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a key role in critical care

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DOI
10.1097/MCC.0000000000000846

Publication date
2021

Document Version
Author accepted manuscript (AAM)

Published in
Current Opinion in Critical Care

Monitoring muscle mass using ultrasound: A key role in critical care

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Abstract

- Purpose of review: The loss of muscle mass in critically ill patients contributes to morbidity and mortality, and results in impaired recovery of physical functioning. The number of publications on the topic are increasing. However, there is a lack of consistent methodology and the most optimal methodology remains unclear, hampering its broad use in clinical practice.
- Recent findings: There is a large variety of studies recently published on the use of ultrasound for assessment of muscle mass. A selection of studies has been made, focusing on monitoring of muscle mass (repeated measurements), practical aspects, feasibility and possible nutrition and physical therapy interventions. In this review, 14 new small (n=19-121) studies are categorized and reviewed as individual studies.
- Summary: The use of ultrasound in clinical practice is feasible for monitoring muscle mass in critically ill patients. Assessment of muscle mass by ultrasound is clinically relevant and adds value for guiding therapeutic interventions, such as nutritional and physical therapy interventions to maintain muscle mass and promote recovery in critically ill patients.

Keywords

Muscle mass, ICU, ultrasound, CT

Introduction

Bedrest, reduced nutritional intake, and inflammation associated with critical illness lead to muscle loss and ICU-acquired weakness (ICU-AW). Muscle loss may amount to 10% or more of rectus femoris muscle area (RFMA) in just a week of ICU stay [1].

This progressive loss of muscle mass leads to morbidity, mortality and long-term diminished physical functioning [2]. Additionally, a low muscle mass on admission to the ICU is associated with increased mortality [3]. Low muscle mass is also part of the malnutrition diagnosis according to the GLIM criteria and ESPEN-guideline on clinical nutrition in the intensive care unit [4]. Furthermore, muscle mass is a key parameter to help guide therapeutic interventions such as nutrition and physical therapy. Therefore, it is essential that muscle mass is measured in clinical practice. While there are several accurate muscle mass measurement methods and techniques (including CT scan, bio-impedance analysis, and ultrasound), not all are routinely feasible in clinical ICU practice [5*]. The use of ultrasound (US) in assessing muscle mass in critically ill patients has gained much attention recently as it is non-invasive and can easily be utilized at the bedside. However, there is a lack of consistent methodology and the most optimal methodology remains unclear, hampering its broad use in clinical practice. The number of publications on the topic are increasing, of which a number of publications have been selected for this current opinion review.

There are two main goals for the assessment of muscle mass: 1. To assess the current muscle mass for the patient as part of (nutritional) diagnosis, and thereby risk stratification and 2. To monitor the progression of muscle loss and/or recovery of muscle mass, and create opportunity to examine the effectiveness of therapeutic interventions to reduce muscle loss and/or promote muscle recovery. This review will focus on the second goal because several aspects, specifically a clear methodology, of monitoring muscle mass (over time) are still unclear. Thus, this review also focuses on feasible methodology for monitoring muscle mass by US in clinical

practice. If applicable, CT is also mentioned. However, CT is currently not a feasible tool for monitoring muscle mass in clinical practice considering its radiation exposure, costs and risks associated with patient transport.

But what muscle should we measure? For nutritional assessment, it is important to assess the mass or volume of the muscle and muscle area as a proxy for whole-body muscle mass. With CT, both the area of total muscle tissue, as well as specific muscles like the rectus femoris (RF), a large proximal extremity muscle, can be assessed as a surrogate for whole-body skeletal muscle mass. The third lumbar level (L3) is often used in CT, while a mid-upper leg measurement might be more representative of whole-body muscle mass. With US, the RF at mid or 1/3 upwards from the patella to the anterior superior iliac spine (ASIS) is often assessed. Cross-sectional area (CSA) of the RF, often referred to as RFMA, may be preferred over combined RF and VI muscle thickness, often referred to as quadriceps muscle layer thickness (QMLT) [6]. In Figure 1, US images on a healthy subject and ICU patient at day 7 are shown.

