



## CRITICAL EVALUATION OF MUSCLE MASS LOSS AS A PROGNOSTIC MARKER OF MORBIDITY IN CRITICALLY ILL PATIENTS AND METHODS FOR ITS DETERMINATION

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**Objective:** Loss of muscle mass in critically ill patients is associated with serious consequences, such as prolonged mechanical ventilation, intensive care unit confinement, and higher mortality. Thus, monitoring muscle mass, and especially its decline, should provide a useful indicator of morbidity and mortality. Performing evaluations according only to body mass index is imperfect, therefore the aim of this article was to evaluate appropriate methods for muscle mass loss determination in ICU patients.

**Methods:** For this review, the literature searches were conducted through Embase and Medline, PubMed and Google Scholar databases up to February 2018 for the following Medical Subject Headings terms muscle atrophy, protein catabolism, ICU-acquired weakness, muscle mass loss, myolysis, critical illness, stress metabolism, computed tomography, magnetic resonance imaging, dual-energy X-ray absorptiometry, neutron activation analysis, anthropometric examination, determination of endogenous metabolites of the skeletal muscles, bioimpedance spectroscopy, ultrasound.

**Result:** It appears that ultrasound, which is widely available in hospitals, is the most advantageous method. Muscle ultrasound is non-invasive, relatively inexpensive, and is a bedside method that is free of ionizing radiation. Furthermore, muscle ultrasound also seems to be valid in patients with severe fluid retention, which is a typical complication with other conventional methods.

**Conclusion:** Early detection of critical illness neuromyopathy could be beneficial for improving the standards of intensive care, and thus reducing the risk of mortality in these patients.

**Key words:** muscle atrophy; protein catabolism; stress metabolism; body composition; myolysis.

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Critical illness is a life-threatening multisystem process that can result in significant morbidity and mortality (1). Acute stress response is most often

### LAY ABSTRACT

Every day there are many people around the world who suffer from multiple injuries, burns or serious diseases leading to the hospitalization in the intensive care units. These life-threatening conditions are associated with the muscle mass loss being one of the mortality risk factors. According to the published literature, in critically ill patients wastage of muscle mass is up to 9% daily with harmful consequences such as inability to breathe spontaneously. Therefore, care should include not only medication, but also appropriate nutrition and rehabilitation. The aim of this paper was to evaluate available methods for monitoring muscle mass. Ultrasound seems to be the most advantageous. It is readily available diagnostic equipment in hospitals, which is noninvasive, relatively inexpensive and free of ionizing radiation. Early detection and evaluation of muscle wasting could be beneficial for improving the standards of intensive care and thus reducing the risk of mortality in these patients.

elicited by accidental or surgical injury, sepsis, burns or other serious diseases. This stress state is characterized by the activation of a hormonal response in the hypothalamic-pituitary-adrenal axis, leading to release of cortisol from the adrenal gland. This is a major component of the general adaptation to disease and stress, and contributes to maintaining cell and organ homeostasis. In a stress response, levels of adrenaline, noradrenaline, glucagon, and growth hormone also increase (2). A hypermetabolic stress state is associated with a number of alterations in carbohydrate metabolism (3) through an increase in hepatic glucose production by gluconeogenesis and glycogenolysis, and inhibition of insulin-mediated glucose uptake to skeletal muscles (4). This stress hyperglycaemia ensures an adequate supply of glucose for the brain and phagocytic cells (5). Interestingly, in trauma, non-injured muscle is insulin resistant, while injured muscle is usually not (6). Protein catabolism extends to the peripheral tissues (muscles, skin). It is important for the synthesis of acute phase proteins, including coagulation factors, and as an energy substrate for immune cells, fibroblasts, and for gluconeogenesis (7, 8). Whole-body protein turnover is increased in critically ill patients. Changes in protein metabolism during a stress response increase amino acid oxidation and nitrogen losses. This results

**Table I.** Consequences of lean body mass loss in critically ill patients hospitalized in intensive care unit

Loss of lean body mass	Consequences
10%	Impaired immune system function
20%	Reduced vital lung capacity
30%	Dependence on mechanical ventilation
>30%	High risk of mortality

in a negative nitrogen balance and changes in body composition, with a tendency towards loss of muscle mass (9), which is enhanced by prolonged immobilization of these patients (10).

