Bedside ultrasound measurement of skeletal muscle

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Purpose of review
Skeletal muscle and lean body mass may be vital to prognosis and functional recovery in chronic and acute illness, particularly in conditions in which muscle atrophy is prevalent. Ultrasound provides a precise and expedient method to measure muscle mass and changes in skeletal muscle at the bedside.

Recent findings
Here, we describe the various methodological approaches along with the validation and reliability tests that have been performed in various populations. Current applications of ultrasound in chronic and acute illness as well as its limitations and strengths in quantifying the muscle mass and changes in muscle over time are discussed. To capitalize on the beneficial features of ultrasound for measuring muscle, we describe the work that is needed to optimize the usefulness of ultrasound in chronic disease and acute care.

Summary
Given the precision, practicality, and ease of use, ultrasound is emerging as a highly useful tool in expediently measuring the muscle mass and changes in muscle tissue at the bedside. Ultrasound may be valuable in identifying patients who are at risk of malnutrition, in tracking muscle atrophy for the purpose of calculating nutrient delivery, and in assessing the success or failure of nutrition, pharmacological and rehabilitative interventions that aim to counter muscle atrophy.

Keywords
malnutrition, sarcopenia, skeletal muscle mass

INTRODUCTION

Chronic and acute illnesses are often associated with muscle atrophy [1,2▪,3▪,4▪▪,5▪▪,6▪,7,8], which may lead to deleterious clinical outcomes such as increased risk of mortality [5▪▪], increased hospital length of stay [7], and increased ICU length of stay [2▪]. To better understand the clinical and metabolic implications of low muscularity and the process of muscle atrophy, precise, expedient bedside tools are needed. Here, we evaluate the clinical importance of quantifying muscularity and muscle atrophy, and we briefly discuss the tools that are currently available and used at the bedside. We will then discuss the benefits and limitations of using ultrasound for quantifying muscle atrophy as a bedside modality of body composition.

THE CLINICAL IMPORTANCE OF ASSESSING SKELETAL MUSCLE ATROPHY IN CHRONIC AND ACUTE ILLNESS: COMMONLY USED METHODS

Several features contribute to the development and progression of muscle atrophy, regardless of the diagnosis (i.e. injury, acute or chronic illness), including bedrest and immobilization, systemic inflammation, and changes in blood flow. The magnitude of change in muscle, the timeframe of change, and the impact on clinical outcomes differ in various patient populations. In the critically ill, the greatest muscle losses (~17%) typically occur within the first 10 days of ICU admission [2▪], and these losses are amplified by the severity of illness in the first week of ICU admission (i.e. patients with multiorgan failure experience 16% loss vs. 3% for those with single-organ failure in the first 7 days) [2▪]. Skeletal muscle is essential in inflammation and

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KEY POINTS

- Ultrasound is emerging as a common method for the quantification of muscle and it has recently gained significant attention with the growing importance of understanding the role of skeletal muscle at the bedside.
- Ultrasound can provide precise and reliable measures of muscularity and potentially changes in muscle mass in many clinical populations (i.e. chronic obstructive pulmonary disease and heart disease), but more validation and reliability studies are needed to address the specific issues in body composition analysis in these diverse populations (i.e. edema in critically ill).
- To optimize its capabilities, future work is needed to comprehensively understand its strengths and limitations as well as the development of predictive equations of whole-body muscle mass for specific populations as well as cutpoints for identifying individuals with low muscularity.

cytokine regulation [9,10], and is the largest depot (>75%) for glucose clearance [11,12]. Thus, loss of muscle tissue and deteriorating integrity of muscle may further complicate the existing morbidities in the acute or chronically ill. In cancer, for example, toxicity from chemotherapy is associated with lean tissue mass, whereby patients with the least amount of lean mass typically experience worse symptoms of toxicity [13]. On the other hand, gain or maintenance of muscle through nutrition and exercise or rehabilitative interventions may improve the outcomes in acute or chronically ill individuals and the quality of life in the elderly.