For monitoring, it is essential that: 1. Either loss or gain of muscle is representative for whole-body muscle mass, and possibly more important. 2. That this monitoring assessment has a meaningful relationship with recovery and/or outcome. Here, the relationship with recovery is stressed, as the ultimate goal is to intervene (with nutrition and exercise) in muscle loss to improve long-term physical functioning of critically ill patients.

Normalization of muscle mass index?

Without extensively discussing the normalization issue, it is an important element for comparability of patients as well as studies on the subject. Considering that whole-body muscle mass serves as a proxy for protein reserve, an indexation should not be necessary as the amount of muscle is the 'reserve capacity' of the body. Given that taller patients may have more muscle mass, is not really relevant. However, in order to make a comparison, indexation is still required.

Pita *et al.* [7] studied 50 liver transplant patients, in which they monitored RFMA by using US and assessed psoas muscle area (PMA) at baseline by CT. They showed loss of muscle mass in 10 days of ICU stay ranging from 11% (0.17 cm^2/m^2 versus baseline 1.606 cm^2/m^2) versus 13% when indexed on body surface area (BSA) (0.11 cm^2/m^2 versus baseline 0.837 cm^2/m^2), and 15% when indexed against height squared (0.09 cm^2/m^2 versus baseline 0.601 cm^2/m^2). The question as to which (indexed) version of RFMA is most clinically relevant, remains. There appeared to be slight differences in the relationship between RFMA and overall survival, with BSA indexed RFMA being the only one predictive of overall survival. Nevertheless, the studied sample size was small and p-values of the RFMA were rather at borderline significance. Both the variation in the level of muscle loss as well as the indexation are noteworthy.

Landmark and compression level

Bury *et al.* [8**] studied 52 surgical ICU patients and assessed QMLT by maximal compression US both at the mid-upper leg as well as at 1/3 upwards the superior margin of the patella to the ASIS, therefore closer to the knee (Figure 2). Within 10 days, a second measurement was available in 52 patients, and a third measurement

in 38 patients. The average percentage of QMLT loss per day appeared rather similar or slightly higher for midpoint versus 1/3 landmarks (3.2±3.8% versus 2.9±5.7%). Interestingly, QMLT loss was higher between the second and third measurements (4.0± 8.0% at midpoint and 4.3±9.8% at 1/3 landmarks) compared with loss between first and second measurements (1.7±9.2% and 1.7±9.4%). The percentage QMLT loss per day was modeled as the outcome with baseline QMLT measure, energy and protein intake groups, and nutrition status at the start of therapy as the independent variables. Interestingly, malnutrition was found to be a significant factor in increased QMLT loss in the 1/3 landmark (whilst energy and protein intake were not), but not for the midpoint landmark. It is important to note that they found that it is feasible for registered dietitians to use US monitoring in clinical practice. Although this study does not directly support US measurements at 1/3 landmarks to be superior to other landmarks, the differences between performed measurements appear clinically relevant as malnutrition is a major reason for monitoring muscle mass.

Sabatino *et al.* [9] analyzed 233 sets of measurements in 30 critically ill patients with acute kidney injury, showing a high level of agreement between US and CT (cm thickness) for both the RF and vastus intermedius (VI) muscle, both proximal (upper third) and distal (lower two-thirds). The differential bias (proportional bias) comparing US to CT was +0.26 (82.3%) for RF-proximal, +0.04 (97.7%) for RF-distal, +0.09 (93.7%) for VI-proximal, and +0.05 (97.9%) for VI-distal. This suggests that the RF assessment at the distal level is preferred over the more proximal assessment, while there is no apparent difference for VI. Bland–Altman agreement analysis on pooled results showed that the limits of agreement between the US and CT were narrow,

ranging from −0.34 to +0.36 cm. Overall, there is a high level of agreement, although US appears to be less accurate than CT. The landmark choice may affect the monitoring of US outcomes as well.

Fetterplace *et al.* [10] assessed QMLT by maximal pressure US and L3 CSA by CT in 35 critically ill patients. They found that the L3 CSA increased by 35 cm2 (95% CI 11-59 cm2) for every 1 cm increase in QMLT. However, this was not applicable for minimal pressure measurements, in which an increase of 8 cm2 (95% CI -5-22 cm2) was found. Based on CT, 40% of patients had a low muscle area. It would be interesting to show diagnostic sensitivity and specificity of US versus CT. Insufficient follow-up data were available for the evaluation of monitoring.