The detailed mechanisms of changes in body composition have not been sufficiently described (11). Stress metabolism is necessary for survival, but prolonged duration can contribute to bodily damage, as shown in Table I (2). Muscle mass is a clinically interesting prognostic marker of mortality in these critically ill patients. Many studies have investigated this topic, but no review articles or evaluations of the clinical methods for measurement of muscle mass in intensive care units (ICU) have been published to date.

### MUSCLE MASS AS A POSSIBLE PREDICTOR OF MORTALITY

Based on described metabolic and pathophysiological changes, there are differences in body composition in critically ill patients with multiple injuries in ICU. In the 5-year period after discharge from intensive care, survivors typically have a threefold increase in death rate and a greater incidence of several neuromuscular diseases compared with the general population (11, 12).

Other studies have described how monitoring of body composition changes, specifically that of muscle mass, is a useful indicator of morbidity and mortality (13). Muscle wasting is also statistically significantly correlated with increased periods of mechanical ventilation (14) and prolonged lengths of hospital stay (LOS) (15–17).

Studies have either directly or indirectly evaluated the loss of muscle mass in different ways. Previously, it seemed sufficient merely to describe a patient's condition using body mass index (BMI). Nowadays, we tend to evaluate muscle mass directly. Its loss better estimates patient malnutrition, and its determination seems to be an interesting prognostic marker in polytrauma patients.

Higher BMI has been described in association with a higher percentage of survival in critically ill patients (18–20). This phenomenon is called the obesity paradox (21) and it was confirmed in a large observational cohort study that was conducted over 10 years in 154,308 patients. BMI was found to have a significant association with hospital mortality, with

the risks increasing rapidly for underweight patients (BMI < 18.5 kg/m<sup>2</sup>). The lowest risk of death was seen in obese and seriously obese patients, those with a BMI of 30–39.9 kg/m<sup>2</sup> (22).

There are several explanations for the apparently beneficial effects of obesity for critically ill patients, including higher levels of anti-inflammatory cytokines, more nutritional reserves, and the higher cholesterol and lipid levels common in obese patients, which bind endotoxin during critical illness and provide the precursors for adrenal steroid synthesis (23). However, in a study by Moisey et al. (14), evaluations made using only BMI were demonstrated to be imperfect because 71% of 149 critically ill patients older than 65 years were sarcopenic independently of their BMI when examined by the computed tomography (CT) scan method. Of the sarcopenic patients, 9% were underweight, 44% were of normal weight, and 47% were overweight/obese according to BMI classifications. Measuring muscularity allowed for the early identification of at-risk patients (14). Similarly, Pichard et al. (15) confirmed that malnutrition is better detected by a fat-free-mass index using the bioelectrical impedance method than by using BMI. A patient with muscle atrophy and elevated adipose tissue may be categorized as having a normal nutritional status based on BMI, but would be considered to be undernourished based on a low fat-free-mass index. In fact, they found fewer patients (15%) who were identified as at nutritional risk because of a low BMI (< 20 kg/m<sup>2</sup>) than because of a low fat-free-mass index (37%) (15).

Wasting or defects in skeletal-muscle mass and strength is very common in critically ill patients, and is a risk factor for mortality (24–26). Weijs et al. (13) in their study used a CT scan to determine skeletal muscle area in 240 mechanically ventilated patients during the early stage of critical illness. Low-muscle area was observed in 63% of the patients for both females and males. Mortality was 29%, and was significantly higher in females than in males (37% vs 23%;  $p=0.028$ ). Low-muscle area was associated with higher mortality compared with normal-muscle area in females (47.5% vs 20%;  $p=0.008$ ) and in males (32.3% vs 7.5%;  $p<0.001$ ) (13).

The study by Moisey et al. (14) demonstrated that decreased muscle index, but neither BMI nor serum albumin, was significantly associated with in-hospital mortality (OR=0.93,  $p=0.025$ ). Muscle atrophy on admission to the ICU affects the length of ICU stay and the number of days of mechanical ventilation. They found that patients with lower muscle mass, compared with patients with physiological amount of muscles, had significantly fewer ventilator-free days (median=19 vs median=27;  $p=0.004$ ) and significantly fewer ICU-

free days (median = 19 vs median = 16;  $p = 0.002$ ) (14).