Although skeletal muscle is known as the foundation for functional performance, muscle loss has significant implications on survival and metabolic health [6▪,11,14]. For example, functional impairments are reported up to 5 years following ICU stay [14]. With the growing population of aged individuals, the implications of muscle loss are particularly concerning [6▪,15▪▪]. Moisey *et al.* [15▪▪] demonstrated that 71% of patients over 65 years of age have lower than normal muscularity at ICU admission and this relates to mortality as well as reduced ventilation-free and ICU-free days. Taken together, aged ICU patients who have low muscularity have reduced survival and, of those who survive, they may have significantly reduced functional independence. It is clear that clinically expedient and precise bedside measures of muscle mass are important in assessing the muscularity and changes in muscle tissue in chronic and acute illness, which will permit the identification of those who may be at risk of poor prognosis.

To date, weight (actual or estimated) in addition to BMI has been widely used along with other clinical assessment measures to evaluate nutritional status at the bedside. However, these methods are not only crude, but also they cannot discern between changes in fat and lean tissue. Given that skeletal muscle atrophies in many illnesses and conditions has an important role in clinical outcomes, access to modalities that have the capacity to quantify specific tissue depots is ideal. Tools such as bioelectrical impedance that can segregate fat from lean mass may be ineffective in some populations, like lung and colorectal cancer patients, because measurements are severely compromised by variable hydration status [16]. Fluid retention, as observed in many illnesses [16,17▪], may mask the changes in lean tissue or may confound the overall weight changes. These limitations may consequently underestimate the loss of lean tissue, resulting in failure to correctly identify patients who are malnourished or at risk of losing lean tissue and becoming malnourished. Interpretation of results from the clinical trials that are aimed at preserving muscle through nutritional, pharmacological, and rehabilitative interventions may also be skewed when imprecise tools of body composition are utilized.

Dual energy X-ray absorptiometry (DXA) can provide precise information about whole body and regional distribution of fat and lean tissue compartments; however, DXA may not be clinically accessible and is often impractical, particularly in acutely ill populations. MRI and computed tomography (CT) provide the most precise and specific quantifications of skeletal muscle and adipose tissue depots; however, these modalities present with various challenges, including cost and radiation exposure associated with acquiring and analyzing prospective longitudinal scans, as well as various practical and logistical issues.

Ultrasonography is emerging as a promising tool in measuring skeletal muscle at the bedside by quantifying the muscle thickness of a muscle or muscle group of interest. In general, high-frequency sound waves (1–10 MHz), that are generated by the vibrations of electrically stimulated piezoelectric crystal within a transducer, travel through the skin and are partially reflected by the underlying tissues. The reflection of sound by the tissues is called acoustic impedance and each tissue has a unique characteristic impedance. This information is returned to the transducer as an echo and is converted into electrical signals that are displayed on a monitor or other electrical device. There is a two-step process to analyze the images for body composition: subjective distinction between the muscle

and other soft tissue (i.e. fat–muscle) or muscle and other hard tissue (i.e. muscle–bone) interfaces at the most superficial and deepest point of the muscle of interest, and objective quantification of the thickness of the muscle.

With its portability, low cost, wide availability, minimal training, and ease of use [18▪▪,19], ultrasound is becoming a popular mode for body composition analysis at the bedside. Not only does ultrasound provide measures of muscle thickness in specific regions of the body, but also it may provide valuable information regarding muscle architecture including pennation angle (the angle in which muscle fibers are positioned) and fascicular structures [20▪▪], which may ultimately reveal strength deficits and mechanisms that explain muscle atrophy in patients.