Tourel *et al.* [11] studied 42 critically ill neurological patients in whom US and CT measurements were performed on day 1 of admission. A second evaluation at 3.2 days was present in 25 patients, a third evaluation at 6.6 days was present in 10 patients. They found US to be highly correlated to CT (0.93, 95% CI 0.84-1.02) and reliable, which is a confirmation of other studies. No data on US monitoring was described.

QMLT versus RF CSA

Lee *et al.* [12] assessed both QMLT and RF CSA with minimal compression US at baseline and after day 7 (n=53) and 14 (n=24) in critically ill patients. They also showed high nutrition risk (mNUTRIC score, modified nutrition risk in critically ill patients >5, 53.5%), sarcopenia (SARC-F >4, 30.2%) and frailty (CFS, clinical frailty score >5, 17.4%) at baseline. None of the muscle measurements or change in

muscle status from baseline to day 7 were related to cumulative fluid balance, important information that is often not reported on. QMLT loss was 8.6±19.4% at day 7 and 15.6±23.7% at day 14, while RF CSA loss was 9.8±19.5% at day 7 and 22.7±19.9% at day 14. Overall, there appears to be an almost linear loss of muscle mass, as previously observed by Puthucheary *et al.* [1]. Results of the RF CSA assessment were 1.14 times higher at day 7 and 1.45 times higher at day 14 compared to QMLT. While QMLT has been suggested to underestimate the loss of muscle mass, the importance of this difference remains to be determined. A noteworthy observation is that the only independent predictor of 60-day mortality was the change of QMLT from baseline to day 7: every 1% loss of QMLT over the first week of critical illness was associated with 5% higher odds of 60-day mortality. Also, the relatively simple questionnaire-based assessments mNUTRIC, SARC-F and CFS are associated with both muscle status and mortality. Therefore, lacking any device, they may be of help in the nutritional assessment of the critically ill patient. Even if the RF CSA is a more accurate measurement of muscle loss, an open mind should be kept towards other measurements and possibilities.

Consistency of muscle loss with other markers

Wandrag *et al.* [13] explored a variety of measurements in 43 critically ill patients, including muscle thickness by US on the bicep, forearm and thigh, to explore a possible ‘tipping point’ (catabolism versus anabolism) and roadmap for nutritional intervention. They showed loss of muscle thickness of 1.2% per day over 14 days; 1.1 cm over 7 days (n=43) and 1.67 cm over 14 days (n=17). Other markers of protein metabolism, including urinary urea and 3-methylhistidine, confirmed

continued catabolism up to day 14. No nutritional ‘tipping point’, to distinguish anabolism, could be identified.

Foster *et al.* [14] studied a cohort of 60 major trauma patients from injury to 6-month recovery, performing US at 4 different sites (biceps brachii, forearm, RF and rectus abdominis) at weekly intervals while in hospital and at 3, 4, 5 and 6 months following discharge. Biceps brachii were found to be the most accessible muscle (considering dressings, amputations and wounds on the other measurement sites), and the only one analyzed. The lowest level of muscle thickness was reached at 6 weeks (-22.7%), with onward recovery. Total urinary urea excretion was assessed, which reached its peak at 1 week and returned to baseline only after 6 weeks. Thus, while protein catabolism was most pronounced at 1 week, it remained elevated up to 6 weeks with continuing loss of muscle depth for 6 weeks. This is an interesting finding as most short studies hardly grasp the long-term consequences of major trauma and possibly other (diagnostic) critically ill patient groups.

Chapple *et al.* [15*] assessed QMLT with US in 19 non-mechanically ventilated critically ill patients. They also investigated the feasibility of other nutritional assessment tools including subjective global assessment (SGA), mid-upper arm circumference (MUAC), calf circumference (CC), body weight and bioelectrical impedance analysis (BIA) up to day 5 of ICU stay or ICU discharge. QMLT at baseline was 2.6±0.8 cm (n=15) and 2.5±0.3 cm (n=5) at follow-up. These data for QMLT and other measurements are hardly usable to assess muscle loss, however, the feasibility is more interesting as counted by completed measurements as a percentage of attempted measurements: bed scales 12%, chair scales 15%, SGA

95%, MUAC 100%, CC 92%, US QMLT 81% and BIA 63%. Within this comparison, the US assessment of QMLT could be considered as feasible, while anthropometric measurements only may appear to be more feasible.