Bioelectrical impedance analysis, which was used in a study by Pichard et al. (15) in critically ill patients (525 men, 470 women) demonstrated an association between fat-free mass (FFM) at hospital admission and LOS in the ICU. A low FFM was noted in 37% of the patients hospitalized for 1–2 days, and this increased to 55.6% of the patients hospitalized >12 days (15). Regarding this study, Naber (27) commented that FFM index better predicts a longer LOS than BMI or a Subjective Global Assessment questionnaire. FFM is affected by fluid balance, and therefore patients with oedema, patients undergoing haemodialysis and patients who needed rehydration perfusion or cardiorespiratory resuscitation were excluded from this study. Therefore, the study is limited by its restriction to less seriously ill patients (27).

Another study investigated body cell mass (BCM) as a metabolically active compartment of FFM using multifrequency bioimpedance analysis. Dual-energy X-ray absorptiometry (DXA) was also performed as a reference method, through which FFM, bone mineral and extracellular water were measured. BCM reflects the body's cellular components involved in oxygen consumption, carbon dioxide production and resting metabolism, and is altered by changes in nutritional status and the catabolic effects of disease. In this context, BCM was also shown to be a marker of malnutrition or for making a prognosis in the most critically ill patients (28).

Another method of determining muscle mass was by measuring muscle layer thickness (MLT) of the quadriceps femoris muscle by ultrasound. In the study by Gruther et al. (16), 17 patients were measured at baseline and after 28 days. A decrease in MLT between these days was correlated with the length of stay in the ICU (for the right thigh  $p = 0.006$ , for the left thigh  $p = 0.003$ ). In their study (16), Gruther et al. also used the method of measuring thigh circumference. They found that it cannot be used as a predictor of mortality or LOS, because overhydration, which is common in these patients, may distort the results. Soon after hospitalization, MLT was measured by ultrasound in 101 patients during the first examination, and showed a high significant negative correlation between MLT of both the right thigh ( $p < 0.0001$ ) and left thigh ( $p < 0.0001$ ) and LOS in the ICU (16).

In a study by Puthuchery et al. (17), an ultrasound measurement of the rectus femoris muscle cross-sectional area (CSA) also had a predictive value. As muscle depleted, the LOS in the ICU increased significantly ( $p < 0.001$ ) (17).

## LOSS OF MUSCLE MASS DURING INTENSIVE CARE UNITS STAYS

The above-described loss of skeletal muscle as a defect or wasted strength and mass occur in most critically ill patients with multiple injuries in ICU. This is typically a bilateral deficit of muscle strength in all limbs (29). This can include disorders of skeletal muscle (critical illness myopathy; CIM), as well as disorders of the peripheral nerves (critical illness polyneuropathy; CIP), but in some cases there is a combination of both.

It is clinically important to separate these CIM and CIP, since they have different prognosis and will probably also require specific intervention strategies (30). CIM is significantly more common than CIP in ICU patients. In this patient condition, there are structural and functional changes in skeletal muscle, such as decreased membrane excitability, which results in muscle weakness (26). The reported prevalence of CIM or CIP ranges from 25% to 100% and depends on the population studied, the criteria examined, and the presence of risk factors (31).

There are symptoms typical of CIP, such as symmetrical distal-predominant muscle weakness with atrophy, a loss of deep tendon reflexes, and often a distal reduction of sensitivity to pain, temperature, and vibration, as well those suggestive of CIM, such as muscle weakness and early failure after being weaned from the ventilator (32).

Furthermore, there are serious consequences, including an extended period of mechanical ventilation and longer ICU stays (33–35) and, according to certain studies, higher mortality was found in patients with neuromyopathy compared with patients without this diagnosis (36, 37). Furthermore, patients who survived experienced physical disability for weeks or months (38). Although full recovery has been reported in approximately 50% of people with muscle weakness, improvement is related to the severity of the condition. People with severe weakness may take months to improve, and may remain severely affected (39).

