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Quantitative peripheral muscle ultrasound in sepsis: Muscle area superior to thickness

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ABSTRACT

Purpose: The objective of this study is to describe the relationship between two quantitative muscle ultrasound measures, the rectus femoris cross-sectional area (RF-CSA) and quadriceps muscle thickness, with volitional measures of strength and function in critically ill patients with sepsis.
Materials and methods: We performed a prospective study of patients admitted to a medical ICU with sepsis and shock or respiratory failure. We examined the association of two ultrasound measurements – the RF-CSA and quadriceps muscle thickness – with strength and function at day 7. Strength was determined using the Medical Research Council Score and function using Physical Function in the ICU Test, scored.
Results: Twenty-nine patients were enrolled; 19 patients had outcome testing performed. Over 7 days, RF-CSA and thickness decreased by an average of 23.2% and 17.9%, respectively. The rate of change per day of RF-CSA displayed a moderate correlation with strength (ρ 0.51, *p*-value 0.03) on day 7. Baseline and day 7 RF-CSA did not show a significant correlation with either outcome. Quadriceps muscle thickness did not significantly correlate with either outcome.
Conclusions: Muscle atrophy as detected by the rate of change in RF-CSA moderately correlated with strength one week after sepsis admission.

1. Introduction

Skeletal muscle dysfunction develops early and rapidly during the course of critical illness [1]. This dysfunction, defined clinically as intensive care unit acquired weakness (ICU-AW), is associated with prolonged mechanical ventilation, prolonged intensive care unit (ICU) stays, and increased hospital and one-year mortality [2-5]. Weakness is also a major driver of morbidity after hospital discharge in survivors of critical illness [6-8]. Critically ill patients with sepsis are at increased risk for reduced muscle strength and impaired exercise tolerance after discharge [9]. The diagnosis of skeletal muscle dysfunction in critically ill septic patients, however, remains a challenge. The most widely accepted method of diagnosing ICU-AW requires volitional participation by the patient [2,10,11]. Critical illness itself as well as concomitant delirium or sedation precludes such participation in the majority of patients [2]. As such, the true incidence of skeletal muscle dysfunction in sepsis remains unknown and risk assessment early in the course of critical illness is rarely possible.

Peripheral muscle ultrasound is appealing as a diagnostic and risk stratification tool for skeletal muscle dysfunction in critical illness. Ultrasonography is widely available, performed at the bedside, and does not require patient participation. Quantitative muscle ultrasound measurements have been shown to be reliable in critically ill patients [1,12]. Challenges with this modality, however, still exist. There is inconsistency in the literature about which quantitative ultrasound measurement to use [13]. In addition, it is unknown if the absolute muscle thickness or area on ultrasound or the rate of muscle loss over time more strongly correlates with muscle strength and function [14]. Patients with sepsis are at increased risk for skeletal muscle dysfunction [9,15,16] and, if further developed, peripheral quantitative muscle ultrasound may be an important tool to describe and follow muscle dysfunction

Abbreviations: ICU-AW, intensive care unit acquired weakness; RF-CSA, rectus femoris cross-sectional area; Q-MT, quadriceps muscle thickness; MRC, Medical Research Council; PFIT, Physical Function in the ICU Test; APACHE, Acute physiology and chronic health evaluation.

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specifically in this subset of patients. Prior research has shown that a reduction in cross-sectional area correlates with muscle weakness in a mixed cohort of mechanically ventilated patients [17]. In a cohort including only patients with sepsis, however, static measures of muscle thickness at 10 days post-ICU admission did not correlate with weakness [18].

The objective of this study is to describe the relationship between two quantitative muscle ultrasound measures, the rectus femoris cross-sectional area (RF-CSA) and quadriceps muscle thickness (Q-MT), with volitional measures of strength and function in a cohort of patients with sepsis complicated by shock or respiratory failure, a very high risk population. In contrast to prior studies, we examined these relationships at specific time points within one week after ICU admission to limit the variability in time points assessed.

2. Material and methods

2.1. Study design

We conducted a single-center prospective cohort study of patients with sepsis or septic shock admitted to the medical ICU at an urban academic referral center. The Institutional Review Board at the University of Pennsylvania approved the study, Protocol #820585. This study was approved with a waiver of timely consent. Consent was obtained from patients or surrogates as soon as was feasible.