Mayer *et al.* [16**] studied 41 patients admitted to the medical or cardiothoracic ICU, diagnosed with sepsis or acute respiratory failure. US CSA, muscle layer thickness (LT) and muscle quality (echo intensity, EI) for rectus femoris (RF) and tibialis anterior (TA) were assessed at day 1, 3, 5 and 7. RF muscle was assessed at 2/3 distance from the ASIS to superior patella border. TA muscle was assessed at 1/3 distance from the lateral tibial plateau to inferior border of the lateral malleolus. From day 1 to 7, RF CSA loss was 18.5%, TA CSA loss was 8.1%, RF LT loss was 20.1% and TA LT loss was 9.1%. EI increased 10.5% in RF and 15.4% in TA from day 1 to 7. At hospital discharge, 25.7% of patients (9/35) met the criteria for ICU-AW. Change in RF EI from day 1 to 7 of ICU admission was a strong predictor of ICU-AW at hospital discharge. These changes in muscle quality are clinically meaningful deteriorations in the muscle structure, potentially related to myofiber necrosis. EI is easy to assess and especially a very early assessment that may be predictive of ICU-AW. Although the loss of muscle mass was not predictive for ICU-AW, it may still be a very important predictor of later return of physical function.

Vivier *et al.* [17] studied 35 critically ill patients for US diaphragm and pectoral thicknesses at day 1 and 5 of admission. They found a loss of diaphragm thickness of approximately 12% (0.3 mm of 2.5 mm baseline, $p<0.001$) and a loss of pectoral thickness of approximately 2% (0.1 mm of 5.6 mm baseline, $p=0.308$). Diaphragm atrophy (>10% loss) occurred in 48% (17 of 35) and pectoral atrophy in 29% (10 of

34) cases. Diaphragm and pectoral thickness change were not related. Diaphragm atrophy was not associated with outcome, however pectoral atrophy was associated with less successful weaning at day 14. Such a functional relationship, that indicates the potential of early US assessment and prediction of (intermediate) outcome, is an important finding.

Countermeasures against muscle loss

McNelly *et al.* [18] conducted a randomized controlled trial (RCT) seeking to demonstrate the value of intermittent feeding (IF) versus continuous feeding (CF) in 121 critically ill patients, with 10-day RF CSA muscle loss assessed by US as the primary outcome. Loss of RF CSA during 10 days of ICU admission was similar between arms and amounted 18.7% (IF) and 20.6% (CF) in the intention-to-treat analysis and 17.4% (IF) and 19.8% (CF) in the per-protocol analysis. With a protein target of ≥1.2 g/kg and a pass target of 80%, only 46.5% of patients receiving CF and 57.0% receiving IF met this target.

Berger *et al.* [19] studied 23 critically ill patients that were not reaching an adequate intake by day 3 and received supplemental parenteral nutrition for 5 days (day 4 to 9) in a RCT. RF CSA was assessed by US at day 4, 9 and 15. Median RF CSA loss was 20.4% between day 4 and 15, therefore approximately 1.85% per day. The supplemented group tended to show less loss of RF CSA compared to the control group (-16% versus -23%, p=0.068). The supplemented group (n=11) received more protein (1.11 versus 0.69 g/kg/day, p=<0.001) and energy (24.3 versus 17.8 kcal/kg/day, p=<0.001) compared to the control group during the 5-day intervention.

The reduced loss of muscle mass in the supplemented group seems to be fully in line with the higher level of protein feeding in the supplemented group in this RCT.