According to available study (17), the largest loss of muscle mass occurs during the first week of hospitalization. This has been confirmed using the ultrasound method to measure the rectus femoris muscle CSA (17). In that study, the CSA decreased by 12.5% ( $p = 0.002$ ) over 7 days, and at day 10 there was a decrease of 17.7% ( $p < 0.001$ ) in the rectus femoris CSA. In addition, it was demonstrated that the decrease in the rectus femoris was greater in patients who experienced multi-organ failure by day 7 (–15.7%) compared with single-organ failure (–3.0%) ( $p < 0.001$ ), even by day

3 (−8.7% vs −1.8 %). Within multi-organ failure, it also depends on the number of failed organs. Changes in rectus femoris CSA were greater in those with 4 or more failed organs (−20.3%) than in those with 2–3 failed organs (−13.9%) (17).

Similarly, through the use of CT scans Casaer et al. (40) determined femoral muscle loss over 7 days as being  $6.9 \pm 1.7\%$  of the initial volume. These patients lost a mean body weight of  $1.8 \pm 1.7$  kg over a 7-day period, which correlated positively with the loss of femoral muscle volume ( $R=0.703$ ,  $p=0.02$ ) (40).

Reid et al. (41) also found that patients with the greatest amount of muscle at the start lost significantly more muscle thickness over the first 7 days than those with thinner muscles ( $p<0.001$ ) (41). They described rates of muscle wasting at 1.6%/day, with a range of 0.2–5.7%/day, and Campbell et al. (42) witnessed 6%/day, with a range of 2–9%/day in those who were severely oedematous (41, 42).

After major trauma, hydrolysis of the skeletal muscles with a release of proteins is typical in muscle wasting. Studies show that approximately two-thirds of the protein loss occurred in skeletal muscle, but the remainder came from other sources. In a study by Monk et al. (43), total body protein (TBP) loss was 1.62 kg (16%) over 21 days and 1.09 kg of this came from the skeletal muscles. That is, 67% of the protein originated from skeletal muscle. It was also found that, over the first 5 days of the study, there were large losses of proteins from skeletal muscles in patients, although after this time, it appears that the protein loss was shared between non-muscle tissues and skeletal muscles (43).

TBP was determined in multiple studies by another method, neutron activation analysis (IVNAA) (43–46), and they observed similar results in polytrauma and

septic patients. The greatest losses of TBP appeared during the first week of hospitalization, after which muscle mass decreased more slowly (46). In patients with severe sepsis, the loss of TBP was approximately 1.5 kg/12.5% 10 days after admission to the ICU (44). The decrease in TBP was even greater in patients with multiple injuries. During these 10 days, the loss of muscle mass was thus approximately 1.2% of TBP/day (43). Patient monitoring and measuring their muscle mass was usually conducted during 21 days of hospitalization. During this study period, the TBP decreased by 13.1% (46), while in another study it was approximately 1.58 kg (approximately 15%) in septic patients (45), and in patients with major polytrauma the decline ranged from 14.6% (46) through 1.624 kg (approximately 16%) (43) to 1.66 kg (45).

## METHODS TO DETERMINE MUSCLE MASS

Several methods have been used in the aforementioned studies to determine muscle mass, but they differ in many aspects (see Table II). Each of the methods has its own specific benefits (e.g. economic, accuracy, validity, effect on the body, time constraints, and feasibility). Some of the methods are highly accurate (CT scan, magnetic resonance imaging (MRI), DXA, IVNAA) in comparison with others, but have usually come at a higher cost. These methods are generally not used routinely in all patients, but are very important in research. For clinical practice, less expensive and time-consuming methods, such as anthropometric examination, determination of endogenous metabolites of the skeletal muscles (creatinine, 3-methylhistidine, excretion of creatinine in the urine), bioimpedance spectroscopy and ultrasound, are preferable.