METHODOLOGICAL APPROACHES TO SKELETAL MUSCLE MEASUREMENT USING ULTRASOUND

There are several methodological approaches that have been reported among diverse populations, summarized in Table 1 with references included. Although this is not a complete list, it captures the common procedures and concepts used in the recent studies on various populations. Research in select populations, such as coronary artery disease [21▪▪] and chronic obstructive pulmonary disease [22], has validated and utilized bedside ultrasound for the measurement of skeletal muscle. However, other populations, such as critically ill patients, may benefit from the expediency and portability of ultrasound, but validation studies have yet to be performed. The lack of validation or reliability studies in such groups as the critically ill does not preclude the use of ultrasound; simply, additional work is needed to facilitate interpretation of results from this tool. In particular, identification of a methodological procedure that is practical and provides the most accurate predictions will be key in producing reliable measures at the bedside, particularly in populations that may present with several confounding features including edema.

There are several considerations when choosing a procedure for measuring muscle thickness and volume using ultrasound, especially when comparing results across the studies. Some factors are obviously not applicable at the bedside, whereas other factors should be considered in such a way that balances accuracy with expediency. For example, standing measures may potentially yield more accurate predictions than measures obtained in supine position [25]; however, this procedure is not feasible for all acutely ill or hospitalized patients. It is also likely that including more than three landmarks for analysis may provide more accurate predictions [25], but this draws away from the expediency of using ultrasound. Here, one would need to decide on whether to compromise on accuracy or expediency, depending on the purpose in using ultrasound (i.e. determining nutritional status in clinic vs. research). Determining the muscle groups or individual muscle that one is interested in is important as various study designs focus on and validate different muscles. Deciding on whether to perform unilateral or bilateral measures will have implications on reliability and applicability, if compared across different studies. Importantly, identifying the effects of fluid retention toward the accuracy of measurements will be essential in interpreting these results, given that many hospitalized patients experience edema. It is thought that fully compressing against the tissue of interest may improve accuracy in measurements in which there is edematous tissue. This consideration is a unique challenge to measuring muscle, especially in the critically ill population in which fluid shifts are variable and warrants future work. As a demonstration of the practical application of ultrasound to measure lean body mass in the acute care or critical care or ICU setting, the training video referenced here provides a useful practical training demonstration of bedside lean body mass determination by ultrasound: https://www.youtube.com/watch?v=hP-UQmhuzk4 – created by Clinical Evaluation Research Unit, Kingston, Ontario for TOP-UP Trial as found on www.criticalcarenutrition.com.

VALIDATIONS OF SKELETAL MUSCLE MEASUREMENT USING ULTRASOUND

The validation and reliability studies outlined in Table 1 generally demonstrate a high degree of accuracy and reliability. However, validation and reliability studies have not been published in some populations, including critically ill and cancer patients, whereas other populations have some initial validation studies but could benefit from additional studies. Further, studies are needed in determining the smallest detectable change in muscle using ultrasound for longitudinal analysis at the bedside to evaluate the frequency in which measures can be taken to examine the changes over a period of time.

THE FUTURE OF ULTRASOUND AT THE BEDSIDE: LIMITATIONS AND USEFULNESS

As with any bedside tool, there are certain limitations that need to be considered in performing and interpreting muscle measurements derived

Table 1. Summary of the common methodological approaches with validity and reliability measures for measuring muscle using ultrasonography

