Longitudinal changes in anthropometrics and impact on self-reported physical function after traumatic brain injury

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Critical illness is associated with significant and rapid loss of muscle early in the hospital admission.[1-3] In survivors of critical illness, these marked changes in body composition result in weakness, which may have significant consequences on functional outcomes and quality of life well after discharge from the intensive care unit.[4]

Patients admitted to the ICU with a traumatic brain injury (TBI) are hypermetabolic and hypercatabolic, and thus may be particularly susceptible to marked changes in anthropometric measurements and body composition.[5] A recent study reported that underfeeding of patients with TBI in the ICU is commonplace and is associated with a longer time to discharge.[6] Nutritional deficits have been shown to persist throughout hospitalisation[6] and a large proportion of patients with TBI remain malnourished 2 months after their injury.[7,8] Additionally, patients with TBI are frequently bed-bound and there are barriers to participation in physiotherapy sessions within the ICU and after ICU discharge.[9,10] Given that patients with TBI stay in hospital for prolonged periods, coupled with the fact they have poor nutritional intake and immobility, it is likely that anthropometric measurements will substantially diminish over this time. However, changes in anthropometric measurements, particularly body composition and muscle mass, after discharge from the ICU during the acute phase of recovery, have not previously been described. This information may identify key time points to target nutrition and/or physiotherapy interventions.

Appropriate methods to assess longitudinal changes in anthropometric data are needed. Significant changes in bodyweight have been reported in patients with TBI[11] but bodyweight is only a surrogate measure of change in muscle mass, and may not relate to functional outcomes.[12] Gold standard body composition imaging methodologies, such as magnetic resonance imaging (MRI) and computed tomography (CT), are challenging to perform in critically ill patients, as they require transfer of the patient out of the ICU, require expensive equipment and may involve radiation exposure. Dual-energy x-ray absorptiometry (DXA) provides an accurate, lower cost alternative and is often used as a reference standard, but this also requires transfer of the patient out of the ICU.[13,14]

ABSTRACT

Background and aims: Patients admitted to the ICU with a traumatic brain injury (TBI) are at risk of muscle wasting but this has not been quantified. Our aims were to describe longitudinal changes in anthropometrical data, compare the accuracy of non-invasive methodologies to the validated dual-energy x-ray absorptiometry (DXA), and assess the relationships between anthropometrical data and self-reported physical function.

Methods: In a prospective observational study, we recruited patients admitted to the ICU with a moderate-to-severe TBI over 12 months. Anthropometric measurements included the subjective global assessment (SGA), bodyweight and ultrasound-derived quadriceps muscle layer thickness (QMLT), which we performed weekly in hospital and 3 months after admission. We assessed total body composition using DXA within 7 days of ICU discharge, and compared the total lean muscle mass with ultrasound-derived QMLT taken within 5 days of the DXA measurement. We assessed functional outcomes at 3 months using the physical component score of the Short Form-36 (SF-36) and the Extended Glasgow Outcome Scale (GOS-E).

Results: Thirty-seven patients were included, with a mean age of 45 years (SD, 16 years), and 87% were men. Participants were admitted to the ICU for a mean of 13 days (IQR, 6–18 days) and to hospital for a mean of 38 days (IQR, 19–52 days). They had significant weight loss in hospital (mean, 4.9% [SD, 7.7%]; $P = 0.001$). Malnutrition, measured with the SGA, was twice as prevalent at hospital discharge than at admission ($P = 0.005$). A reduction in QMLT occurred in the ICU but stabilised after ICU discharge. DXA-derived total lean mass taken within 7 days of ICU discharge strongly correlated with ultrasound-derived QMLT taken within 5 days of DXA measurements ($\rho = 0.74$, $P = 0.037$). Improvements in self-reported physical function, using the SF-36 and GOS-E at 3 months, were associated with a greater QMLT at hospital discharge (SF-36: $\rho = 0.536$, $P = 0.010$; GOS-E: $\rho = 0.595$, $P = 0.003$, $n = 23$) and at 3 months (SF-36: $\rho = 0.658$, $P = 0.020$; GOS-E: $\rho = 0.642$, $P = 0.025$, $n = 12$).