**Table II.** Evaluation of different methods to monitor muscle mass in critically ill patients

Method	Advantages	Disadvantages
Computed tomography and magnetic resonance imaging	Highly accurate; highly reliable; possibility of detecting infiltration of muscle by adipose tissue; applicable in patients with a high degree of fluid overload	Time consuming; higher cost; relatively high level of radiation exposure; transport to special department; inappropriate for repeated monitoring of muscle mass loss
Dual-energy X-ray absorptiometry	Highly accurate; fast examination	Transport to the center specialized personnel; radiation exposure; expensive; the result is affected by tissue hydration; inappropriate for repeated monitoring of muscle mass loss
Neutron activation analysis	Accurate measurement; can be used in patients with severe fluid retention	Time-consuming; certain amount of radiation exposure; few centres have necessary technical equipment; inappropriate for repeated monitoring of muscle mass loss
Anthropometry	Simple and cheap technique; does not expose patients to radiation; can be repeatedly used in one patient	Time-consuming; unbalanced state of hydration distort results; operator dependent
Endogenous metabolites of skeletal muscle	Inexpensive and easy; no special equipment; does not expose patients to radiation; can be repeatedly used in one patient	Time-consuming; many factors typical for critically ill can influence results (trauma, infection, renal insufficiency,...)
Bioimpedance spectroscopy	Inexpensive; rapid application portable device; easily performed at the bedside; does not expose patients to radiation; can be repeatedly used in one patient	Distortion by hydration status and the presence of oedema; skin temperature and different body position can influence; special device
Ultrasound	Simplicity and ease of application; free of ionizing radiation; relatively inexpensive widely available piece of equipment; portable device; applicable in patients with a high degree of fluid overload; easily measured in supine, unconscious patients; can be repeatedly used in one patient; can detect fatty infiltration and changes in muscle architecture	Operator dependent

### *Computed tomography and magnetic resonance imaging*

There are highly accurate imaging techniques available; CT and MRI. Usually, these methods provide an estimate of regional skeletal muscle using cross-sectional images. These methods can detect infiltration of muscle by adipose tissue and quantify skeletal muscle without fat. CT and MRI can calculate total muscle area and total fat-free skeletal muscle area. These measures are considered highly reliable. Moreover, they are the only techniques that can directly assess abdominal visceral fat content. The disadvantages of these methods include their high cost and the requirement for highly specialized staff, a relatively large amount of time, and specific software. CT is limited by its associated relatively high level of radiation exposure. On the other hand, CT and MRI are very accurate methods and they have been used mainly in research to determine muscle mass (47). It has also been shown that CT provides a more accurate determination of visceral adipose tissue than MRI and that the scan times for CT are shorter than for MRI (48). However, both methods are inappropriate for repeated monitoring of muscle mass loss in routine clinical practice.

### *Dual-energy X-ray absorptiometry*

In research, DXA has also been used to estimate body composition. Originally, DXA was developed to measure bone mineral content, but it can also be used to estimate soft tissue (lean and fat content) (49). In contrast to the methods described above, the radiation exposure associated with DXA is minimal. Other advantages include the short time required to take the measurement and the fact that it is easily tolerated. However, DXA cannot be used routinely because it is expensive, it requires patients to travel to the centre, and it must be applied by specialized personnel. DXA provides a 3-component model of body composition, comprising fat, bone mineral, and lean tissue according to the differential tissue attenuation of X-ray photons. DXA allows for whole-body scans, as well as separation into regional measurements of the upper and lower extremities (47). An underexplored area of DXA technology when assessing body composition is the influence of hydration on soft tissue component estimates. DXA assumes that the hydration of lean body mass is uniform and fixed at 0.73 ml/g, or 73% (50). If a subject contains more than the average amount of water, as in the case of critically ill patients, DXA will overestimate the fat content (51, 52). Therefore, the use of DXA in these patients is not ideal.

### *Neutron activation analysis*

Neutron activation analysis is one of the oldest methods for determining body composition, especially chemical content. This technique measures the action of neutrons on various chemical elements in the body. When an atom is exposed to a neutron, the atom may become radioactive and will release detected gamma radiation. This measurement can be performed immediately after activation or after a certain amount of delay (51). The radiation is detected by gamma-spectrography. IVNAA is a very accurate measurement that takes approximately 1 h (53). Its main disadvantages are a certain amount of radiation exposure and the fact that only a few centres are equipped with the necessary technical equipment. Similarly, using a potassium  $^{40}\text{K}$  isotope can measure total-body potassium content and can be used to determine lean body mass (53). The greatest advantage for patients in ICU is the fact that IVNAA can be used in critically ill patients who have severe fluid retention (16). The multi-compartment elemental models based on IVNAA have become the reference norms most often preferred for evaluating and/or calibrating the alternative techniques (51).