	Population	Methodological approach	Validation and reliability
Analysis of a single landmark			
Ema *et al.* [20▪▪]	Healthy ($n=14$) Age: 24 + 1 years old (mean + SD)	Measurement: thickness of rectus femoris Landmark: 60–70% of the thigh length from the popliteal crease to the greater trochanter Position: supine with legs fully extended Leg(s): right leg Compression: none	Validation against cadaveric specimens: <1% of true value of thickness Intrarater reliability of US: Same day variation (CV) = 2.4 + 1.4% Variation over 2 days (CV) = 2.3 + 1.8%
Thomaes *et al.* [21▪▪]	Coronary artery disease patients ($n=45$) Age: 68 + 6 years old (mean + SD) BMI: 26.6 + 2.9 kg/m^2 (mean + SD)	Measurement: thickness of rectus femoris Landmark: half point of the length between epicondylus lateralis and trochanter major of the femur Position: supine with knees extended but relaxed with toes pointed up Leg(s): right leg Compression: minimal Additional notes: five pictures taken and averaged	Validation against CT ($n=20$): Difference between US and CT = 0.01 + 0.12 cm; ICC = 0.92 (95% CI = 0.81–0.97) Bland–Altman plot limits of agreement: 0.01 + 0.24 cm, $P=0.77$ Intrarater reliability of US ($n=25$): Variation over 2 days (minimal detectable difference) = 0.24 cm Average difference = −0.02 + 0.10 cm, $P=0.4$; ICC = 0.97 (95% CI = 0.92–0.99)
Seymour *et al.* [22]	Healthy ($n=26$) and COPD ($n=30$) Age: 40–90 years old	Measurement: cross-sectional area of rectus femoris Landmark: 3/5 of the distance between ASIS and superior patellar border Position: supine with legs extended Leg(s): not indicated Compression: minimal [23] Additional notes: contraction–relaxation maneuvers were employed to delineate muscle septa prior to image acquisition; averaged three consecutive measurements within 10% CV	Validation against CT ($n=10$ COPD, 8 healthy): Intraclass co-efficient $r=0.88$ Rectus femoris vs. total quadriceps cross-sectional area $r^2=0.55$, $P<0.001$ Intrarater reliability of US ($n=19$): Variation over 2 days: Bias = 12 + 43 mm^2; limits of agreement −72 to +96 mm^2 Interrater reliability of US ($n=10$): Bias = 2 + 32 mm^2; limits of agreement −61 to +65 mm^2
Analysis of two landmarks			
Tillquist *et al.* [18▪▪]	Healthy participants ($n=78$; 7 centers) Age: 30.6 + 8.4 years old (mean + SD; range = 21–55 years old) BMI: 24.1 + 4.4 kg/m^2 (range = 16.9–40.7 kg/m^2) 42 Trainers	Measurements: muscle thickness of quadriceps Landmarks: mid-point of ASIS and upper pole of the patella, lower one-third and upper two-thirds of ASIS and upper pole of the patella Position: not indicated Leg(s): both legs Compression: maximal compression Additional notes: Manual and training video used to standardize procedures Averaged both landmarks for both legs	Intrarater reliability of US ($n=42$): ICC = 0.98; mean difference between two measures = 0.033 cm; 95% CI = 0.004–0.061, $P=0.0247$ Interrater reliability of US ($n=78$): ICC = 0.95; mean difference = −0.028 cm, 95% CI = −0.067 to −0.011, $P=0.1607$
Analysis of three or more landmarks			
Baldwin *et al.* [24]	Healthy volunteers ($n=13$) Age: 33 years old (median); range = 20–73 years old	Measurements: between most superficial aspects of fat–muscle interfaces and limiting tissues (i.e. bone) Landmarks: acromiale, radiale, stylion, trochanterion, tibiale laterale	Intrarater reliability of US: ICC for mid-upper arm = 0.998 (95% CI = 0.993–0.999) for left and 1.0 (95% CI = 0.999–1.0) for right

Table 1 (*Continued*)

	Population	Methodological approach	Validation and reliability
		Position: supine Leg(s): both Compression: none Additional notes: Segment lengths and girths measured in triplicate and averaged to obtain mid-segment point. Landmarks imaged in triplicate	ICC for mid-forearm = 0.997 (95% CI = 0.989–0.999) for left and 0.985 (95% CI = 0.945–0.996) for right ICC for mid-thigh = 1.0 (95% CI = 0.999–1.0) for both legs; greater variability on right vs. left leg
Sanada *et al.* [25]	Healthy Japanese participants ($n = 72$) Age: 18–61 years old	Measurements: distance between bone–muscle interface and muscle–fat interface of rectus femoris and vastus intermedius combined and height was used to relate muscle length Landmarks: nine sites total – lateral forearm, anterior and posterior upper arm, abdomen, subscapula, anterior and posterior thigh, anterior and posterior lower leg Position: standing [26] Compression: none	Validation against MRI ($n = 48$): $r^2 = 0.96$, $P < 0.001$