Nickels *et al.* [20] conducted a RCT in 72 critically ill patients with 30 minutes of daily in-bed cycling in addition to usual-care physiotherapy (n=37) versus usual-care physiotherapy (n=37). US RF CSA was blindly assessed at day 10 after enrollment. The used landmark was at 1/3 distance from the superior patella to the ASIS. Additionally, RF LT and VI LT were assessed at baseline, day 3, 7 and 10 post-study enrolment, and 7 days after ICU discharge. While this is termed a negative study (no significant between-group differences), the figure on RF CSA clearly shows muscle atrophy up to 7 days post ICU discharge: 12% with and 23% without in-bed cycling. This seems to be an underpowered study, however, some attention to nutrition (protein) might have been worthwhile as well.

Conclusion

The use of US in clinical practice is feasible for monitoring muscle mass in critically ill patients. Choice of muscle and landmark, compression level, and other factors affect the assessment to a variable extent. Therefore, consistency of methodology in clinical practice is key. Assessment of muscle mass by US is clinically relevant and of added value for guiding therapeutic interventions, such as nutrition and physical therapy interventions to maintain muscle mass and promote recovery in critically ill patients.

Key points

- Using ultrasound in clinical practice is of added value and feasible for monitoring muscle mass in critically ill patients.
- Choice of muscle and landmark, compression level, and other factors affect the assessment to a variable extent, therefore consistency in the application in clinical practice is key.
- Assessment of muscle mass by ultrasound is clinically relevant and of added value for guiding therapeutic interventions, such as nutrition and physical therapy interventions to maintain muscle mass and promote recovery in critically ill patients.

Reference section

1. Puthucheary ZA, Rawal J, McPhail M, et al. Acute skeletal muscle wasting in critical illness. JAMA 2013; 310:1591-1600.
2. Herridge MS. Legacy of intensive care unit-acquired weakness. Crit Care Med 2009; 37:S457-61.
3. Weijs PJM, Looijaard WGPM, Dekker IM, et al. Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients. Crit Care 2014; 18:R12.
4. Singer P, Reintam Blaser A, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019; 38:48-79.
5. * Looijaard WGPM, Molinger J, Weijs PJM. Measuring and monitoring lean body mass in critical illness. Curr Opin Crit Care 2018; 24:241-247.

A previous review on monitoring lean body mass in critically ill patients, showing the potential of using ultrasound.

6. Puthucheary ZA, McNelly AS, Rawal J, et al. Rectus Femoris Cross-Sectional Area and Muscle Layer Thickness: Comparative Markers of Muscle Wasting and Weakness. Am J Respir Crit Care Med 2017; 195:136-138.
7. Pita A, Ziogas IA, Ye F et al. Feasibility of Serial Ultrasound Measurements of the Rectus Femoris Muscle Area to Assess Muscle Loss in Patients Awaiting Liver Transplantation in the Intensive Care Unit. Transplant Direct 2020; 6:e618
8. ** Bury C, DeChicco R, Nowak D, et al. Use of Bedside Ultrasound to Assess Muscle Changes in the Critically Ill Surgical Patient. JPEN J Parenter Enteral Nutr 2020; 0:1-9.

A study showing not only the results of both mid-upper leg as well as 1/3 ultrasound measurements but also the differences in clinical relevance between the two landmarks.

9. Sabatino A, Regolisti G, di Mario F, et al. Validation by CT scan of quadriceps muscle thickness measurement by ultrasound in acute kidney injury. J Nephrol 2020; 33:109-117.
10. Fetterplace K, Corlette L, Abdelhamid YA, et al. Assessment of muscle mass using ultrasound with minimal versus maximal pressure compared with computed tomography in critically ill adult patients. Aust Crit Care 2020; 24: S1036-7314.
11. Tourel C, Burnol L, Lanoiselé J, et al. Reliability of standardized ultrasound measurements of quadriceps muscle thickness in neurological critically ill patients: a comparison to computed tomography measures. J Rehabil Med 2020; 52:jrm00032.