### *Anthropometric measurements*

Skeletal muscle can be assessed using standard, but time-consuming, anthropometric measurements. Anthropometry is a simple and cheap technique, easily applied in clinical practice or in large population-based surveys. Measuring skinfold thickness as subcutaneous fat is one of the anthropometric methods that can be used to estimate body fat, but not visceral (54). The second method is measuring limb circumference to estimate limb muscle and the protein nutritional state. Both these methods rely on a balanced state of hydration and cannot therefore be used with critically ill patients due to their typical fluid retention. Skeletal muscle wasting in critically ill patients is often masked by overhydration (41, 42). These measurements are therefore unreliable as a marker for acute muscle loss in ICU patients (25, 55).

### *Endogenous metabolite measurements*

Estimates of total body muscle can be obtained from endogenous metabolites of skeletal muscle (creatinine, 3-methylhistidine, urinary creatinine, and D3-creatine). Creatine is relatively constantly converted non-enzymatically into creatinine (56), and 3-methylhistidine derives from the breakdown of actomyosin (57). Creatinine concentration in a 24-h urine collection has been proposed

as an indirect measure of body skeletal muscle mass. However, there are many factors that can influence this value, and this limits its accuracy for this purpose. Diet, exercise, infection, trauma, renal insufficiency, and age can decrease creatine production. Furthermore, these factors are typically present in polytrauma patients in the ICU, and hence unfortunately this method is not applicable here. Recently a new method has been tested in preclinical studies, which is based on the oral administration of deuterium-labelled creatine (D3-creatine), followed by measurements of the concentration of urinary  $^2\text{H}$  isotopic enrichments of D3-creatinine. Scientists suggest that D3-creatine is found only in skeletal muscle, and that its turnover is relatively constant, but further research is needed in this area (58).

#### *Bioelectrical impedance measurements*

Measuring bioelectrical impedance is another method of body composition analysis, which is non-invasive, inexpensive, rapid, portable and highly acceptable to patients and easily performed at the bedside. This method does not expose patients to radiation. It is appealing for both research and clinical practice (59). The current techniques of bioelectrical impedance measure electrical resistance and reactance across one or more signal frequencies. Resistance is proportional to the fluid and electrolyte content of the body, whereas reactance is thought to be a measure of the capacitance of cell membranes. It can measure total body water, thus allowing for the calculation of total muscle mass, which is the largest water-rich tissue in the body (60). Bioelectrical impedance analysis has been validated indirectly in healthy human subjects (61). However, it has a major drawback, since muscle mass measurements can be distorted by hydration status and the presence of oedema (62–64). There are also other factors that can influence an impedance measurement, including skin temperature and body position (65).

#### *Ultrasound*

Recent attention has focused on the utility of ultrasound to monitor muscle wasting in critically ill patients (11). The main advantages of this method are its simplicity and ease of application in clinical practice. Ultrasound is a widely available piece of equipment in hospitals. It is useful for bed-ridden or mobility impaired individuals. It is also effort-independent and free of ionizing radiation (55), but it does not measure muscle mass and is operator-dependent. It is important to observe some aspects while taking the measurement to ensure that the results are reproducible. Firstly, it is important to ensure that ultrasound is performed in exactly the same place on the body every time. The solution may be to

place a small permanent mark on the patient's body. Secondly, small adjustments in the angle of insonation can affect muscle echotexture measurements, so it is important to ensure that the transducer is perpendicular to the imaged muscle. Thirdly, serial studies require maintaining the same ultrasound device settings. Finally, subcutaneous tissue thickness is increased during ICU hospitalization, which is a parameter that needs to be measured and controlled for making quantitative ultrasonographic assessments of muscle (66).

Ultrasound evaluates not only muscle mass, but also its quality, as enhanced echo intensity represents changes caused by increased intramuscular fibrous and adipose tissue (67). Ultrasound measures a muscle's transection rather than muscle volume (40). A number of characteristics of peripheral skeletal muscle architecture can be measured; for example, CSA, fibre pennation angle, MLT and echogenicity (55).