2.2. Study population

Eligible patients were admitted to the medical ICU at the Hospital of the University of Pennsylvania between June and December 2015 with a diagnosis of sepsis. In order to identify the most severely ill patients with sepsis, we also required patients to have sepsis complicated by respiratory failure or shock requiring vasopressors for a minimum of 6 h, and an anticipated ICU length of stay >48 h. Sepsis was defined by the American College of Chest Physicians (ACCP) and Society of Critical Care Medicine (SCCM) consensus criteria for severe sepsis and septic shock [19]. Respiratory failure was defined as the need for invasive mechanical ventilation, non-invasive mechanical ventilation, or high flow nasal cannula with fraction of inspired oxygen >50%. Patients were sampled consecutively. To minimize the impact of premorbid muscle dysfunction, patients were excluded if they were transferred to our ICU from a long-term acute care facility or outside hospital >48 h after the onset of their critical illness, if they had a tracheostomy in place at the time of admission, or were admitted to the ICU for at least 7 days in the prior 3 months. Patients who were non-English speaking or cognitively impaired and unable to follow physical therapy commands were also excluded from the study. Finally, we excluded patients with preexisting neuromuscular disease including multiple sclerosis, amyotrophic lateral sclerosis, preexisting paresis of bilateral lower extremities, and acute spinal cord injury.

2.3. Ultrasound protocol

A standardized ultrasonography protocol was adapted from previously published protocols (see supplementary appendix) [1,20-22]. A portable ultrasound machine (SonoSite$_{TM}$ Edge) was used with a 5–10 MHz linear transducer and 2–5 MHz curvilinear transducer. One experienced critical care physician obtained all of the images (JP). This physician underwent training by a fellowship-trained musculoskeletal radiologist and a subset of the images was reviewed with the radiologist to ensure accurate image capture. Initial ultrasound measurements were performed within 48 h of ICU admission. Follow-up images were obtained within 48 h of day 7 after ICU admission. All ultrasound measurements were taken with the transducer placed perpendicular to the long axis of the thigh. The site at two-thirds of the distance between the anterior superior iliac spine and the superior patellar border was marked with a skin marker. Light pressure was used and an image was obtained with the entire rectus femoris muscle within view. At each time point, measures were repeated until three measures were made within 10% of each other. These three measures were then averaged for analyses. Ultrasonography was performed on both lower extremities and the right lower extremity was used in the analysis unless there was technical inferiority of the right-sided images.

2.4. Quantitative muscle ultrasound measurements

We examined two quantitative peripheral ultrasound measurements (Fig. 1). Quadriceps muscle thickness (Q-MT) was defined as the thickness of the rectus femoris-vastus intermedius complex and measured as the linear distance from below the subcutaneous tissue down to the level of the femur. Rectus femoris cross-sectional area (RF-CSA) was defined as the area of the rectus femoris muscle calculated by planimetric technique. The linear array probe was used to obtain the Q-MT measurements. We chose to use the curvilinear probe for the RF-CSA measurement to allow for greater window width and depth penetration because during pilot testing it was noted that the entire muscle was often not visible in a single view with the linear array probe. Utilization of the curvilinear probe for RF-CSA measurement has been previously validated [23].

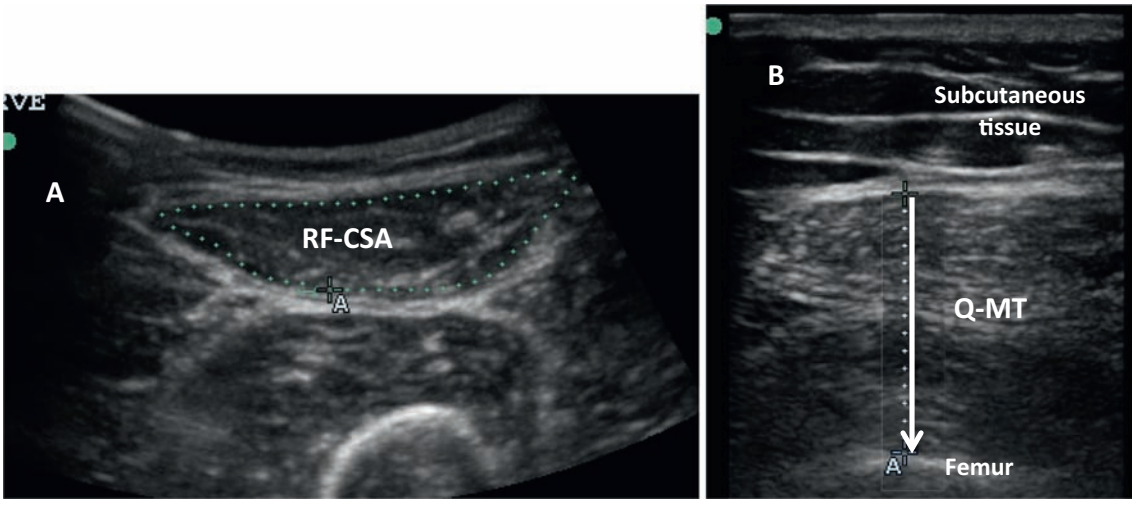

Fig. 1. Representative ultrasound images. A. Ultrasound Image of Rectus Femoris Cross-Sectional Area (RF-CSA) using curvilinear probe. The area is outlined by dotted line. B. Ultrasound Image of Quadriceps Muscle Thickness (Q-MT) using linear array probe. The thickness measure is the linear distance from below the subcutaneous tissue to the level of the femur as labeled with the arrow.