ASIS, anterior superior iliac spine; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CV, coefficient of variation; ICC, intra-class correlation coefficients; US, Ultrasound.

from ultrasound. It is important to recognize that ultrasound measurements typically comprise muscle thickness of one or more individual muscles, with the quadriceps muscle group being the most commonly measured tissue. It is possible that muscle measurements derived by ultrasound may not be as accurate or precise as CT and MRI analysis, which are modalities that include a larger field of view and can provide consecutive, automated scans that quantitate various muscle groups and fat depots. Studies using CT and MRI for body composition analysis have been well established in various populations [4▪▪,5▪▪,7,8,13,16,27]. Although ultrasound may not provide the detailed measures that CT and MRI can, understanding the limitations of ultrasound is important and still permits useful identification of patients who are sarcopenic [28▪▪], or otherwise are malnourished or vulnerable to becoming malnourished in inpatient and outpatient settings. The portability, wide availability, lack of radiation, and noninvasiveness of ultrasound allow for multiple longitudinal measures to track changes in the body composition during ICU or hospital stay, which may be difficult to achieve with MRI or CT.

Predictive equations for whole-body measures are needed to better understand the impact of muscle atrophy on the whole body. Given the large and variable fluid shifts observed in various illnesses, including cancer and ICU patients [12,14], it is not known whether edema may confound muscle measurements; using full compression of the ultrasound head and probe against the body segment (i.e. thigh for quadriceps measures) may help counter this issue [18▪▪]. Without compression during ultrasound use, there is evidence indicating that edema may be identified (and possibly quantified) in ultrasound scans of the anterior thigh [29]; this has yet to be comprehensively investigated and would be invaluable at the bedside.

Ultrasound presents the novel assessment methods for quantifying skeletal muscle at the bedside. Future work may focus further on characterization of patients with low muscularity as they may be prone to malnutrition, comorbidities, and poor clinical outcomes if hospitalized. Muscle measures derived from ultrasound may also be used to deliver protein based on muscle mass rather than using weight measurements. In cancer, in which chemotherapy toxicities are associated with lean tissue mass [13], measures of muscle using ultrasound may be a future direction for calculating chemotherapy doses. Moreover, ultrasound may become an important tool for measuring the success or failure of nutrition and rehabilitation interventions that aim to preserve muscle in acute and chronic illness in which muscle wasting is prevalent.

To optimize on the capabilities of ultrasound equipment for the evaluation of muscle atrophy, there are several areas that warrant investigation.

Universal landmarks are essential for comparable evaluations of muscularity and muscle atrophy across different studies within or even across different populations. Choosing landmarks that are not only most practical, but also provide reliable and useful information is also important for multicenter studies. Methodological and validation studies that examine the precision of muscle measurements, precision in the detection of small changes, and effects of edema on muscle are important issues to address in methodological investigations. The development of whole-body skeletal muscle predictive equations that can provide insight on the overall impact of muscle atrophy on patients will be fundamental. And finally, developing cutpoints or ranges of muscularity that identify patients who are at risk of malnutrition will be imperative.

CONCLUSION

Ultrasound has been utilized in the quantification of muscle over the last 20 years, but only recently has it gained significant attention with the growing importance of understanding the role of skeletal muscle at the bedside. Overall, it can provide precise and reliable measures of muscularity and potentially changes in muscle mass. To optimize on its capabilities, future work is needed to comprehensively understand its strengths and limitations.

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Conflicts of interest

There are no conflicts of interest.

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- ■ of special interest
- ■■ of outstanding interest

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