Unlike the anthropometric methods, bioimpedance analysis and DXA, the ultrasound method is applicable in patients with a high degree of fluid overload. Campbell et al. (42) in their study on 9 patients with multiple organ failure suggest that measuring muscle layer thickness using ultrasound can be used to estimate the muscle wasting in oedematous patients. According to histological evidence, it appears that oedematous patient fluid is not retained in the body's muscles. The ultrasound technique was proposed on the basis of this hypothesis. It was found, in practice, that when excess fluid accumulates in the subcutaneous tissue, the positions of the tissue interfaces were still readily identifiable via ultrasound, but the depth gain compensation often required an adjustment (42).

When taking ultrasound measurements, various locations are used. Campbell et al. (42) described taking ultrasound measurements at 3 sites (over the biceps, the anterior forearm, and the anterior thigh), which leads to a better indicator of loss of muscle mass than taking a measurement at only one location. These 3 sites where muscle thickness could be easily measured in supine, unconscious patients correlates with lean body mass derived by DXA (42). In another study with 50 patients, this method also worked in the majority (48/50) of patients who had severe fluid retention (41). Gruther et al. (16) also concluded that ultrasound seems to be a valid and practical measurement tool for daily routine use in the ICU for documenting muscle mass (e.g. MLT) (16).

Several studies (16, 41, 42) have demonstrated that the method of measuring the circumference of the limb may distort the results due to retained fluid, but the method of ultrasound in these patients is still applicable. Furthermore, ultrasound has already been used in monitoring the effectiveness of rehabilitation strategies (68).

In addition, ultrasound measurements of muscle architecture have been shown to correlate closely with data obtained via MRI (69) and CT scanning modalities (70). Several studies have demonstrated that muscle ultrasound is able to reliably detect pathological changes, including muscle atrophy, fatty infiltration and intramuscular fibrosis. Grimm et al. (32) investigated whether muscle ultrasound could be useful for screening illness neuromyopathy, because its early detection could be beneficial for improving the standards of care (24, 71). Muscle or nerve biopsy may be useful for definitive diagnosis. The typical pathological findings in CIM include relative selective loss of myosin. Nerve biopsy in CIP will demonstrate widespread axonal degeneration of both motor and sensory nerves (30, 66). Due to its invasiveness, this method is not suitable for repeatedly monitoring the development of this condition. Therefore Grimm et al. (32) performed the first feasibility study in patients with an electrophysiologically-proven critical illness neuromyopathy to evaluate whether muscle ultrasound allows for the visualization of changes in muscle echotexture during the early course of sepsis. The results of this first pilot study suggest a promising role for bedside ultrasound as an additive non-invasive procedure for detecting changes in muscle architecture in patients with either septic shock or severe sepsis (32).

### CONCLUSION

As a consequence of the previously-described stress metabolism, changes in body composition occur in polytrauma patients. The loss of skeletal muscle and wasting of muscle strength evolves during the stress response in the majority of patients admitted to the ICU. The largest loss of muscle mass occurs during the first week of hospitalization and is, on average, 10% of the initial muscle volume. Studies describe a muscle mass loss of 0.2–9% per day depending on the severity of the patient's condition. In addition, the extent of these losses is greater when multiple organs have failed. Approximately two-thirds of protein loss was from skeletal muscle and the remainder from other sources. The mean loss of body protein is 13–16% after 3 weeks of hospitalization. Furthermore, there are serious consequences of these body composition changes, such as an extended period of mechanical ventilation, longer ICU stays, longer LOS and higher mortality. Therefore, according to many studies, determining muscle mass, and especially its decline, provides an interesting prognostic marker of morbidity and mortality in polytrauma patients. Determining this parameter could help to diagnose patients at high risk of muscle weakness and allow their therapy, together

with rehabilitation, to be adjusted as soon as possible. In order to accomplish this, the use of ultrasound is the most advantageous of the evaluated methods in clinical practice according to recent studies in critically ill patients, because it is a widely available piece of equipment in hospitals. In addition, this bedside method is non-invasive, simple, free of ionizing radiation and relatively inexpensive. The patient does not have to be transferred to another department. The main advantage of this method is the applicability of the procedure in patients with major oedema, which is very common in the ICU. Muscle ultrasound is able to reliably detect pathological changes, including muscle atrophy, fatty infiltration, intramuscular fibrosis and changes in muscle architecture. Early detection of critical illness neuromyopathy could be beneficial for improving the standards of intensive care and thus reducing the risk of mortality in these patients.

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