Conclusions: Patients with a TBI lose muscle thickness while in the ICU but the trajectory of loss stabilises after ICU discharge. Ultrasound-derived QMLT is related to total lean mass and physical function after discharge. Further studies are needed to confirm that ultrasound measurement of QMLT is a useful surrogate measure of muscle mass and functional outcomes after trauma and critical illness.

Muscle size, estimated with structural measurements, has been shown in a heterogeneous cohort of ICU patients to be associated with long-term function.[15] Ultrasonography of quadriceps muscle layer thickness (QMLT) is feasible, has been shown to be a reliable measurement in healthy populations, and may be a useful method of monitoring changes in muscle size at the bedside.[16] The quadriceps muscle provides the greatest proportion of total skeletal muscle mass,[17] and mass relates to strength,[15] so QMLT may be a better indicator of functional outcome than muscle thickness in other muscle groups.[18] One recent study reported an association between muscle thickness, using this technique, and the cross-sectional area of abdominal muscle at the third lumbar level, obtained by CT.[19] However, this technique has not yet been validated against a gold standard method of measurement of total muscle mass in the setting of muscle wasting, and may not be feasible in patients with TBI who are frequently agitated and unable to cooperate with the investigation.

Our objectives were to:
- describe changes in anthropometric measures in patients with moderate-to-severe TBI over the period of hospitalisation and 3 months from admission
- compare the accuracy of non-invasive anthropometric methodologies with a validated reference, DXA
- assess relationships between anthropometric measures and quality of life and functional outcomes.

Methods

Study design and population

To evaluate anthropometric changes in patients admitted to the ICU with moderate-to-severe TBI, we conducted a prospective observational study at a single university-affiliated hospital that is the major acute neurotrauma referral centre for South Australia. All patients admitted throughout a 12-month period were eligible to participate if they had a moderate TBI (Glasgow coma scale [GCS] score, 9–12) or a severe TBI (GCS score, 3–8); were ≥ 18 years of age; and were in the ICU for ≥ 48 hours. Patients were excluded if they were expected to die imminently.

Ethics, consent and permissions

Consent was obtained from all participants. For patients deemed not competent to provide consent, the patient's legally authorised representative was approached. The protocol was approved by the Royal Adelaide Hospital Human Research Ethics Committee (HREC/14/RAH/100).

Data collection

We collected patient demographic data, injury severity data and clinical outcome data (including ICU and hospital lengths of stay). Inpatient data was censored at 90 days. Study participants were invited back to be studied 3 months after admission.

Anthropometry

Anthropometric measurements, including ultrasound for assessment of QMLT, subjective global assessment (SGA) and bodyweight measurements, were conducted by a single trained investigator at Day 7 after ICU admission and then on a weekly basis until hospital discharge.

Quadriceps muscle layer thickness

Bedside ultrasound measurements were conducted with a portable ultrasound machine (SonoSite X-Porte) and a 13-6 MHz transducer, using a protocol described previously.[16] The patient was in a supine position with legs relaxed, lying flat in extension. Measurements of QMLT were taken bilaterally at:
- the border between the lower one-third and upper two-thirds between the anterior superior iliac spine (ASIS) and the upper pole of the patella
- the midpoint between the ASIS and the upper pole of the patella.

A still image was taken with the transducer held perpendicular to the skin and maximal pressure applied. Duplicate measurements were taken by one researcher and a third measurement was taken if the first two measurements differed by > 10%. We calculated the means of all measurements to provide the total mean QMLT, and calculated weekly means for the total patient population.