12. Lee ZY, Ong SP, Ng CC, et al. Association between ultrasound quadriceps muscle status with premorbid functional status and 60-day mortality in mechanically ventilated critically ill patient: A single-center prospective observational study. Clin Nutr 2020; 28:S0261-5613.
13. Wandrag L. Brett SJ, Frost GS, et al. Exploration of muscle loss and metabolic state during prolonged critical illness: Implications for intervention? PLoS One 2019; 14:e0224565.
14. Foster MA, Taylor AE, Hill NE, et al. Mapping the Steroid Response to Major Trauma From Injury to Recovery: A Prospective Cohort Study. J Clin Endocrinol Metab 2020; 105:925-937.
15. * Chapple LA, Gan M, Louis R, et al. Nutrition-related outcomes and dietary intake in non-mechanically ventilated critically ill adult patients: A pilot observational descriptive study. Aust Crit Care 2020; 33:300-308.

A study showing a higher feasibility of ultrasound measurements compared to classical anthropometric measurements in clinical practice.

16. ** Mayer KP, Thompson Bastin ML, Montgomery-Yates AA, et al. Acute skeletal muscle wasting and dysfunction predict physical disability at hospital discharge in patients with critical illness. Crit Care 2020; 24:637.

A study assessing muscle cross-sectional area, muscle layer thickness, echo intensity and the development thereof during ICU stay by ultrasound measurements. Furthermore, showing the clinical relevance of echo intensity as a predictor for ICU-acquired weakness.

17. Vivier E, Roussey A, Doroszewski F, et al. Atrophy of Diaphragm and Pectoral Muscles in Critically Ill Patients. Anesthesiology 2019; 131:569-579.

18. McNelly AS, Bear DE, Connolly BA, et al. Effect of Intermittent or Continuous Feed on Muscle Wasting in Critical Illness: A Phase 2 Clinical Trial. Chest 2020; 158:183-194.
19. Berger MM, Pantet O, Jacquelin-Ravel N, et al. Supplemental parenteral nutrition improves immunity with unchanged carbohydrate and protein metabolism in critically ill patients: The SPN2 randomized tracer study. Clin Nutr 2019; 38:2408-2416.
20. Nickels MR, Aitken LM, Barnett AG, et al. Effect of in-bed cycling on acute muscle wasting in critically ill adults: A randomised clinical trial. J Crit Care 2020; 59:86-93.

