critically ill patients. There was no relationship between nutritional intake and the quadriceps femoris muscle thickness in critically ill patients. Protein intake has a moderate relationship with the quadriceps femoris muscle thickness in critically ill patients.

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