Subjective global assessment

The SGA is a bedside assessment tool that categorises malnutrition status (well nourished, mild-to-moderately malnourished or severely malnourished) based on a visual physical assessment and dietary, anthropometric, and clinical histories. The SGA has been shown to be predictive of nutrition-association morbidity in hospitalised patients.[20-22]

Bodyweight

We measured the patient's weight, when possible, using the Multi Point Weighing System bed scales (A&D Weighing), a ward-specific chair or floor scales. When it was not possible to weigh a patient because their condition prevented it, we used their most recently documented weight, a weight reported by a family member or the patient, or a weight estimated by the primary investigator. We estimated the patient's height using a measurement of ulna length.[23]

Body composition

We conducted total body DXA scans within 7 days of ICU discharge using the Prodigy bone densitometer (GE Healthcare) to evaluate total body composition, specifically, the percentage of total body lean muscle mass.[24]

At the 3-month follow-up of patients, we measured their QMLT (by ultrasound), conducted an SGA, measured bodyweight and conducted a DXA scan.

Quality of life and functional outcomes

We assessed the patients' health-related quality of life 3 months after ICU admission, using the Short Form-36 Version 2 (SF-36v2).[25] The SF-36 has been validated in an ICU population and is commonly used in studies of critical illness.[26] Total population data were compared with South Australian population norms because the population norms were readily available.[27]

We conducted the Extended Glasgow Outcome Scale (GOS-E) measurement 3 months after the patient's injury. The GOS-E is often used in studies of TBI as a measure of global functional outcome.[28] We used the structured interview to improve the consistency of ratings, and dichotomised the results into favourable (GOS score 5–8) or unfavourable (GOS score 1–4).[28,29]

Both questionnaires were conducted by the researcher in person, when possible, or via telephone. When the patient was unable to complete the questionnaires themselves, their next of kin provided surrogate responses.[30]

Statistical analysis

Data are shown as means with standard deviations, or medians with interquartile ranges (IQRs), unless otherwise stated. Because of our small sample size and assuming a constant linear change in values over time, when a single ultrasound measurement was missing, we averaged the previous and subsequent weeks' measurements for the missing value. We acknowledge that the assumption of a linear relationship between muscle loss and time is a limitation of our study, but our approach to managing missing values was a conservative one. To evaluate changes in ultrasound QMLT measurements in the ICU and in the post-ICU acute ward, individual patient ultrasound measurements were time-aligned, with time zero being ICU discharge. We used a mixed-effects linear model, allowing a random intercept on patient to account for multiple datapoints per individual. In order to describe differences in the mean trajectory between periods, a linear spline was introduced at time zero, and the mean model profile and 95% confidence intervals added.

We assessed the associations between DXA lean body mass (total and leg) and the closest measured ultrasound-derived QMLT using the Pearson correlation. We used the McNemar–Bowker test to assess the association between SGA category at baseline and SGA at hospital discharge, and used paired-samples t tests to assess the significance of weight changes over time. We analysed the associations between the anthropometric results and 3-month questionnaires using the Pearson correlation. We performed statistical analyses using SPSS, version 23 (SPSS Inc), and considered $P < 0.05$ to be significant. We did not make adjustments for multiple tests. Data are available on request.

Results

Demographic data

A total of 37 of 47 eligible patients participated in the study. The patient participation algorithm and number of patients contributing data to each measurement are shown in Figure 1. The mean age of patients on admission was 45.3 years (SD, 15.8 years), and 87% were men. A total of 67% of patients had a severe TBI, and the median Acute Physiology and Chronic Health Evaluation II score was 18 (IQR, 14–22). The median ICU length of stay was 13.4 days (IQR, 6.4–17.9 days), and the median hospital length of stay was 37.8 days (IQR, 19.4–52.4 days). Over the entire duration of hospitalisation, the mean daily nutritional intake was 1916 kcal of energy (SD, 880 kcal), and 86 g of protein (SD, 43 g). Detailed patient demographic and nutritional intake data have previously been published.[6]