Acknowledgements

None

Financial support

None

Conflicts of interest

None

Figure 1

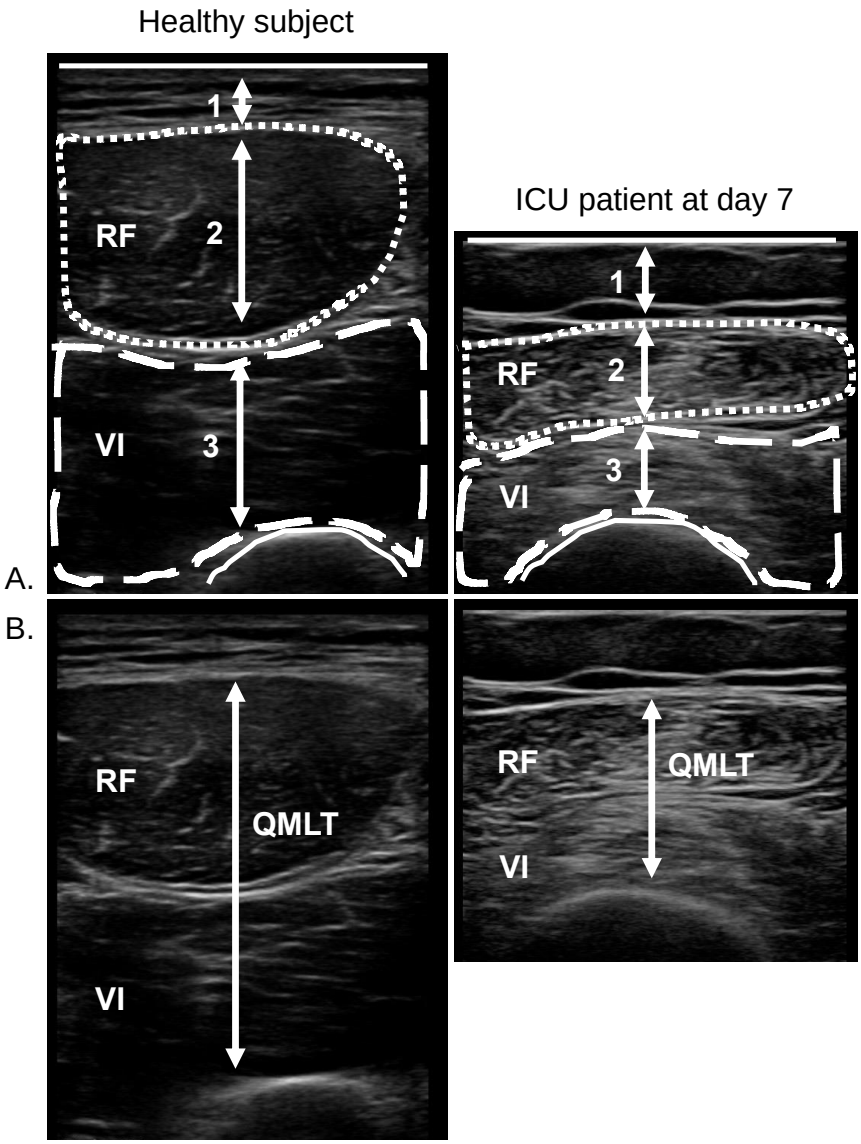

Figure 1. Ultrasound images on a healthy subject and ICU patient at day 7

A: 1. subcutaneous fat layer, 2. rectus femoris (RF), 3. vastus intermedius (VI). RF cross sectional area (CSA) is drawn in the dotted line. RF and VI arrows represent muscle thickness.

B: Quadriceps muscle layer thickness (QMLT) as RF and VI muscle thickness combined.

Figure 2

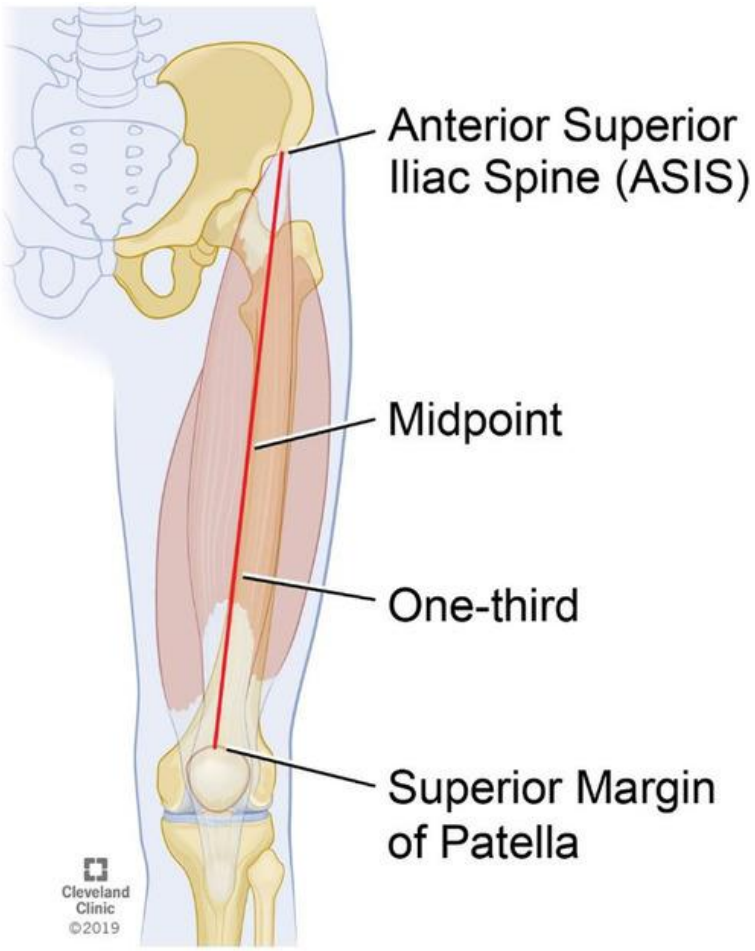

Figure 2. Quadriceps muscle layer thickness measurement landmarks

Previously published by: Bury C, DeChicco R, Nowak D, et al. Use of Bedside Ultrasound to Assess Muscle Changes in the Critically Ill Surgical Patient. JPEN J Parenter Enteral Nutr 2020; 0:1-9.