Figure 1. Recruitment and number of patients participating in each element of the study*
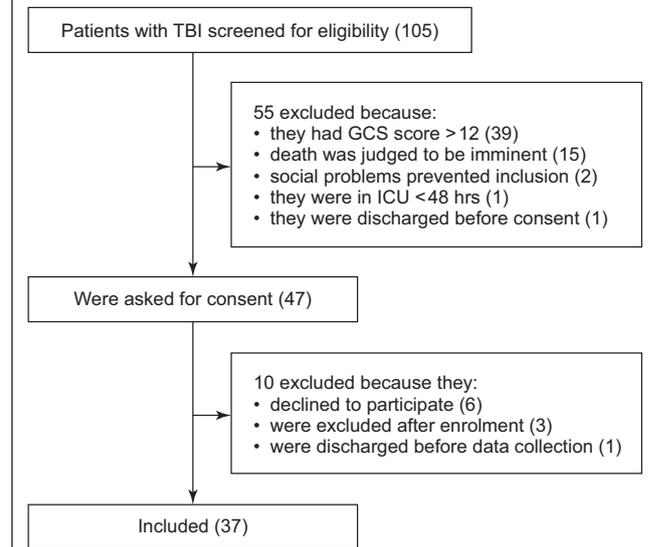
TBI = traumatic brain injury. GCS = Glasgow coma scale. ICU = intensive care unit. * Patients contributing data components as follows (*n*). Ultrasound: ICU, 19; ward, 31; 3 months, 13. Weight: ICU admission, 37; hospital discharge, 32; 3 months, 18. Subjective global assessment: ICU admission, 33; hospital discharge, 27; 3 months, 15. Dual-energy x-ray absorptiometry: ICU discharge, 8. Questionnaire: 3 months, 24.

Figure 2. Changes in quadriceps muscle layer thickness, per patient, before and after discharge from intensive care unit
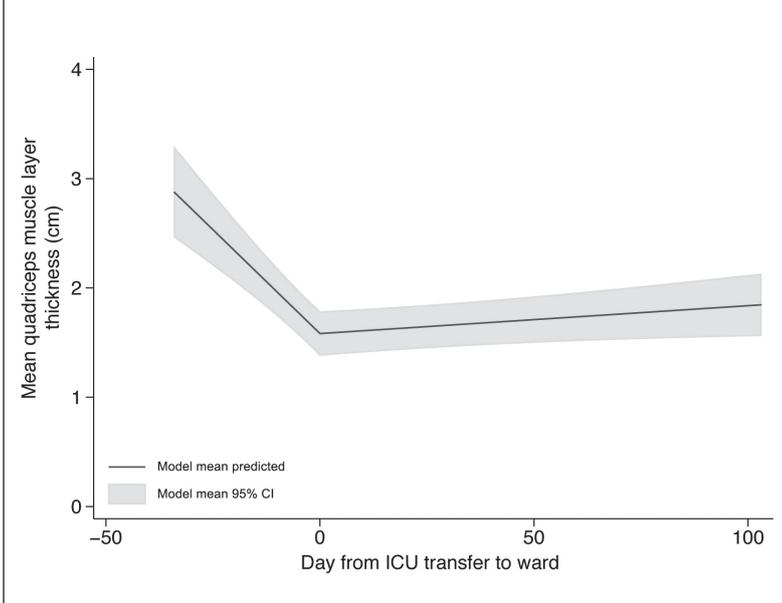
Anthropometry

Quadriceps muscle layer thickness

Over the study period, 123 ultrasound scans were performed on 33 patients; 30 (24%) in the ICU and 93 (76%) on the post-ICU acute ward. A mean of 3.7 ultrasound scans per patient were conducted (one for five patients, two for nine patients, three for five patients, and ≥ four for fourteen patients). An ultrasound scan of the QMLT was possible at 79% of time-points in hospital and in 39% of patients at the 3-month follow-up. During hospital admissions, the primary reason for missed ultrasounds was agitation or restlessness, particularly on waking from sedation and early in the recovery period on the ward. At the 3-month follow-up, the primary reason for missed measurements was inability to attend a hospital appointment.

For patients who had > 1 ultrasound scan conducted (28 patients), the mean baseline measurement was 1.78 cm (SD, 0.72 cm), and the mean proximate (final hospital) measurement was 1.59 cm (SD, 0.57 cm), a 3.91% (SD, 33.06%) decrease in QMLT.

We compared the trajectories of ultrasound scans for QMLT in the ICU and on the post-ICU acute ward, and this showed a sharp reduction in the mean QMLT in the ICU, followed by a slow increase in the QMLT until hospital discharge (Figure 2).

Three months after ICU admission, we measured the QMLT in 13 patients, six of whom (46%) had remained in hospital. The mean 3-month QMLT was 2.0 cm (SD, 0.7 cm) with a mean decrease from baseline in these patients of 0.1 cm (SD, 0.5 cm) and 3.2% (SD, 26.0%) (P = 0.64).

Subjective global assessment

At ICU admission, patients were well nourished (Table 1). From ICU admission to hospital discharge, 33% of patients moved to a more malnourished category of SGA (P = 0.005; Table 1).

Bodyweight

Anthropometric data at hospital discharge were not available for five patients because of agitation or patient refusal. There was considerable weight loss from hospital admission to hospital discharge, with a mean weight loss of 4.2 kg (SD, 6.5 kg) (4.9% [SD, 7.7%]; P = 0.001) (Table 1). Three months after ICU admission, we were able to perform these measurements again for 18 patients (five remained as inpatients, nine returned for investigation, and four were contactable by telephone). Weight loss persisted at 3 months, with a mean weight loss of 2.9 kg from baseline (SD, 6.8 kg) (2.5% [SD, 8.9%]; P = 0.074) (Table 1).

Body composition

We assessed total body composition for eight patients using DXA. The reasons that DXA was not performed for other patients were: refused consent (10), agitation (eight), patient discharged (3) and medically unstable (4). Mean total bone mineral density was 1.01 g/cm^2 (SD, 0.07 g/cm^2), mean total fat mass was 19.5 kg (SD, 7.3 kg), mean total lean mass was 46.7 kg (SD, 8.1 kg), and mean total body fat mass percentage was 32.9% (SD, 5.6%). There was a significant correlation between total lean mass from the DXA and the ultrasound-derived QMLT measurement

Table 1. Anthropometric data at ICU admission, hospital discharge, and 3 months after injury

Variable	Time point		
	ICU admission (n = 37)	Hospital discharge (n = 32)	3 months (n = 18)
Mean weight, kg (SD)	81.9 (17.8)	75.4 (14.9)	75.1 (11.4)
Mean BMI (SD)	26.7 (6.5)	24.9 (5.6)	24.3 (4.0)
SGA category,* n (%)	(n = 33)	(n = 27)	(n = 15)
A	28 (85)	15 (56)	9 (60)
B	3 (9)	10 (37)	6 (40)
C	2 (6)	2 (7)	0 (0)
Mean QMLT, cm (SD)	1.84 (0.71) (n = 33)	1.59 (0.58) (n = 28)	2.00 (0.70) (n = 13)

ICU = intensive care unit. BMI = body mass index. SGA = subjective global assessment. QMLT = quadriceps muscle layer thickness.
* A = well nourished; B = mild-to-moderate malnutrition; C = severe malnutrition.

Table 2. SF-36v2 component scores at 3 months after admission to the intensive care unit (*n* = 25)

SF-36v2 domain*	Mean (SD)	Population norm
General health	49 (12)	70
Physical functioning	39 (15)	84
Role (physical)	34 (12)	82
Bodily pain	46 (12)	76
Vitality	48 (12)	60
Social functioning	34 (15)	84
Mental health	43 (12)	79
Role (emotional)	40 (15)	90
Mental component summary	43 (13)	na
Physical component summary	41 (12)	na

SF-36v2 = short form 36 health survey. na = not applicable. * SF-36v2 component scores across all 8 domains, compared with population norms, with mental and physical health component summary scores.

conducted within 5 days (ρ = 0.74, *P* = 0.037, *n* = 8), but not leg muscle mass from the DXA and QMLT measurements (ρ = 0.59, *P* = 0.12, *n* = 8).

Functional outcomes

Three months after ICU admission, in the 25 participants (68%) for whom data were available, the mean results from the SF-36v2 were well below population norms for all domains (Table 2). Further, 3 months after injury, 13 of 26 participating patients (50%) were classified as severely disabled (using the GOS-E); eight (31%) were moderately disabled, and five (19%) had a good recovery (Figure 3).

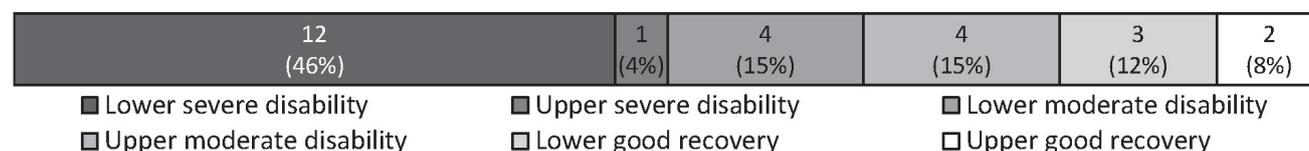## Relationship between anthropometry and self-reported outcomes

The SF-36v2 physical component summary score at 3 months was positively correlated with the QMLT at hospital discharge (ρ = 0.536, *P* = 0.010, *n* = 22) and at 3 months (ρ = 0.658, *P* = 0.020, *n* = 11). There was also a positive correlation between GOS-E score at 3 months and QMLT at hospital discharge (ρ = 0.595, *P* = 0.003, *n* = 23), and at 3 months (ρ = 0.642, *P* = 0.025, *n* = 12).

Discussion

Our longitudinal observational study shows that patients with head injuries who are admitted to the ICU experience deterioration in their body composition over the hospital stay, including significant weight loss, increased prevalence of SGA-categorised malnutrition, and muscle wasting. However, the trajectory of body composition changes improved after ICU discharge. The observed ultrasound-derived QMLT correlated with DXA-derived total body lean muscle mass. Therefore, ultrasonography, although logistically challenging to conduct in this population, shows potential as a portable, non-invasive method to measure longitudinal changes in muscle size in hospitalised patients, representative of total muscle mass. Additionally, QMLT at hospital discharge and 3 months after injury correlated with self-reported functional status at 3 months, which may provide a useful surrogate measure of the effectiveness of hospital-based interventions that will translate to improvements in patient-centered functional outcomes.

Our findings support and expand on other recent studies performed in the ICU reporting that significant changes in body composition, specifically muscle size, in critically ill patients occur rapidly in the early hospital phase.[1-3] Two retrospective studies of patients with head injuries report that patients are underweight and have high rates of clinically determined malnutrition on admission to their rehabilitation facility.[7] Patients in our study did not have high rates of malnutrition at hospital discharge, and these differences in results may be because of differences in study designs, such as prospective versus retrospective recruitment, head-injury severity inclusion criteria, sensitivity of measurement techniques used, site-specific feeding practices and time of assessment for severity of malnutrition. We used more sophisticated measurement techniques to quantify anthropometric changes in our study population.

Other studies have shown that ultrasound-derived muscle size is correlated with clinical outcomes within the ICU. Gruther and colleagues showed a negative correlation between QMLT and ICU length of stay;[31] and Parry and colleagues showed correlations between cross-sectional area and thickness of particular muscle groups (eg, vastus intermedius) and measures of physical function and mobility within the ICU.[2] However, to our knowledge, ours

Figure 3. Glasgow outcome scale scores at 3 months after admission to the intensive care unit (*n* = 26)

12 (46%)	1 (4%)	4 (15%)	4 (15%)	3 (12%)	2 (8%)

■ Lower severe disability ■ Upper severe disability ■ Lower moderate disability
□ Upper moderate disability □ Lower good recovery □ Upper good recovery

is the first study to show the relationship between QMLT throughout the hospitalisation period and longitudinal functional outcomes. No other study has shown the effect of muscle thickness on self-reported physical function after critical illness, but ultrasound-derived muscle thickness has been correlated with quadriceps strength in elderly patients and patients with pulmonary disease.[15,32] A retrospective observational study of patients with a severe TBI also reported a correlation between clinical features of malnutrition within 3 weeks of hospital admission and unfavorable outcome on GOS-E at 6 months, but these investigators did not measure body composition.[8] Studies in other populations suggest that muscle mass, not bodyweight, predicts functional outcomes.[12] Further exploration of the influence of body composition on longitudinal function is needed. In particular, it remains to be established whether increased muscle bulk leads to improved function, or rather that increased function improves activity which in turn increases muscle bulk.

Several studies have validated the use of ultrasound to measure muscle size in a range of populations against gold standard techniques, and these studies have tended to measure the cross-sectional area of specific muscle groups, instead of a linear measurement. Measurement of cross-sectional area is more time-consuming to conduct, may be difficult to visualise in the context of muscle atrophy, and its interpretation requires extensive training. All these factors reduce its applicability for use in large studies of critically ill patients. There are only three published studies that validate ultrasound-derived linear measurements against gold standards. Sipila and colleagues validated the use of ultrasound to measure QMLT in elderly female athletes, using the CT-derived cross-sectional area as the reference.[33] Worsely and colleagues validated ultrasound-derived thickness of the vastus medialis muscle group against MRI-derived measurements in 12 young healthy males.[34] Recently, Paris and colleagues reported ultrasound-derived QMLT measurements to be associated with CT-derived abdominal muscle cross-sectional area in critically ill patients. In that study, measurements were taken early in the ICU stay, (within 5 days of admission) in a relatively healthy ICU cohort (median ICU stay, 3 days [IQR, 2–7 days]); 30% mechanically ventilated). Our study complements these previous data and provides additional evidence that ultrasound-derived muscle thickness is an effective method when compared with gold standard measurements of total body muscle mass, even in the presence of muscle atrophy.

To our knowledge, ours is the first study to describe longitudinal changes in anthropometric data of critically ill patients, with a focus on muscle size, and to show the relationship between those changes and functional outcomes. Patients with head injuries are frequently excluded from studies relating to muscle strength or function

due to compliance issues which mean that they are unable to participate in studies involving common measurement methods, such as walk tests or hand-grip strength. Our study shows the feasibility of clinician-conducted bedside ultrasonography after critical illness in a usually neglected, but important, subpopulation.

The major limitations of our study are the relatively small sample size and missing data. Specifically, measurements of weight, ultrasound-derived QMLT and DXA were not feasible in all subjects, mostly because of injury-related agitation. Additionally, follow-up of patients at 3 months was not possible for all participants. Therefore, the correlations between results of DXA and QMLT, and between body composition and outcome measures, need confirmation in a larger study. Correlations between DXA-derived leg muscle mass and ultrasound-derived muscle thickness may be shown with a larger patient sample.

Another limitation of our study is that measurements of bodyweight were not feasible at all time-points, so we used some estimates. We also conducted our study at a single centre in a specific patient population, which would have affected the generalisability of results. However, it is possible that other groups with augmented metabolism (eg, patients with burn injuries) may have similar trajectories in body composition changes. It is important to recognise that the baseline measurements were taken on Day 7 of the ICU admission, and a significant degree of muscle loss may have already occurred by this tthen.[3] It is therefore possible that we underestimated the degree of muscle wasting during the ICU stay.

Bedside ultrasound is a promising technique to measure changes in muscle thickness in the context of muscle atrophy during and after critical illness, and may correlate to total body muscle mass and longitudinal functional outcomes. Our findings need confirmation in a larger prospective study. Future research should determine whether there are specific therapies that may attenuate muscle atrophy in this population. These therapies may include nutrient provision with a focus on protein; exercise; and pharmacological interventions. The ability for ultrasound to detect clinically relevant changes in muscle thickness in response to therapy needs exploration.

Conclusions

In patients admitted to the ICU with a moderate-to-severe TBI, ultrasonography provides a useful technique to measure changes in muscle size over time. These patients experience muscle atrophy in the ICU but this trajectory stabilises after ICU discharge. Ultrasound-derived changes in muscle size correlate with measurements obtained from the validated DXA technique and are associated with changes in physical function.

Competing interests

None declared.

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